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South Dakota medicine

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2600 W. 49th Street, Suite 100
Sioux Falls, SD 57105
605.336.1965
Fax 605.274.3274
www.sdsma.org

Editor
Keith Hansen, MD

SDSMA President
Kara Dahl, MD

Chief Executive Officer
Barbara A. Smith

Staff Editor
Elizabeth Reiss, MS
–ereiss@sdsma.org, 605.336.1965

Advertising Representative
Elizabeth Reiss, MS
–ereiss@sdsma.org, 605.336.1965

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For the past two years, my wife has been lobbying to get a Peloton. I didn't see the need since we already had a stationary bike in the basement, nor did I want to pay for ongoing access to instructors that would tell me how to work out. I know what I'm doing. I've spent years working out. I could certainly push myself as hard, if not harder, than these fitness professionals could. I don't need to pay an additional dime for some instruction and accountability. Right?

You have to be nodding your head in agreement. Or, you probably know what's coming next. Well, Santa got hold of her wish list and brought a Peloton to our house in December (actually January…thanks supply chain).

And, when I gave it a try, I quickly realized I was wrong about the effect of coaching and accountability. While this is not a commercial, nor an endorsement for Peloton, I don't think I'm getting paid, I found myself working out harder than I had in years. The competitive nature that comes with the on-line features played a part.

But the biggest contributing factor has been the accountability the online instructor provides. Accountability with how hard I was pushing myself. Accountability with sticking to the details of the workout. Accountability with not spinning the tension lever lower than the instructor was otherwise advising. Accountability with seeing results/metrics improve on each ride. I now see what all the hype is about, and my thank you note to Santa (and my wife!) is in the mail.

This story shares strong parallels with that of deciding to engage a financial advisor. Most individuals presume they can manage investments on their own and navigate life's financial decisions without help. They aren't wrong. Some people can do this.

The better question is whether or not your results would improve with a financial "coach," an objective fiduciary guiding the way. Are you really saving as much as you could without someone pushing you? Are you really investing in the most appropriate manner without someone advising you? Are you really on track toward financial independence at the earliest age possible without someone mapping out the path?

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Rising to the Challenges

Kara Dahl, MD
President, South Dakota State Medical Association

Physicians in South Dakota have faced many challenges this past year and will likely encounter similar ones in the future, likely with a unique twist. There will also be new challenges due to unforeseen circumstances as healthcare and the politics surrounding it continues to evolve. As I begin reflecting on my year as president, I thank all of you for your dedication and hard work in the face of many of these difficult situations. As I write this, COVID-19 numbers are down and there is a sense of hope. However, we endured another large surge just months ago, which highlighted how difficult this virus is to manage. Thank you for your leadership and advocacy supporting public health measures to fight the spread of COVID-19.

This year's intense legislative session was full of proposed legislation that centered around public health and the practice of medicine. Several bills took aim at vaccinations. This is likely due to the unfortunate politicization that has taken place regarding the COVID vaccinations. Both the bill that would have allowed for employees to bring claims against their employer for perceived injury due to vaccines required for employment and a bill that would have expanded vaccine exemptions failed.

Additionally, many of the bills this legislative session were surrounding marijuana for medicinal purposes. The SDSMA staff along with many of our members advocated for putting in place safety measures and was successful in achieving physician access to the marijuana registry. There will be ongoing discussions surrounding the implementation of marijuana for medicinal purposes in our state and continued advocacy from the SDSMA will be needed.

Scope of practice is another area that will need ongoing discussions and advocacy. The SDSMA will continue efforts to find meaningful solutions to improving rural healthcare in the setting of physician shortages. We believe that a physician-led healthcare team is the best model for patient care and will continue to advocate for that.

I am excited for all that we have to look forward to in the future as physicians practicing in South Dakota. We have a strong medical association that is committed to improving the practice of medicine in our state and dedicated to strengthening the patient-physician relationship. The wellness program for physicians seeking extra assistance during difficult times or feeling at risk for burnout or moral injury is a great example of the ongoing evaluation of physician needs in our state and the desire to strive for improvement in these areas.

As we look toward the future of medicine, it is imperative to look at our medical students and residents. We must support and encourage the future generation of physicians. This starts even prior to medical school, with inspiring college or high school students to shadow or gain more knowledge about the practice of medicine. We are fortunate to have such an excellent medical school in South Dakota and many of you have been integral in the education of these students; thank you for your ongoing dedication to these future physicians. I also want to highlight the SDSMA Foundation which provides financial assistance to the students at the USD Sanford School of Medicine. All contributions go toward scholarships, grants, and low interest loans for these students in South Dakota. Your contributions are greatly appreciated – thank you.

In summary, I would like to thank all of you for the strength, courage, and resilience you have demonstrated in the past couple years as we have faced uncertain and extremely difficult times as physicians. The SDSMA will continue to advocate for you and your patients, despite the challenges that we face. Please reach out if there are important issues that we need to focus on more moving forward. I have faith that the physicians in our state will continue to rise to the challenges in front of us while continuing to plan for the betterment of medicine in the future.

Cutting Deep: Debriefing Cases

Schae Hanson, MS IV

Time out. This is a mother, in today for laparoscopic extended ascending colectomy with the surgeon. No known allergies. Ancef has been given. Time out is completed.

A father has died after a trip to the emergency department following a head trauma with suspected myocardial infarction causing his death but with otherwise unknown history.

Hands are scrubbed and sterilized. Techs, assistants, and surgeons are gowned. The patient lies naked, betadine covering the abdomen. The field is draped. Cautery, suctioning, camera and light are hooked up to their appropriate homes. We are ready to begin.

The aluminum tray is slid onto a cart. The body bag is heavy. I hold my breath as we unzip the bag and am surprised to see a younger man, blood coming from his mouth around his endotracheal tube and nose as we slide him onto the table. He is cold and in rigor mortis. I watch his chest, how it does not rise and fall with each breath he does not take. He has multiple lines placed with stickers from the EKG covering his upper chest and back. Let's begin.

Cautery is used to make incisions on the left side of the abdomen for port placement. With the help of the camera, numbing medicine is placed to provide an abdominal block in the hopes this will help with post-operative muscular pain. We look around the abdominal cavity. Loops of bowel are pink with yellow fat glistening in-between. The liver's edge is maroon-red, healthy. Aha. There is the tattoo left by the gastroenterologist locating the mass that was unable to be endoscopically removed. Dissection begins to free enough length of bowel to make a connection after removing the piece with the mass. The surgeon's hands show efficiency and precision. I guide the camera and retract as instructed. I imagine the symptoms faced by this patient prior to her surgery. Was she experiencing blood in her stool? Constipation? Nausea and vomiting? Will this mass be cancerous?

Photos show every abrasion and bruise. Every notable thing about him is drawn on a sheet of paper by the forensic pathologist. The assistant and pathologist make incisions simultaneously and bilaterally to expose the innards of his body. Immediately, the metallic smell of blood and a putrid odor fill the air. He is already decomposing. The pathologist is methodical in their approach to dissection. They start with the thoracic organs. Blood is found surrounding his heart, suffocating it. Bingo, we've found the culprit: an aortic dissection. Next, I help take out the abdominal organs. The brain is normal and reminds me of all the anatomy I have forgotten. The pathologist weighs, biopsies, and places each organ back into a bucket. I imagine his life prior to now. What did he do for work? Who did he love? How did he get that scar on his forehead? What if this was my dad? He's the same age.

The dissection has been tricky due to the location of the mass indicated by the tattoo. It takes two hours to comb through mesentery, bowel, blood vessels. Finally, the surgeon frees the length of bowel needed, staples each end, and creates the anastomosis. Her incisions are put back together with a series of stitches and glue. She is undraped, cleaned off, gown placed back on, extubated, moved over to the rolling bed. She awakes, unaware of the time that has passed, still dreaming with her eyes open, mouth dry from the tube. I will see her tomorrow when I round.

His bag of organs is placed back into his empty cavity. A large, S-shaped needle is used with thick string to stitch his wide incision back together. Gaps are wide, and you can still see the subcutaneous fat peeking between. This stitch isn't meant for anything more than functionality; get him to the morgue in one piece. A hose is used to wash him off. He is placed into a clean, plastic bag and wheeled back onto the tray in the cooler. I will never see him again.

The mother's family is sitting in a room where the surgeon gives them the good news: Her mass has been removed, and he believes that the anastomosis was some of his best work. They breathe a sigh of relief.

The father's family is on the other end of a telephone call. It is the police, telling them what the autopsy showed. Gasps followed by silence are imagined as they grapple with the reality of his death.

As a medical student, I may or may not witness the surgeon's

update to the mother's family. More often, I stay behind in the operating room to help clean up the patient, move them to their post-operative bed, clean the room, and thank the rest of the team. If this is the final case of the day, I may not even see the surgeon until the following day if my schedule allows it. If I can remember to ask or if the surgeon remembers something to share with me in regards to family updates, we will debrief further on the subject. That is an if though. Otherwise, it fades from my memory as quickly as the Krebs metabolism cycle did from the first year of medical school.

After the autopsy, I quickly change out of the paper gown taking care of not getting anything on my clothing or on the floor of the room. I do not even ask what the next steps are for the deceased father. The pathologist quickly waves me off to 'grab some food while I have the time'. And the surprising thing is that I am actually hungry and eat without a single thought of what I had just witnessed in that autopsy room.

As a medical student, I oftentimes find myself in the background of an encounter or a case. Much is obvious, much is not. Reflecting on what I witnessed for both the mother and the father, I find myself wondering what questions I would ask the doctors if we had taken the time. How do you find the right words when speaking with the family? What if something had not went according to plan? Does the pathologist call the family following the autopsy or is it up to the police? How do you console someone with such staggering news over the phone?

Debriefing is an important aspect of patient care, particularly in the educational setting. I wonder how my views of patient cases would have changed if I had further discussed what happened with the doctors afterwards. Do we stray away from debriefing because of the time it takes or because we are protecting ourselves from delving further into emotions we rarely let ourselves feel in medicine?

I will contemplate this further as I eat my quick lunch and revel in the fact that I am merely a medical student, learning with every encounter.

About the Author:
Schae Hanson, MS IV, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota.

The Impact of Kindness in Medical Student Education in Rural South Dakota

Emily Endres, MD; Jamie Messerli, MS; Susan Anderson, MD; and Jerome W. Freeman, MD

Abstract

All medical students at the University of South Dakota Sanford School of Medicine (SSOM) have rural healthcare rotations. Because SSOM has adopted kindness as a focal point in its new five year strategic plan, we designed a qualitative study to assess students' perception of kindness in the rural setting.

Introduction

University of South Dakota Sanford School of Medicine (SSOM) has made a commitment to promote kindness among its medical students, faculty and staff. Each of these groups agrees that kindness is important, but the definition of kindness can seem a bit elusive. In science and medicine, precise working definitions are generally helpful. But kindness is in a different realm of human activity. All of us are aware and appreciative of times when we are treated kindly, but articulating the defining characteristics of kindness can be challenging. The Kindness Project at SSOM stresses that the term means action, not merely sympathy or empathetic feelings. More specifically, kindness is defined as reflecting both *what* we do and *how* we do it. Kindness seems trivialized a bit by implying that it represents merely "being friendly and nice", terms that could be judged to lack sufficient gravity. The challenge of *how* we treat people demands that each individual be approached with respect and dignity, not as a means to an end. The *what* aspect of kindness should be tangible and observable. In a sense, less time need be spent on defining kindness and more on recognizing and promoting kind action, particularly as it relates to showing kindness to patients.

Our focus on kindness has particular relevance given the growing realization that effective medical practice requires more than just sophisticated medical knowledge and cutting-edge technology.[1] Increasingly, Americans have come to expect quality with respect to *how* their care is delivered. A patient-centered care approach is advocated.[1,2] The 2001 report "Crossing the Quality Chasm: A New Health System for the 21st Century," defined patient-centered care as "providing care that is respectful of and responsive to individual patient preferences, needs, and values and ensuring that patient values guide all clinical decisions."[2] Providing patient-centered care includes "using, eliciting understanding and validating the patient's perspective; understanding the patient within his or her psychosocial context; reaching a shared understanding with the patient of the problem and its treatment; and creating a partnership in which 'activated' patients share in decision making, power, and responsibility."[3] Arguably, at its core, patient-centered care is based on treating patients with kindness.[4]

At SSOM one aspect of the Kindness Project is a commitment to study the implications of kindness. All of our students have clinical experiences in rural medicine and primary care. After 18 months of basic sciences (Pillar 1), the medical students spend 10 months in the longitudinal integrated curriculum (LIC) for their Pillar 2 experience. At the beginning of Pillar 2 every medical student completes a three-week family medicine preceptorship at a rural location. Students also have the option of requesting the Frontier and Rural Medicine (FARM) program that provides the entire LIC experience in selected small communities throughout the state. In Pillar 3, students spend 18 months mainly devoted to elective rotations and also do an additional required four week rural family medicine rotation. For the purposes of this study, we decided to look at students' perception of kindness during any time spent on rural rotations.

Methods

Approval for this qualitative study was obtained from the University of South Dakota's Institutional Review Board. This study utilized focus groups and key informant interviews of medical students from each of the three pillars. Open-ended, semi-structured questions were created that ask about kindness and the barriers of kindness in respect to being a medical student. These seven main questions and their follow-up questions were developed by a team of content experts and were utilized for the focus groups and key

informant interviews. The interviewer read from the sheet of questions for each focus group and for individual interviews to ensure uniformity. The interviewer has had extensive training in conducting focus groups and key informant interviews.

A total of 44 students were involved in this project. 35 students participated in focus groups and 9 students did key informant interviews. As Pillar 1 includes two different class years, there were 16 participants from the class of 2023 and 15 participants from the class of 2022 who took part in one of two focus groups. Four key informant interviews were gathered from the class of 2021 and the class of 2020 had four participants take part in a focus group and five participants took part in key informant interviews. All participants signed informed consent documents before commencing their participation in this study. Focus groups were conducted in private meeting rooms, while key informant interviews took place by telephone in a private office. All interactions were tape-recorded and transcribed verbatim and each participant received a $50 stipend. The authors made minor edits to several of the student quotations to enhance clarity.

Two independent coders (Co-PI and a study assistant) assessed the transcripts to identify consistent themes. Themes on the issue of kindness in the medical field were uncovered through reading all interview and focus group transcripts. A conventional content analysis methodology was used. Analyzing the data by way of a qualitative content analysis approach allowed for further examination into the subthemes relating to rural medical education and its relationship to kindness.

Results

Based on input from focus groups and key informant interviews, three primary themes relating to kindness in a rural setting were identified: 1. *enhanced relationships between physicians and medical students*; 2. *a culture of kindness*; 3. *a personal knowledge and dedication to patients in the rural setting by their physicians.*

Enhanced Relationships

During both the key informant interviews and the focus groups, the most commonly mentioned benefit of learning medicine in a rural community was the enhanced relationships medical students felt between them and the physician and between the physician and patient. Rather than perceiving a power hierarchy that made the faculty physicians seem unapproachable, students who participated in the FARM program felt comfortable approaching their mentoring physicians for advice and questions. One Pillar 2 student noted:

> *"I'm fortunate enough in FARM, I can call or text my attendings at any time. They are super respectful and receptive to any questions I have. When we are doing rotations in [large city], there's definitely that power hierarchy that is much more evident. I've been fortunate in FARM to have great attendings in this small community who are very receptive to me and have always treated me kindly and with respect."*

Not only does this type of open communication lead to the medical student feeling more comfortable in their learning environment, it allows the student to play a more active role as a member of the medical team and gives students a better lens as to what their life could potentially look like as a future physician working in a rural setting. This sentiment was also felt by students who had a more abbreviated experience in a rural setting, such as a clinical half day rotation during Pillar 1:

> *"I spent a weekend in [rural town], South Dakota and one thing I noticed about them or how they interact here is everyone knew each other. So that helped kindness and it really made me feel welcome when I only knew one of them; but then he introduced me to three, four other doctors, and PAs, and they all offered to spend the day with me and show me around. I got to hop between different areas and I think that was all facilitated through the kindness initiative and the rural setting.*

As members of a small community, physicians have often spent time with their patients in social settings and can better understand the situations and difficulties that their patients encounter. With this understanding, physicians are able to connect with patients and help patients feel comfortable sharing their emotions or opinions that physicians in a larger practice may not be able to. This unique relationship was described by a Pillar 3 student reflecting on their time in a rural rotation:

"I had a particular physician out in [rural town], South Dakota who really was able to connect with her patients and she could tell by their demeanor or how they were looking or acting that something was not quite right. They were not telling her something and she knew it and a lot of times in those situations if the patient's not going to bring it up, physicians are like, "see ya" type of thing. She always would take the time and be like, 'Okay, what else is going on?' And she was able to oftentimes get out these underlying kinds of stories that were going on. It wasn't about her and her schedule and how many patients she had to see."

Culture of Kindness

During the interviews, it was evident that medical students at all levels of training highly valued kindness. They spoke of the kindness demonstrated between students, the kindness shown to them by professors, and their experiences of kindness in the clinical setting. Although kindness was displayed differently in various settings, they all agreed on one thing; kindness is evident in South Dakota. A Pillar 2 student highlighted this when she said,

> *"I think we're lucky in South Dakota to have a culture that is more respectful of students and patients."*

Although treating others with kindness is imbedded in South Dakota's culture, participants commonly highlighted how health care providers in rural areas seem to display an additional level of kindness beyond those in more urban settings. Students felt that this kindness stemmed from the familiarity between the providers, other staff members, and patients. Pillar 1 students described their experience in observing this unique understanding:

> *"It's easier to see kindness with people that you are familiar with and that you have a relationship with."*

> *"And I would say that at the clinic here, they definitely take the time because everyone knows each other here. Usually, the doc is like, 'Oh, saw you in the grocery store last night.' And so, that makes it a lot easier for them to be kind because they're not talking to a stranger anymore... it does seem like in rural settings, having that friendship between the patient and the doctor or the patient and the nurse is easier, and the bond happens earlier on because they're neighbors or that kind of thing."*

The kindness that physicians show can permeate to all of those with whom they interact. It can boost the morale of the healthcare team and improve the patient's compliance with their treatment. When physicians allow medical students to work with them, they are not only agreeing to teach the student about how they practice medicine but are also agreeing to lead the student by example. The actions of an attending physician can inspire a student to emulate observed behaviors, as well as highlighting the conduct the student does not want to adopt in future practice. One Pillar 2 student commented on the impact their attending physician's kindness had on them,

> *"Out here, I feel like they're exceptionally kind. And so, that's motivated me to think about how I react to patients and how I treat patients."*

Personal Knowledge and Dedication to Patients

Throughout much of South Dakota, patients' local options for who to choose as a primary care provider are limited. This can become difficult for patients who have complex medical problems or have diagnoses that require close monitoring or for those seen as "difficult patients." Because patients may not have abundant options of physicians, rural physicians have an extra responsibility to care for these individuals. A Pillar 2 FARM student reflected on this situation during their interview:

> *"Because I'm out in a [rural town], and there aren't that many provider options, one of the biggest examples of kindness I can think of is with our chronic pain patients. The physicians out here are exceptionally kind and patient with them and they've never fired any of their patients, which I think says a lot about just having that knowledge of being like, "These people need cared for. I'm the only one out here who can care for them.'"*

The dedication is evident in the level in which a physician gets to know each patient. In a rural setting, the physician has the extra benefit of interacting with patients outside of clinical settings. Instead of treating the patient as a disease, this allows the physician to have a better understanding of the person they are treating. It should be acknowledged that interacting with patients in small communities in social settings while also being confidantes of patients, where "everybody knows everybody," can be a challenge for the physician. Trust must be established and confidentiality ongoing. Physicians need to be cautious and thoughtful in sharing their own personal attitudes and experiences. But at times this can be powerful. Relationships are a big part of life and while challenging it is also rewarding, humbling, and a gift to be able to take care of one's friends and neighbors. And, in fact, Hogue and Huntington found that those practicing in rural areas were less likely to report burnout than those in urban areas or medium-sized towns.[5]

Another Pillar 2 FARM student noticed this deeper level of understanding by the primary care doctor:

> *"I do get to follow a lot of specialists out here. And I think they don't get the chance to know these patients like the primary care doctors do. Specialists don't know a patient's background, history, and story in detail and they only get to meet a patient in a 15 or 30 minute appointment. So, I think there is a more personalized kindness seen in the rural setting."*

Discussion

Students often mentioned that they could sense the kindness in a very tangible way when in rural settings. In these small

communities, students found that not only were physicians closer to their patients, but the physician was also able to become more familiar with the student. This familiarity opened lines of communication that enabled students to feel comfortable asking their attending physician questions as well as asking them for advice. Students also noticed that patients seemed to be more open with their physician when discussing their health problems. If a patient did not fully divulge concerns, the rural physician seemed attuned to relevant issues and often prompted beneficial discussion with the patient. When students were comfortable with the physician and the rest of the care team, they felt more confident actively participating in patient care and felt like a valued member of the healthcare team, further validating their educational experience.[6] In rural, and often remote settings, students regularly witnessed the dedication physicians had for serving their patients and students were inspired by these actions.

Although kindness is mentioned among various elements of professionalism in the missions of other medical schools, at present no other medical school has chosen to make kindness a central focus of its curriculum and culture.[7] This focus on kindness that the SSOM has adopted is creating a positive environment in the medical school as well as in the state's clinics and hospitals. The goal of this initiative is to establish a culture in which kindness permeates into the interactions between students, staff, and faculty physicians throughout all stages of medical education. Ultimately, a reverberation of this kindness will hopefully be seen throughout the clinic and hospital settings, leading to an increase in patients' satisfaction with their care and a decrease in burnout among healthcare providers. The narratives of the students interviewed for this study highlight the positive impact that kindness has had on their educational experiences and patients' experiences, especially while in rural settings. These results emphasize the importance of kindness and the need to continue to advocate for kindness in all healthcare settings.

SSOM's FARM program and rural family medicine rotations were established in an effort to expose students to the practice of rural medicine with the hope of one day attracting those students back to rural areas to establish their practice. An unforeseen benefit of this program is that students who participate in rural rotation, and especially those in the FARM program, have frequent opportunities to witness kindness through the interactions between small town healthcare providers and patients. After conducting focus groups and key informant interviews, it was apparent that kindness in rural settings is emphasized through such relationships.

One theory that may account for the students' perceptions is the nature of the rural track including an immersion experience in which the student spends a majority of their time with one or two primary care physician coordinators identified in each community. The physician coordinators at each site are the main contact faculty members who are tasked with ensuring that the student achieves all the objectives of the curriculum and that each student receives both formative and summative feedback. Thus, this more continuous exposure might lead to the students' perception of kindness on the part of the physician.

Not all the medical students interviewed in this study explicitly addressed experiences of kindness in the rural setting. However, as the foregoing quotations note, kindness was a theme of many student responses. Certainly, kindness can be demonstrated in multiple hospital and outpatient settings in communities large and small. Our study suggests that the rural experiences of SSOM students frequently prompt students to specifically articulate the impact of kind behavior.

Our focus in this study on kindness in the rural setting is certainly not meant to imply a lack of kindness in other clinical settings. Rather, the medical student comments we report serve to illustrate that students' education in rural settings may be uniquely conducive to promoting kind behavior between faculty, students and patients.

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About the Authors:

Emily Endres, MD, Family Medicine Residency Program, Rapid City, South Dakota.

Jamie Messerli, MS, Sanford Health Research and Department of Neurosciences, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota.

Susan M. Anderson, MD, Department of Family Medicine, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota.

Jerome W. Freeman, MD, FACP, Department of Neurosciences, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota.

Magnesium Citrate Toxicity: A Case Report of a Patient With Significantly Altered Gastrointestinal Anatomy

Meghan Grassel, MS III; and Michael Koch, MD

Abstract

Magnesium citrate is a widely used over the counter drug with little to no safety concerns. This case study describes the development of magnesium toxicity after a single dose of magnesium citrate in a patient with extensive prior gastrointestinal surgery for pancreatic adenocarcinoma. The surgery resulted in extensively altered gastrointestinal physiology and several mechanisms could have influenced the abnormal absorption of magnesium seen in this patient. The patient had normal renal function pointing to a different mechanism than previously reported magnesium toxicities.

Introduction

Oral magnesium citrate is a medication typically used for constipation relief and as a bowel cleanse before surgical procedures. It increases the frequency and force of peristalsis and is also an osmotic laxative that retains water in the colon[1]. Normally, it is well tolerated. The magnesium component is not detected in the blood after use, as it is not absorbed in quantifiable amounts.[1]

Magnesium is a necessary cation for the body, and 1.7 to 2.3 mg/dl, or 0.75-0.95 mmol/l, is considered normal serum concentrations, with approximately 20 percent of serum magnesium bound to albumin.[2,3] Serum magnesium levels, however, do not always correlate with total body magnesium content.[2,3] The small intestine absorbs 30-50 percent of dietary magnesium through a transport channel and passive diffusion with water.[2,3] The small intestine decreases its absorptive capacity with increasing amounts of magnesium and in chronic renal disease.[2,3] Absorption can alternatively be increased with higher levels of PTH.[2] Serum magnesium is filtered at the glomerulus, but only 3 percent of magnesium is typically excreted in the urine.[3] The filtration rate and tubular reabsorption determine the final elimination rate of magnesium in the kidney. Sixty to seventy percent of Mg is passively reabsorbed in the ascending loop of Henle.[2,3] A calcium receptor senses increased plasma calcium or magnesium and can activate an arachidonic acid cascade that subsequently inhibits the NaK2Cl cotransporter and augments magnesium excretion.[3] Natriuresis, osmotic load and metabolic acidosis can all increase magnesium excretion rates.[3] Metabolic alkalosis, parathyroid hormone, and calcitonin can all reduce excretion.[3] Hypermagnesemia is rare clinically and usually occurs with increased magnesium ingestion in the setting of renal insufficiency.[3] In healthy individuals, serum magnesium levels are generally well maintained until the glomerular filtration rate decreases to less than 20 ml/min.[2,3] Although magnesium levels are normally not a problem, when levels reach a higher threshold, toxicity can become significant.

Clinically, magnesium toxicity can be uncomfortable to deadly for a patient.[2] Magnesium toxicity becomes evident after serum concentrations reach 4-6 mg/dl or 1.74-2.61 mmol/l.[2] Symptoms can include nausea, vomiting, headaches, hypotension, urinary retention, lethargy, flushing, and abnormal heart rhythms and asystole.[2,3] Severe cases have demonstrated coma, paralysis, hyporeflexia, bradyarrhythmia, respiratory depression, and cardiac arrest.[2] Diuresis can enhance renal excretion of magnesium and, in severe toxicity events, IV Ca can be administered for further treatment.[2] Treatment with calcium antagonizes the effects of magnesium at neuromuscular junctions, preventing the side effects of hypermagnesemia.[2] It does not decrease the amount of magnesium, however, and continued diuresis is still needed. Magnesium toxicity from ingested magnesium usually only occurs in patients with renal dysfunction.[4,5]

Magnesium can cause more acute physiologic disruption. However, the citrate component of magnesium citrate is also important. Citrate metabolism varies based on acid-base status. Alkalosis increases citrate excretion and acidosis inhibits excretion.[6] Small changes in pH can greatly affect citrate metabolism. Normal urine citrate is 1.7 mmol (320 mg) in men.[6] Importantly, citrate can also be converted

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to bicarbonate further influencing acid-base balance and complicating tracking citrate levels.[6]

Our case study follows a patient with significant gastrointestinal surgery. Dumping syndrome frequently effects patients after gastric or esophageal surgery.[7,8] Disturbance of normal gastric emptying through altered anatomy or disruption of innervation can greatly increase the speed of transit of chyme.[7,8] The food bolus reaches the intestine much faster, in greater quantities, and with different pH values than it would have with normal gastric physiology.[7,8] This causes fluid shifts into the intestine from the plasma to offset the hyperosmolality of the food bolus, furthering the dumping syndrome.[7,8] Dumping syndrome also activates the sympathetic nervous system.[7] Symptoms include abdominal pain, bloating, nausea, and diarrhea.[7,8] In addition, patients can experience fatigue, flushing, sweating, and hypotension.[7,8] Hyperinsulinemic responses can also stimulate late dumping syndrome one to three hours after a meal.[7,8] Multiple hormones are released when dumping syndrome occurs including enteroglucagon, peptide YY, vasoactive intestinal polypeptide, glucagon-like peptide, and neurotensin.[7,8] These hormones can alter motility, absorption, and secretion of the small intestine. Vasoactive hormones cause splanchnic vasodilation, increasing blood flow to the small intestine.[7] Interestingly, hormonal imbalances from early dumping syndrome cause delayed motility, increasing the time food spends in the small intestine.[8]

This case study will inform readers of a patient with significant gastrointestinal surgery that experienced magnesium toxicity following treatment with magnesium citrate.

Case Report

Our patient, a 53-year-old male, was diagnosed in November of 2014 with locally advanced pancreatic cancer, T4, NX, MX. He was scheduled to receive 10 rounds of pre-operative adjuvant FOLFIRINOX but was able to tolerate only seven rounds due to the development of severe, life threatening diarrhea, pneumatosis, and colitis. FOLFIRINOX contains leucovorin calcium, fluorouracil, irinotecan hydrochloride, and oxaliplatin. The patient then completed pre-operative radiation therapy with capecitabine and three intratumor injections of gemcitabine. He completed radiation therapy over three months and received a total of 540cGy in 28 fractions. Following this adjuvant therapy, the patient then underwent surgical resection of the neoplasm that included a total gastrectomy, pancreatectomy, duodenectomy, splenectomy, left adrenalectomy, cholecystectomy, and vascular reconstruction of celiac trunk, hepatic artery, and portal vein. Post-surgical treatment for the patient included a continuous glucose pump, insulin monitor, and Creon supplements. Creon is a capsule of porcine lipase, protease, and amylase.

The patient presented December 2018 with constipation and past medical history of post-operative, transient bowel obstructions. 10 oz Magnesium citrate (1.745 g Mg per oz) was prescribed to alleviate symptoms.

The patient returned to hospital after taking the magnesium citrate and appeared to be in worse condition. Patient was nauseated, fatigued, and confused. Magnesium blood levels were elevated at 4.5 mg/dL, normal 1.7-2.3 mg/dL. Potassium, sodium, calcium, phosphorus, and chloride levels were normal. Bicarbonate was elevated at 35 mEq/L, normal of 22-29 mEq/L. The anion gap was normal at 7 with normal range of 7-15. BUN was 11 mg/dL, normal 8-24 mg/dL. Creatinine was 1.05 mg/dL, normal 0.74-1.35 mg/dL. eGFR was estimated using the 2009 CKD EPI creatinine equation and was 81 with normal being above 60 mL/min/BSA. Albumin was 3.6, normal at 3.5-5 g/dL. AST, ALT, and alkaline phosphatase were all elevated in this patient; however, this patient has had elevated levels since his surgery years prior. Bilirubin was normal. The patient had two known kidney stones that were unchanged. Urinalysis showed normal pH, protein, and osmolality. Glucose was elevated, which was unsurprising given the patients history of pancreatectomy and subsequent diabetes mellitus. Urine microscopy revealed RBC and WBC and urinalysis showed hemoglobin which are likely related to the patient's known kidney stones. Magnesium toxicity was diagnosed, and the patient was monitored in the hospital using labs and a cardiac monitor until he recovered. After a day, magnesium levels returned to normal. The patient reported having taken magnesium citrate before his surgery without any side effects.

Discussion

As this patient had a total gastrectomy and duodenectomy, the change in gastric physiology or altered intestinal physiology could have led to his presentation. This altered physiology could have led to toxic levels of a normally safe ion. As this event happened years after the patient's extensive operation for pancreatic adenocarcinoma, the intestine could have adapted to less gut space by increasing receptors for absorption in the small intestine. Additionally, normal feedback loops for gastrointestinal hormones are altered in this patient because of his extensive surgery. The patient replaces some of his pancreatic hormones with Creon; however, his body is not able to respond to changes as they

occur. Thus, any alteration to normal digestion could greatly affect his physiology.

A difference in anatomy and physiology from the surgery likely caused this presentation as the patient had taken magnesium citrate prior to the surgery without incident. Gastric dumping syndrome from his altered gastric anatomy is another possible cause. The increased transit time in the small intestine from dumping syndrome could have caused magnesium absorption beyond normal parameters.[7,8]

This patient has had elevated liver enzymes since surgery; however, his albumin level has remained normal. Thus, his liver is not a likely source of dysfunction. The kidneys could have been another source of the hypermagnesemia in this patient. The kidney excretes the body's magnesium over time, but it also is involved in its reabsorption to maintain normal levels.[3] It is possible that a decreased GFR would diminish magnesium excretion, leading to sustained hypermagnesemia. However, the patient's GFR and creatinine remained normal, so this is not a likely source for this particular case.

Magnesium citrate is a widely used drug that is considered safe for almost all patients. Patients with altered anatomy and physiology, particularly gastric and intestinal, should potentially use caution when using this medication, as GI absorption and renal excretion could be altered and lead to toxicity, as seen in this case.

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About the Authors:

Meghan Grassel, MS III, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota.

Michael Koch, MD, Department of Pathology, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota; Sanford Health, Sioux Falls, South Dakota.

Erdheim-Chester Disease: A Mysterious Illness Causing Obscure Neurologic Syndromes

Alex Hanson, MS IV; and Jerome W. Freeman, MD, FACP

Abstract

Erdheim-Chester disease (ECD) is a very rare form of non-Langerhans histiocytic disorder which affects multiple systems and can present in a variety of different ways. We present two patients diagnosed with ECD whose symptoms, progression and treatment differ dramatically.

Introduction

Erdheim-Chester disease (ECD) is a very rare form a non-Langerhans histiocytic disorder which manifests in a variety of different systems, representing a diagnostic challenge. Fewer than 1,000 cases have been reported in medical literature and our understanding of the disease process is limited, often leading to delayed diagnosis.[1] Somatic mutations involving MAPK genes have been found to be involved in the pathogenesis of the disease, most commonly BRAFV600E in CD34+ stem cells.[2,3] Its most common presentation involves sclerotic lesions of the bones, with possible histiocytic infiltration of other tissues such as the cardiovascular system, central nervous system (CNS), kidney, lungs, skin and others.

Due to the rarity of the disorder and the variety of presentations, specific diagnostic criteria have not yet been established. Consensus recommendations for the workup of ECD include a biopsy to identify BRAF mutation status as that directs treatment. Disease without bone lesions is less common and can be considered when there is histopathological evidence of the disease. However, cases in which biopsy does not demonstrate classic histopathological findings do occur. In such cases, osseous imaging for lesions is along with mutational analysis for BRAF and MAPK pathway mutations is important. Once diagnosis is established, PDG-PET-CT is recommended to define the extent of the disease.[4] We present two patients, both with CNS involvement but with differing initial presentations, progression of disease, prognosis and treatment.

Case Reports

Case 1 is a 42-year-old male who was seen in the neurology office for evaluation of a two-week history of numbness of the feet and thighs and lower chest. He felt he had "less tone" in his abdomen and that he was having more difficulty urinating. He had a sensory level at T4. He noted that two weeks earlier he had been in a small aircraft in very turbulent weather. He had been jolted up and down vigorously. A magnetic resonance imaging (MRI) of the thoracic spine revealed a mass that was initially felt to be a hematoma. At surgery a fibrous mass was removed from the epidural space and the pathologic assessment was histiocytic proliferation that was felt to be consistent chronic hypertrophic pachymeningitis. His symptoms improved after surgery.

Nine months earlier he had presented to an urgent care and then a primary physician complaining of chest pain for two weeks. When the pain persisted a computerized tomography (CT) of the chest was done that showed homogenous soft tissue densities around the thoracic aorta. The possibility of adenopathy was considered and a testicular sonogram was recommended. This study showed irregular, hypoechoic lesions in both testes. An abdominal CT scan showed no diagnostic abnormalities. He was referred to urology and a left orchiectomy was done. The pathology was described as showing a nonspecific granulomatous orchitis with a histiocytic inflammatory component.

Several months after his thoracic surgery his symptoms returned with numbness in the legs and a shooting pain in his spine that was aggravated by exercise. A repeat MRI of the thoracic spine was stable. He was referred to another tertiary center where a positron emission tomography/computed tomography (PET/CT) was performed. This showed increased uptake in the testicles, aortic arch, descending thoracic aorta and several abdominal densities. A differential diagnosis included granulomatous vasculitis with polyangiitis (Wegener's). He was started on high dose prednisone which initially helped his thoracic pain although it worsened again with steroid taper. He was switched to rituximab and his pain decreased over the next several months. A review of the patient's pathologic samples from his prior orchiectomy was undertaken, staining positive for CD68. The sample was negative for a BRAF mutation but positive for a BRCA1 mutation. At that point, the diagnosis was changed to ECD. Treatment with cladribine was begun and following six cycles

of chemotherapy, the patient entered clinical remission.

Case 2 is a 55-year-old male who complained of dysarthria that had gradually worsened over several months. His words become more slurred as the day progressed and increased with fatigue. His exercise tolerance decreased and he began to have mild dysphagia. An MRI and labs revealed no abnormalities. A tensilon test was preformed and was normal. Concern for possible amyotrophic lateral sclerosis (ALS) led the patient to be seen at a major tertiary center. ALS was excluded and instead a diagnosis of tongue myopathy/inclusion body myositis was made.

The patient then developed intermittent thigh pain in the distal portion of the quadriceps above the knees over the next couple of weeks which only occurred at night. Gabapentin was started. A few days later, he developed hematuria and flank pain. An abdominal CT was obtained revealing symmetric fluid/soft tissue stranding suggesting thickening of the capsule of the kidneys. This was quite pronounced near the ureteropelvic junction causing hydronephrosis. Renal function tests were normal. An abdominal lymphoma or possible paraneoplastic process was considered, and he was seen again at the tertiary center where a tissue sample from a kidney biopsy was interpreted as IgG4 sclerosing disease. He was treated with high dose prednisone. A month later, symptoms of flank pain, and weakness had not improved, and involuntary jaw-clenching began. The biopsy samples were revisited revealing a positive BRAF V600E mutation and ECD was suspected as an explanation of the patient's symptoms of leg pain, flank pain, and dysarthria. Treatment with vemurafenib was started. A repeat MRI showed nine 2-3mm lesions in the brain and PET/CT revealed renal and adrenal involvement. After weeks of treatment, the flank pain resolved with residual dysarthria and disequilibrium persisted. A repeat PET/CT showed treatment response to all known areas of involvement.

After a year on the vemurafenib, the patient had increased arthralgias and myalgias, a known side effect of the drug. He was switched to trametinib in hopes that the side effect profile would be more favorable and this drug might be more effective in resolving his dysarthria. However, his dysarthria has persisted despite sustained remission of the disease from a radiological standpoint. In our review of the literature, we did not find a comparable case of ECD presenting with a prominent tongue dysfunction/dysarthria.

Discussion

These cases demonstrate the diagnostic challenge that ECD poses. Both patients had somewhat confusing symptoms leading down various diagnostic paths. These cases showcase the wide range of systems that ECD can affect.

When ECD is suspected, it is important to document the extent of the disease including the number of organ systems affected and determine the functional status of the disease. Clinical symptoms vary greatly as emphasized in these case studies. Non-specific symptoms across multiple organ systems are common and can involve constitutional symptoms, bone pain, and multiple organ involvement.

Typical laboratory studies for ECD are non-specific. CRP and ESR are often elevated. Labs indicating hypopituitarism are possible. Imaging studies are essential and can reveal a mass in the chest, abdomen, and pelvis. PET/CT can demonstrate bone involvement. MRI with contrast of the brain, spinal cord, and heart can reveal lesions.

Tissue biopsy, histological analysis, and immunohistochemical staining establishes the diagnosis. Genetic studies of biopsied tissue can identify mutations that allow for more targeted therapies. Characteristic histopathological findings include inflammatory infiltrates in the affected tissue containing lipid-laden histiocytes and Touton giant cells.[5] However, biopsy findings may be highly variable and there may be an absence of foamy histiocytes, non-specific inflammation with mixed fibrosis or fibrosis alone.[6] Ideally, a skin biopsy of cutaneous lesions provides the least invasive way to establish diagnosis. As with our patients, this may not be possible and surgical excision of tumors from various locations is done. Molecular testing should be done following biopsy that should be able to identify mutations consistent with ECD (MAPK, BRAF) as well as the detection of CD receptors expressed on histiocytes (CD68, CD163, factor XIIIa, and fascin).[4,7] A key characteristic is the absence of Birbeck granules usually found in Langerhans cell histiocytosis.[8]

Differential diagnosis of ECD includes other histiocytic cell disorders, metastatic solid tumors, hematopoietic neoplasms, and macrophage activation syndromes. Langerhans cell histiocytosis (LCH) and ECD are both histiocytic neoplasms that commonly affect the skeletal system. Key differences, however, include the presence of Birbeck granules on histopathological examination as well as common skin involvement with LCH.[9] Paget's disease includes osteosclerotic lesions of bone that may be confused for bone involvement of ECD, but Paget's disease lesions are less likely to be symmetric. Hemophagocytic lymphohistiocytosis (HLH) shows tissue infiltration by non-neoplastic histiocytes unlike ECD as well as other hematological findings.[10] Other disorders on the differential include Juvenile xanthogranuloma (JXG) and Rosai-Dorfman disease.

The management of ECD varies based on patient presentation. As demonstrated by our two patients, treatments can also vary. Asymptomatic patients with no evidence of organ or CNS dysfunction may not need treatment and observation

is recommended. Symptomatic patients require treatment. Enrollment in a clinical trial is recommended wherever possible and targeted therapy based on the mutation present in tissue pathological examination when enrollment is not possible.

When a BRAF mutation is present, the treatment is the BRAF-inhibitor vemurafenib.[11-13] Other mutations that affect other common signaling molecules required treatment with a MEK inhibitor, most commonly cobimetinib.[14] If no mutation is detected, then treatment with interferon alfa is recommended as opposed to systemic chemotherapy which is reserved for patients who do not respond initially to interferon alfa. Systemic chemotherapy regimens usually consist of cladribine, methotrexate, IL-1 receptor antagonists, sirolimus, Infliximab, ALK inhibitors, or Imatinib.[15-17] Surgery and radiation are used primarily for symptomatic treatment such as relief of mechanical compression of the CNS.

There is no real consensus as to how often patients should have follow-up. Clinical evaluation every three to six months is the general rule or sooner if symptoms reappear. Generally, monitoring is focused on organ and CNS involvement. There is no cure for ECD, and the prognosis is generally poor. However a case series of patients treated with targeted therapy showed five-year survival rates of 70 percent with CNS involvement associated with worse outcomes.[17]

Conclusion

ECD presents a diagnostic challenge clinically, in imaging studies and even pathologically. The variety in organ systems it affects causes vastly different presentations. Patient 1 presented more classically for a histiocytic cell disorder in the form of chest pain with organ involvement of the testicles and finally, a CNS mass compressing the spinal cord. Patient 2 had a much more unusual and possibly unique presentation with dysarthria. Later he developed hematuria/renal involvement, jaw-clenching, and lesions in the cerebral white matter. Their varied symptoms started each patient on convoluted diagnostic paths and the correct diagnosis was only appreciated over time. Long-term prognoses remain poor for patients with ECD. Our patients had differing treatment regimens but were able to achieve clinical remission.

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About the Authors:

Alex Hanson MS IV, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota.

Jerome W. Freeman, MD, FACP, Department of Neurosciences, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota; Sanford Health, Sioux Falls, South Dakota.

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Myocardial Infarction with Nonobstructive Coronary Arteries (MINOCA) in a Patient Taking Lisdexamfetamine

Swaminathan Perinkulam Sathyanarayanan, MD; Muhammed Hamza Saad Shoukat, MD; Jeffrey Wilson, MD; and Marian Petrasko, MD

Abstract

Stimulant medications like amphetamines have been associated with various cardiovascular complications like coronary artery spasm, coronary dissections and thrombus formation, the pathophysiology of which is theorized to be the endothelial damage induced by the medication and the inflammatory cascade that follows. We report a case of 52-year-old male on lisdexamfetamine, a newer stimulant agent used for attention deficit hyperactivity disorder (ADHD) who presented with sudden chest pain and ECG changes concerning for myocardial infarction and mildly elevated troponins. However, coronary angiogram showed no obstructive coronary artery disease and there was spontaneous resolution of his symptoms and ECG changes.

Introduction

Myocardial infarction with nonobstructive coronary arteries (MINOCA) is a clinical entity characterized by features of myocardial injury without any obstructive lesions in the artery (≤ 50 percent stenosis) as seen in coronary angiogram and without any other overt causes of MI like cardiac trauma. Plaque disruption, coronary artery spasm, coronary artery dissections, microvascular dysfunction and coronary embolism are some of the common causes of MINOCA.[1] Drug induced coronary artery spasm leading to myocardial injury is commonly seen in young adults with overdose of stimulants like amphetamines.[2] Lisdexamfetamine is a new long-acting stimulant prodrug of amphetamine that is approved for use in ADHD with a convenient once daily dosing. It offers an alternative treatment option for those who have not responded to other ADHD therapies. With an elimination half-life of less than one hour, it is converted into dextroamphetamine which has a half-life of approximately 10-13 hours. Common adverse effects of this medication include insomnia, decrease in appetite, tachycardia and hypertension.[3]

Case

A 52-year-old man presented to the emergency department (ED) with acute onset of non-radiating substernal chest pain, dull in nature and moderate in severity. There was no relation to exertion, respiration, change in body position or caloric intake. He had a past medical history of ADHD and hypertension. He was a lifelong non-smoker and there was no family history of heart diseases. His home medications included lisdexamfetamine and lisinopril. Electrocardiogram (ECG) in the ED was notable for hyperacute T waves in V2 – V6, I, II and aVF with ST segment depressions in I, II, aVF, V3 – V6 concerning for ST elevation myocardial infarction (STEMI) equivalent (De Winter pattern). He was immediately transferred to the cath lab. Coronary angiogram showed minimal non obstructive atherosclerotic coronary artery disease – 20 percent lesion in mid left anterior descending artery. There was no evidence of aortic dissection on the aortogram. His troponins were mildly elevated and peaked at 0.236 ng/ml (normal < 0.028 ng/ml). The patient's chest pain subsided after the procedure and repeat ECG showed resolution of previously noted changes. His transthoracic echocardiogram showed normal biventricular function, left ventricular ejection fraction 60-65 percent and normal valves. He was discharged home the next day in a hemodynamically stable condition on aspirin, high intensity statin and sublingual nitrates. Because there

Figure 1. Patient's ECG taken in the ED.

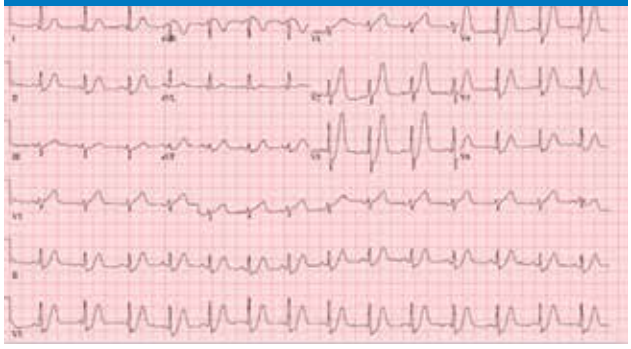
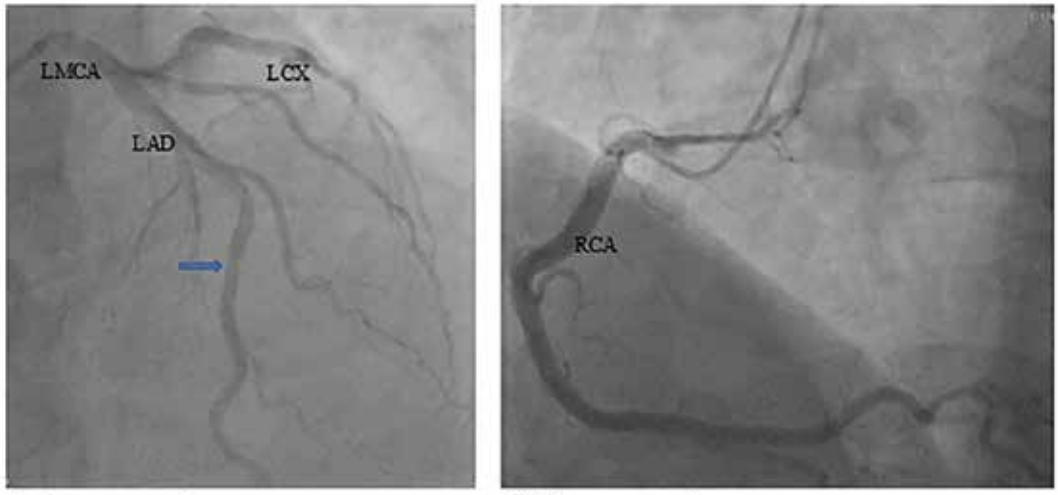


Figure 2. Left coronary angiogram and right coronary angiogram. Left main artery dividing into the left anterior descending (LAD) and left circumflex; there is a 20 percent lesion in the mid LAD artery (blue arrow). Right – the RCA appears free of any disease.

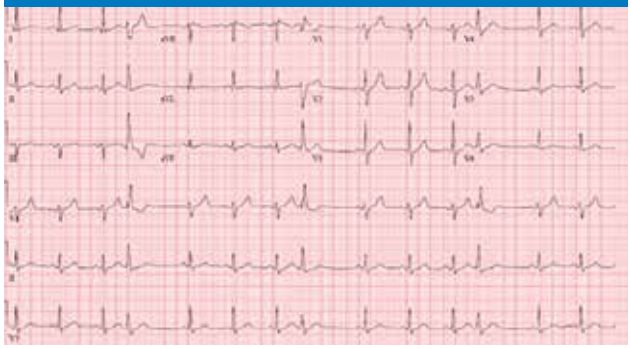


was no significant myocardial injury sustained as evidenced by the mild troponin elevation and normal left ventricular systolic function and because his ADHD symptoms were controlled only on lisdexamfetamine, it was decided to be continued with close follow up and monitoring. He was followed up at one month and four months without any further recurrences.

Discussion

Medications used for ADHD are central nervous system stimulants causing catecholamine release which include amphetamine salts, methylphenidate, lisdexamfetamine, atomoxetine, and methamphetamine. Excessive sympathetic nervous system activity from these medications causes hypertension, endothelial dysfunction, left ventricular hypertrophy, and episodes of arrhythmia.[4,5] Amphetamines cause cardiovascular toxicities like coronary artery spasm, myocardial infarction, coronary artery rupture, aortic dissection, aortic valve thrombosis etc. in the setting of abuse and overdosing from catecholamine surge.[5-7] Lisdexamfetamine is a newer prodrug stimulant used to treat attention-deficit hyperactivity disorder. It is usually started at 30 mg daily and can be titrated to a maximum dose of 70 mg daily.[8] Although short term studies show minimal cardiovascular side effects with lisdexamfetamine,[9] there have been case reports of lisdexamfetamine associated coronary artery spasm[10] coronary artery dissection[11] and takutsubo cardiomyopathy.[12] This case report highlights the potential of newer stimulant medications to cause MINOCA even at therapeutic doses.

Figure 3. Repeat ECG after chest pain subsided.



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About the Authors:

Swaminathan Perinkulam Sathyanarayanan, MD, Department of Internal Medicine, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota.

Muhammed Hamza Saad Shoukat, MD, Department of Cardiology, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota

Jeffrey Wilson, MD, Department of Cardiology, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota.

Marian Petrasko, MD, Department of Cardiology, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota; Associate Program Director, Cardiovascular Disease Fellowship Program, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota.

Acute Rheumatic Fever: Case Report and Literature Review

Ken Noguchi, MD, PhD; Nofil Arain, MD; and Carl Galloway, MD

Abstract

A previously healthy 8-year-old Native American female presented with right-sided weakness and joint pain for two weeks. Following an initially unremarkable workup including negative brain and spine MRI she was noticed to have chorea and subsequently diagnosed with acute rheumatic fever (ARF). ARF is a group A streptococcus-related disease that most commonly is a sequelae of pharyngitis. The diagnosis of ARF utilizes the Jones criteria which includes heart disease, arthritis, chorea, the characteristic rash of erythema marginatum, and subcutaneous nodules. The most serious consequences of ARF include rheumatic heart disease and chorea. ARF can be treated with a combination of antibiotics and anti-inflammatories like aspirin.

Case Presentation

A previously healthy 8-year-old Native American female presented with right-sided weakness for two weeks. The patient's initial complaint was diffuse joint pain and myalgias, which the family attributed to growing pains. In addition, she had a two-day history of right-sided weakness which manifested as difficulty writing and eating with a fork. Her parents also reported that she had difficulty walking. At this time the family was concerned by her odd behavior and presented to an outside hospital for evaluation.

At the outside facility, her comprehensive review of systems was negative other than an unintentional 10 lb weight loss over the last couple months and occasional constipation for which she took polyethylene glycol. Her developmental history was only notable for speech difficulties which resolved after speech therapy. She was adopted at a young age and lived at home with her two siblings and parents. There was no reported exposure to pets, exotic animals or history of recent travel.

Upon presentation to the outside emergency department physical examination revealed temperature of 99.6 F, heart rate of 120, respiratory rate of 22, and O_2 saturation of 100 percent. She appeared well and was in no apparent distress. Her neurologic exam was notable for dyscoordination of her right hand and foot, diffuse poor muscle tone, hyperreflexia at her right knee, normal cranial nerve function. Musculoskeletal exam was notable for bony nodules on her knees and elbows, in addition to a subtle nodule on her right parietal region. The remainder of the physical exam was unremarkable. Labs at that time showed CRP 2.7 mg/dL (normal 0-0.9), ESR 32 mm/h (normal 0-20), and thrombocytosis with platelet count 406 k (normal 152-364 k). Her other labs including a CBC, electrolyte panel, liver function tests, and thyroid studies were unremarkable. CT head and spine revealed no acute findings. Due to the persistent and unexplained neurologic findings and at the recommendation of pediatric neurology service, decision was made to directly admit her to the pediatric hospitalist service for further evaluation and management.

At the time of transfer our differential diagnosis included: central nervous system pathology such as brainstem glioma or other intracranial mass, peripheral nervous system pathology such as Guillain-Barre, transverse myelitis, or rheumatologic disease such as juvenile idiopathic arthritis. Considering her dyscoordination our greatest concern was for a posterior fossa mass.

Upon arrival to our hospital, physical examination showed a temperature of 98.3 F, heart rate of 107, respiratory rate of 17, O_2 saturation of 99 percent, and weight of 25.2 kg. She was notably anxious but otherwise in no distress and clinically stable. Her neurologic exam was notable for right-sided dyscoordination in her upper and lower extremities as seen on heel-to-shin and finger-to-nose, 5/5 strength in bilateral upper and lower extremities although this required substantial motivation of the patient, reflexes symmetric and 2+ in bilateral upper and lower extremities, normal cranial nerve function, gait which was limited by right foot pain, and speech which was normal. Musculoskeletal exam was notable for prominent bony nodules on bilateral knees and elbows, as well as a subtle nodule in the right parietal region. She had normal muscle tone. The remainder of the physical exam was unremarkable.

During hospital admission day one her greatest concern was pain which was managed with acetaminophen, ibuprofen and IV ketorolac. The following day, a brain and spine MRI with and without contrast was obtained at the recommendation of pediatric neurology. These studies were largely unremarkable with an incidental finding of disc desiccation at T4-5 which was considered unrelated to her symptoms. Recommendations from neurology at this time were to pursue a broader differential diagnosis including autoimmune etiologies as well as myositis or encephalitis secondary to influenza infection. Additional labs were obtained including CBC, electrolyte panel, liver function tests, CK, ANA, influenza A and B, uric acid, LDH, urinalysis, ESR, and CRP. These labs were largely unremarkable, except for a slightly elevated ESR at 24 mm/h (normal 0-20). Her previously elevated CRP and thrombocytosis had resolved.

At this time we were thoroughly puzzled and the mother showed our team a video from home of the patient attempting to eat. In the video she was trying to feed herself with her left hand (she is right-handed) and was having choreiform movements with her right arm. When observed, she displayed similar choreiform movements while eating. The mother stated that she had never seen these movements prior to this illness. A low frequency grade I/VI systolic cardiac murmur was also auscultated at the left lower sternal border on exam that day.

In light of these new findings, pediatric cardiology was consulted. An ECG (Figure 1) revealed sinus rhythm, with no conduction delays. There were non-specific ST segment changes likely related to normal early repolarization pattern. Transthoracic echocardiogram revealed mild prolapse of the anterior mitral valve leaflet with moderate mitral valve regurgitation (Figure 2A). There was no leaflet thickening, dysplastic changes or valve stenosis. There was mild left atrial and left ventricular enlargement (Figure 2B) with preserved cardiac function.

The choreiform movement and the cardiac findings were highly suggestive of acute rheumatic fever (ARF). An ASO titer obtained was elevated to 1297 IU/mL (normal <200) and a group A streptococcus (GAS) throat swab was positive, thus confirming the diagnosis. Although the family denied any recent illnesses, upon detailed questioning they did mention her throat scratching for a day about four to five weeks ago. Based on her clinical diagnosis, all her family members were tested with GAS swabs, which were found to be negative.

She was treated with high dose aspirin (80 mg/kg/day) for inflammation, omeprazole 1 mg/kg/day for GI ulcer prophylaxis, furosemide 1 mg/kg/day for mild congestive heart failure, and penicillin G injection 600,000 U. Within 24 hours of starting therapy, she had a marked improvement in her symptoms (polyarthritis and gait disturbance) and started

Figure 1. 12-lead electrocardiogram demonstrating non-specific ST elevation in inferior and lateral leads.

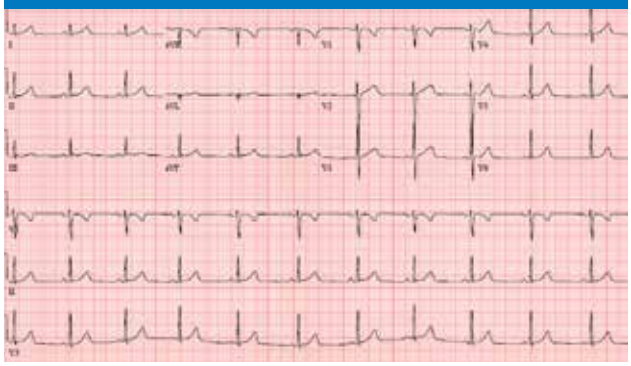
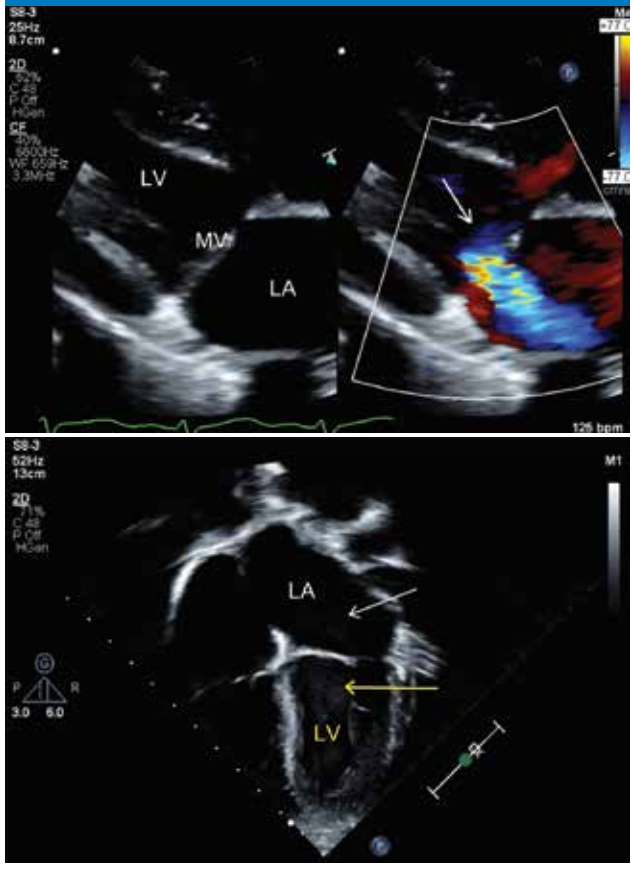


Figure 2. Echocardiogram. A: 2D and color Doppler echocardiogram images from parasternal long axis view. Arrow indicates significant mitral valve regurgitation. B: 2D echocardiogram images from apical four chamber view. Arrows indicate left atrial and left ventricular enlargement, respectively.

LA: left atrium, MV: Mitral valve, LV: left ventricle.



ambulating. Once her pain was adequately controlled, she was discharged in stable condition with established follow-up appointments at a separate facility due to geography and convenience.

ARF Literature Review

ARF is part of a progression of GAS-mediated diseases which starts with pharyngitis or skin infection (scarlet fever). 0.06 percent of patients with a superficial GAS infection will develop ARF due to an aberrant autoimmune response driven by molecular similarity between GAS antigens and host antigens.[1] ARF is a clinical diagnosis determined by the Jones criteria which are summarized below (Table 1).[2] Sixty percent of ARF patients will have an autoimmune response that targets the heart and its valves and progress to rheumatic heart disease (RHD).[1] RHD drives the mortality of GAS-related disease, with global estimates of 300,000 deaths per year.[1] As with most communicable diseases, improvements in living conditions and healthcare access has driven rates of ARF lower.[2] However, there is evidence both within the U.S. and worldwide that ARF is becoming a disease of the lower socioeconomic communities. In the U.S., the incidence of ARF has been estimated at 0.64 per 100,000 children age 5-17 years old, but a 7-fold increased prevalence in African Americans as compared to Caucasian children has been reported.[1] Other studies have shown an increased incidence in American Samoa with rates of up to 150 per 100,000 children less than 18 years old.[2] Globally, the highest rates of ARF have been reported in the indigenous populations of Australia that report an incidence of 194 per 100,000 children age 5-14 years old.[3] When compared to the non-indigenous population there was a 68-fold increased relative risk of acquiring ARF. It has been suggested that in poorer communities the first event of GAS pharyngitis goes undiagnosed and untreated so these patients finally present for care only after substantial carditis has already taken place.[4] In addition, socioeconomic status indirectly contributes to established risk factors for ARF including crowded living conditions, barriers to healthcare access, and low maternal literacy.[5]

Acute rheumatic fever is most common in the 5-14 year old age group.[6] The most common complaint at initial presentation is joint involvement (typically, migratory polyarthritis of large joints) which is present in 77 percent of patients, followed by carditis at 27 percent, and chorea at 19 percent.[1] These three complaints make up three of the five major Jones criteria, while the other two are subcutaneous nodules (usually small, painless, firm and transient nodules occurring a few weeks into the illness) and erythema marginatum (pinkish, nonpruritic rash usually involving the trunk early in the course of the disease) (Table 1; Figure 3). The latter two findings are much less common, although the exact number varies based on the study population. Although the carditis may reflect a classic picture of pancarditis, most often the endocardium, specifically the mitral and aortic valve, is predominantly involved. The latest American Heart Association guidelines for ARF diagnosis expand the definition of carditis from a solely clinical diagnosis including symptoms of heart failure or auscultation of cardiac murmur, to the addition of imaging findings of mitral or aortic valve regurgitation. This decision was made based on the progress of echocardiography techniques and with the hope of detecting subclinical ARF prior to progression to RHD. Minor criteria for ARF include arthralgia, fever, elevated inflammatory markers, and PR elongation. In order to apply the Jones criteria, a patient must have evidence of previous GAS infection either by ASO titer or throat swab. However, two out of every three cases of ARF is not preceded by a

Figure 3. Findings of acute rheumatic fever. A: Erythema marginatum. B: Subcutaneous nodules.
Images appear with permission from VisualDx (www.visualdx.com).

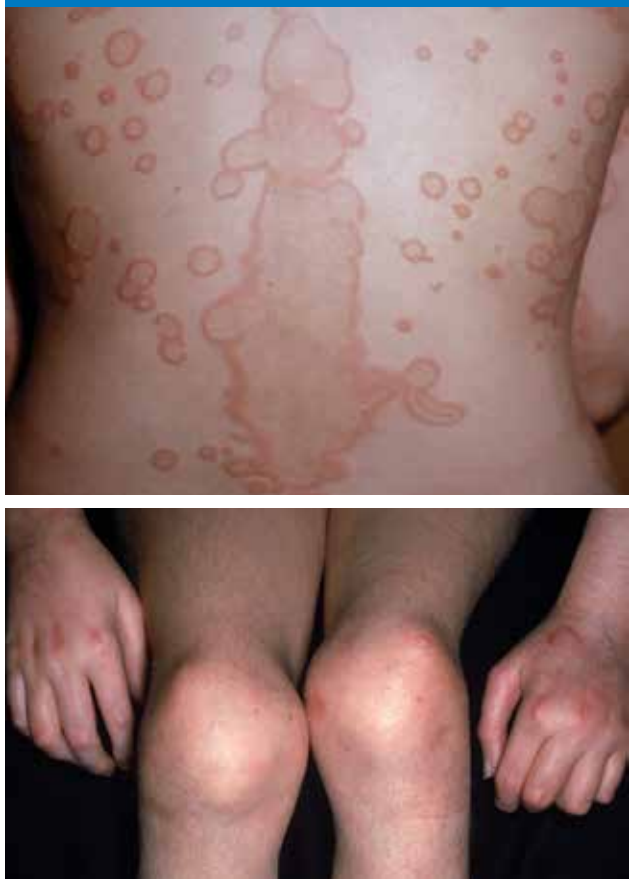


Table 1. Revised Jones criteria.*

A. Major criteria	
Low-risk**	**High-risk**
Carditis (clinical or subclinical)	Carditis (clinical or subclinical)
Polyarthritis	Polyarthritis, monoarthritis, or polyarthralgia
Chorea	Chorea
Erythema marginatum	Erythema marginatum
Subcutaneous nodules	Subcutaneous nodules
B. Minor criteria	
Low-risk	**High-risk**
Polyarthralgia	Monoarthralgia
Fever > 38.5F	Fever > 38F
ESR > 60mm or CRP > 3mg/dL	ESR > 60mm or CRP > 3mg/dL
Prolonged PR (unless carditis is present)	Prolonged PR (unless carditis is present)

*Adapted from Gewitz et al[5]
**Low-risk populations must have an incidence of <2 per 100,000
To be considered with Jones criteria, patients must have evidence of preceding GAS infection.
Initial ARF requires two major OR one major + two minor.
Recurrent ARF requires two major OR one major + two minor OR three minor.

Table 2. Secondary prophylaxis for rheumatic fever – duration of therapy.

Category	Duration after last attack
Rheumatic fever with carditis and residual heart disease (persistent valvular disease*)	Ten years or until 40 years of age (whichever is longer) Sometimes lifelong prophylaxis
Rheumatic fever with carditis but no residual heart disease (no valvular disease*)	Ten years or until 21 years of age (whichever is longer)
Rheumatic fever without carditis	Five years or until 21 years of age (whichever is longer)

* Clinical or echocardiographic evidence.
Modified with permission from: Gerber MA, Baltimore RS, Eaton CB, et al. Prevention of rheumatic fever and diagnosis and treatment of acute streptococcal pharyngitis: a scientific statement from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young, the Interdisciplinary Council on Functional Genomics and Translational Biology, and the Interdisciplinary Council on Quality of Care and Outcomes Research. Circulation. 2009;119(11):1541-51. Copyright 2009 Lippincott Williams & Wilkins.

clinically significant case of sore throat so its absence should not rule out ARF.[2]

In the diagnostic process of ARF the most notable characteristic is chorea, which most often occurs a few weeks – months after the initial GAS infection. The word chorea is derived from the Greek word for dance, and chorea is observed as a set of movements that is jerky and unpredictable. It is most commonly due to basal ganglia pathology and it can be broken down into inherited and acquired causes. Inherited causes include Huntington's disease, mitochondrial disorders, and Wilson's disease. Acquired causes include ARF, intracranial mass, encephalitis, hyperthyroidism, and conversion disorder.[3,4] An acute onset of chorea most commonly suggests an inflammatory etiology so the workup should focus on inflammatory markers, autoimmune markers such as ANA, and GAS testing. If an inflammatory etiology is unlikely a genetic cause must be strongly considered.

The core tenants of management of ARF include antibiotic treatment of GAS pharyngitis and prophylaxis against recurrent GAS infections, nonsteroidal anti-inflammatory drugs (NSAIDs) for symptomatic relief of inflammation, and finally treatment of carditis and chorea.[5,6]

The treatment of choice for GAS pharyngitis includes oral penicillin V or amoxicillin for 10 days, or a single dose of intramuscular (IM) benzathine penicillin G. Alternatively, cephalosporins, clindamycin or macrolides may be used in penicillin allergic individuals. For the inflammation, high dose aspirin (80-100 mg/kg/day in four divided doses) has been used. However, NSAIDs like naproxen with a better safety profile and easier dosing are now preferred. These are used until resolution of symptoms (typically two to three weeks), but occasionally longer treatment for persistent inflammation is necessary. Appropriate consultation with sub-specialists is needed for the symptomatic treatment of carditis and chorea. Detailed management is beyond the scope of this review, but may include anti-heart failure therapy, or use of other anti-inflammatory and immunomodulating agents e,g. glucocorticoids, intravenous immunoglobulins (IVIG). Since the incidence and severity of recurrent episodes of ARF, especially carditis, is related to the severity and number of ARF episodes, secondary prevention with ongoing prophylaxis is extremely crucial. Other risk factors for recurrent attacks include young age at onset, carditis and individuals with high risk for future streptococcal infection exposure.[7] Prophylactic therapy requires administration of IM benzathine Penicillin G every 21-28 days, until at least 21 years of age, but may be extended longer based on exact clinical presentation (Table 2).

In summary, acute rheumatic fever or ARF is part of a progression of GBS-mediated diseases. The most common clinical findings are described by the Jones criteria and include acquired heart disease, arthritis, chorea, erythema marginatum, and subcutaneous nodules. This disease is most common in 5-14-year-old children of low socioeconomic status. Management of ARF includes antibiotic and anti-inflammatory treatments and could potentially require lifelong treatment. Given this serious diagnosis it is important to consider ARF in the differential diagnosis of any patient with acquired heart disease, abnormal neurologic findings such as chorea, or common complaints such as joint pain.

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About the Authors:

Ken Noguchi, MD, PhD, Clinical Instructor, Department of Family Medicine, University of South Dakota Sanford School of Medicine; PGY-2, Family Medicine Residency Program, Center for Family Medicine, Sioux Falls, South Dakota.

Nofil Arain, MD, Associate Professor, Department of Pediatrics, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota; Sanford Children's Hospital, Sioux Falls, South Dakota.

Carl Galloway, MD, Clinical Associate Professor, Department of Pediatrics, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota; Sanford Children's Hospital, Sioux Falls, South Dakota.

Erosive Tophaceous Gouty Arthropathy of the Hand: A Case Report

Robert E. Van Demark, Jr., MD; Justin Brown, MD; Meredith Hayes, MD; Matthew Hayes, MD; and Vanessa J.S. Smith, PA-C

Abstract

The presence of tophaceous gout in the hand is a classic finding seen in uncontrolled gout. Occasionally gouty tophi can be the initial physical finding in asymptomatic hyperuricemia. Composed of monosodium urate (MSU) crystals, gouty tophi can cause significant soft tissue and joint pathology. In addition, tophaceous gout and hyperuricemia are associated with increased mortality. We present a patient with tophaceous gout causing erosive arthropathy of the proximal interphalangeal (PIP) joint. The diagnosis and treatment for tophaceous gout is reviewed.

Introduction

Gout is distinguished from septic joint, trauma, or calcium pyrophosphate deposition (CPPD) by the presence of monosodium urate (MSU) crystals on arthrocentesis. Tophaceous gout is a common finding seen with uncontrolled gout. The gouty tophus is composed of MSU crystals which forms due to chronic hyperuricemia. Over time, the MSU crystals form a granuloma-like structure that can cause erosion of soft tissues , cartilage, and bone which can result in degenerative joint disease.[1] The presence of tophaceous gout and hyperuricemia is also associated with increased mortality.[1,2] The first-line treatment of tophaceous gout is medical management to lower serum urate levels.[1,3-5] If medical management fails, there are limited indications for surgery.[3-5]

Case Report

A 64-year-old right-handed female was seen in our clinic with a swollen right index finger. She was referred by her primary care physician for evaluation of a finger mass. The finger had been swollen for several years and the mass had slowly increased in size. She denied any pain and only complained of finger stiffness. On physical examination, the soft tissue mass involved the proximal interphalangeal joint (PIP) of her right index finger causing a fixed flexion contracture of the finger (Figures 1A, 1B, and 1C). The mass measured 5cm x 4cm and was nontender. There was no redness or drainage from the mass. Multiple smaller tophi nodules were noted on the long, ring and small fingers.

She denied any history of gout. Her medical history was significant with a history of hypertension, hyperlipidemia,

Figure 1A, 1B, 1C. Clinical photograph of right hand demonstrating large tophaceous gout deposit of the index finger PIP joint. Smaller nodules noted in the long, ring and small fingers.

Anyone taking opioids is at **risk** for an **overdose.**

Help your patients recognize the symptoms of an opioid **overdose.**

Most opioid overdoses in South Dakota are *accidental*. If your patients have opioids in their homes, *remind them* of what to look for if an overdose is suspected.

What to watch for:

- Small, constricted "pinpoint pupils"
- Falling asleep or loss of consciousness
- Slow, shallow breathing
- Pale, blue, or cold skin or fingernails
- No response when they rub the middle of the chest with knuckles
- Vomiting, choking, or gurgling sounds

What can be done:

Suggest to patients that they keep naloxone on hand. **It can save a life.** Encourage them to keep their loved ones safe by taking these easy, preventative steps:

- Get naloxone for FREE from any pharmacy
- Order a FREE medication lock box for safe storage
- Order a FREE Dispose Rx packet to safely get rid of unused or expired medication or find a take-back location

Refer your patients and their families to the

Resource Hotline
1-800-920-4343

It's FREE, confidential, and available 24/7

For more about the State Unintentional Drug Overdose Reporting System (SUDORS) data, visit **AvoidOpioidSD.com**

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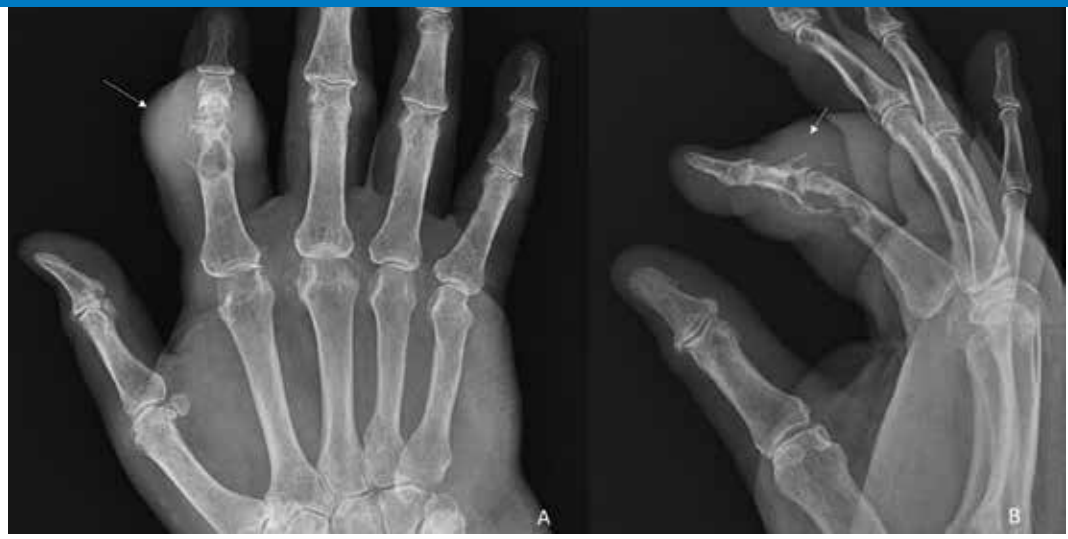
Figure 2A and 2B. PA and lateral radiographs demonstrating lytic lesions of the proximal and middle phalanx with PIP joint arthropathy with overhanging edges (white arrow).

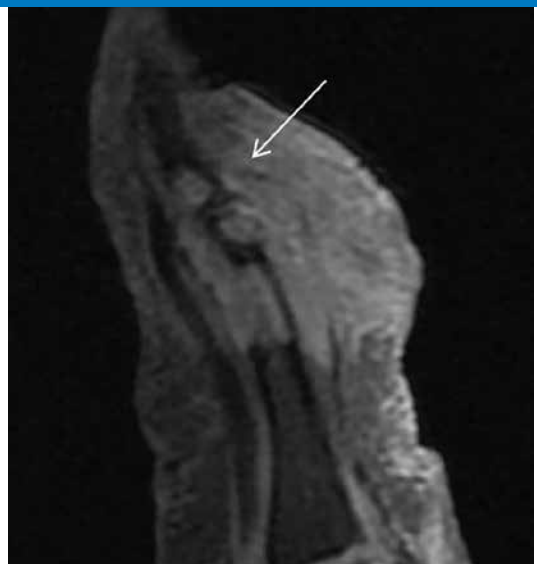


coronary artery disease, hypothyroidism and a BMI of 66.8. Recent laboratory findings showed a normal white blood count of 8.3K/uL, an elevated fasting glucose of 107mg/dL, normal estimated glomerular filtration rate (eGFR) of 40 ml/min/1.73 m2, and an elevated serum urate level 11.7 mg/dL (Normal range 3.5-8.5 mg/dL).[1]

Radiographs of the index finger showed erosive destruction of the middle and proximal phalanges with overhanging edges along with nodularity of overlying soft tissue (Figures 2A and 2B). Magnetic resonance imaging (MRI) scan revealed soft tissue changes with an extensive enhancing intraarticular mass and intraosseous tophi involvement of the proximal and middle phalanges. The tophus also involved and disrupted the index finger extensor tendon (Figure 3).

Due to her lack of pain and minimal functional loss, surgery was not recommended. She was referred to her primary care physician for medical management of her gout.

Figure 3. Sagittal T1 FS post gadolinium images demonstrate intraosseous tophus (white arrow) with marked erosive changes of the PIP joint with surrounding minimally enhancing soft tissue mass.



Discussion

Gout is a chronic medical condition affecting between 1-2 percent of adult males in the Western World.[3] Gout is characterized by hyperuricemia which is defined as a serum urate level above 6.8 mg/dl. Elevated serum urate levels can be caused by excessive intake or by overproduction or underexcretion of purines. The clinical syndrome of pain and swelling is caused by the inflammatory response to the MSU crystals.[3,6] Approximately 5 percent of patients with uncontrolled gout may develop tophaceous gout.[7] The MSU crystals in the tophus cause thinning of the skin which can lead to drainage and infection. The gouty tophus typically involves the distal interphalangeal (DIP) joint.[3] Less commonly, involvement of the PIP joints can also include both flexor and extensor tendons and joint arthropathy.[3,5] Gouty tophi in the hand and wrist can be commonly seen as the initial presentation of gout.[1,3]

The classic radiographic findings can include asymmetric margins of bone erosion, sclerotic rims, and overhanging edges.[3] MRI, ultrasound, and computerized tomography (CT) scans can be used to evaluate periarticular and soft

tissue involvement. A recent study recommended CT scans for the accurate visualization of gouty tophi. The CT scan can evaluate the volume of both subcutanenous and intraosseous tophi and the amount of bone erosion.[6]

The gold standard for the diagnosis of gout is the presence of needle-shaped urate crystals with strongly negative birefringence under polarized light microscopy in either synovial fluid or gouty tophus.[3]

Chhana and Dalbeth have described the cellular structure of tophaceous gout. The tophus consists of three distinct layers: a central core crystalline structure composed of MSU crystals, an intermediate corona zone and an outer layer or peripheral fibrovascular layer. Multiple pro-inflammatory factors found in the tophus include CD68+, macrophages, plasma cells, mast cells, and T and B lymphocytes.[1]

Local production of growth factors and enzymes in the tophus can degrade soft tissue, bone and cartilage as part of the erosion process. It has been suggested that the joint changes seen in gout might be similar to synovial arthropathies seen with inflammatory arthritis.[6] Tophi also have increased numbers of osteoclast with enhanced activity resulting in bone resorption.[1,6]

Infiltration of bone with the tophus may be another mechanism for bone erosion; there is a direct correlation between bone loss and the presence of intraosseous tophi.[6]

Tophaceous gout is also associated with increased mortality due to cardiovascular disease.[1,3] In a recent study, the presence of tophaceous gout was associated with an adjusted hazard ratio for death of 2.05 (95 percent CI 1.29-3.28).[2]

The recommended treatment for tophaceous gout is medical management of the hyperuricemia.[1,3,5] Lifestyle and dietary modifications are included in the initial treatment. If these options fail, drug therapy is started. Allopurinol, a xanthine oxidase inhibitor, is the first choice for drug treatment. Acute gouty flares can be managed with colchicine, nonsteroidal anti-inflammatory drugs (NSAIDs) or corticosteroids.[1,3,4] The American College of Rheumatology (ACR) guidelines recommend a target level of 6 mg/dL for serum urate levels and less than 5 mg/dL for tophaceous gout reversal.[1,3]

Although medical management of gouty tophi is effective in the majority of cases, some patients may require surgical treatment. Potential surgical indications have included nerve decompression, infection, pain control and to improve joint motion.[1,3-5,7-10] Debulking with partial excision of the tophus is probably the most common surgical procedure.[4]

Kumar et al. reported a series of 45 patients treated with surgery for tophaceous gout. The most common indication for surgery was tophus ulceration with underlying infection. Fifty-three percent of patients experienced delayed wound healing with three patients (7 percent) requiring amputation of the involved digit. The authors stressed the importance of proper medical management of gout and recommended referral to rheumatology services to minimize complications.[4]

Reports on the treatment of tophaceous gout involving PIP joints are limited with most patients treated successfully with medical management.[3,5,7] Straub reported on seven patients with PIP joint flexion contractures who were treated with debulking of the tophus.[7] Gelberman et al. reported their experience of seven patients with gouty tophi involving the PIP joint. Five patients were treated with medical management. Two patients underwent surgery to improve PIP joint motion and to prevent a PIP joint contracture. The operative procedure included tophectomy and extensor tendon reconstruction with lateral band mobilization and centralization of the extensor tendon over the PIP joint. Both patients had improved range of motion with improved hand function.[5]

The recommended treatment for gouty tophi is medical management of the elevated serum urate levels. If unsuccessful, surgical indications for tophaceous gout in the hand are limited: debulking of the tophus is the most common procedure.

There are two important reasons clinicians should be aware of the clinical significance of chronic hyperuricemia and tophaceous gout in the hand. Not only are these patients at increased risk of death but gouty tophi in the hand can be the initial presentation of hyperuricemia. Early diagnosis and appropriate medical management of gout can prevent the potential medical and musculoskeletal issues that can occur with uncontrolled gout.

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About the Authors:

Robert E. Van Demark, Jr., MD, Sanford Orthopedics and Sports Medicine, Sioux Falls, South Dakota.

Justin Brown, MD, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota.

Meredith Hayes, MD, Sanford USD Medical Center, Sioux Falls, South Dakota; Sanford Radiology; Sioux Falls, South Dakota.

Matthew Hayes, MD, Sanford USD Medical Center, Sioux Falls, South Dakota; Sanford Radiology; Sioux Falls, South Dakota.

Vanessa J.S. Smith, PA-C, Sanford Orthopedics and Sports Medicine, Sioux Falls, South Dakota.

Intracranial Hemorrhage Secondary to Vitamin K Deficiency Bleeding in a Newborn

David H. Arendt, MD, PhD; Dane A. Hegdahl, MS IV; Benson S. Hsu, MD, MBA, FAAP, FCCM; and KayeLyn J. Wagner, MD, MME

Abstract

We present a case of a 6-week-old infant who presented with seizure-like activity. Workup revealed abnormal coagulation and imaging confirmed intracranial hemorrhage. Parental refusal of vitamin K treatment at birth suggested vitamin K deficiency bleeding (VKDB) in this newborn. Though VKDB is rare in developed countries, rates have been rising which coincides with an increasing trend of parental refusal of vitamin K prophylaxis at birth.

Introduction

Formerly termed hemorrhagic disease of the newborn, vitamin K deficiency bleeding (VKDB) is a life-threating condition which infants are susceptible to for up to the first six months of life. The mechanism of bleeding is the impairment of the coagulation cascade due to a lack of vitamin K (VK) dependent factors II, VII, IX, and X. While pathologic bleeding due to low levels of VK can affect people of all ages, a variety of factors put newborns at particularly high risk due to low VK levels in this age group. An intramuscular dose of VK at birth substantially lowers the risk of VKDB which is why routine prophylactic VK administration was recommended by the American Academy of Pediatrics (AAP) starting in 1961.[1,2] VKDB often results in intracranial hemorrhage. To date virtually all developed countries recommend some form of VK prophylaxis at birth which has drastically reduced the incidence of VKDB. Despite this, cases of VKDB have been increasing globally in recent years largely due to parental refusal of VK administration at birth. We highlight a case of intracranial hemorrhage in a 6-week-old infant secondary to VKDB followed by a review of VKDB including the major events and hurdles that have guided VK prophylaxis.

Case Report

Patient is an exclusively breast fed 6-week-old male born via cesarean section at 38 weeks and who was brought to the local emergency department by his parents for several episodes of twitching/jerking movements. Starting the night before, these episodes lasted 15-20 minutes and affected his left sided arm, leg, and face. Involuntary movements of tongue and eyes were also noted. Patient was reportedly lethargic after these episodes. Home video of the events showed rhythmic movements of the left sided limbs that were worrisome for focal seizure activity. He was admitted to the inpatient service for further evaluation and management. Family history included a maternal aunt with epilepsy and two siblings positive for febrile seizures in the past. No reported fever or other signs illness preceded current symptoms. Of note, parents declined intramuscular vitamin K (IM VK) at birth.

Physical exam on arrival to the inpatient service revealed an afebrile baby with stable vitals in no acute distress. The child cried during the exam but was consolable by his mother. Fontanelles were flat and the only neurologic finding was occasional fasciculations of the tongue, but no apparent tonic-clonic seizure activity. There were no signs of head trauma. Lab work was significant for decreased hemoglobin of 8.1 g/dL. Due to concern of possible hemorrhage causing seizures, imaging by computed tomography (CT, later confirmed by Magnetic Resonance Imaging (MRI)) revealed a large right frontoparietal intraparenchymal hematoma. The hematoma measured 4 x 5.3 x 3.9 cm with a rim of surrounding edema and a 10 mm right-to-left midline shift with mild subfalcine herniation (Figure 1). The patient was transferred to the pediatric intensive care unit (PICU) due to concerns that the bleed was increasing intercranial pressure.

Once in the PICU, the patient was immediately treated for presumed intracranial hypertension. His airway was secured due to the need to decrease metabolic activity of the brain through aggressive sedation. Given the seizure history, the patient was started on levetricetam (40 mg/kg loading, 20 mg/kg/day maintenance).

Abnormal coagulation panel (PT 93.0 sec, PTT 94.2 sec, INR 11.94) and history of refused vitamin K at birth put VKDB high on the differential. Fresh frozen plasma and 2

Figure 1. Axial and coronal T2 MRI views showing a large intracranial hemorrhage involving the right anterior quadrant in the right frontal lobe with mild left to right herniation.

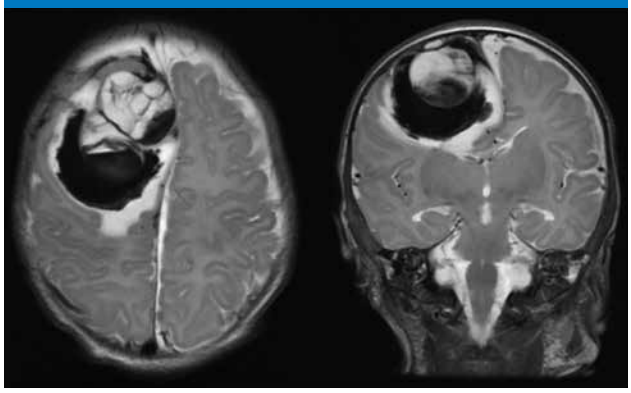
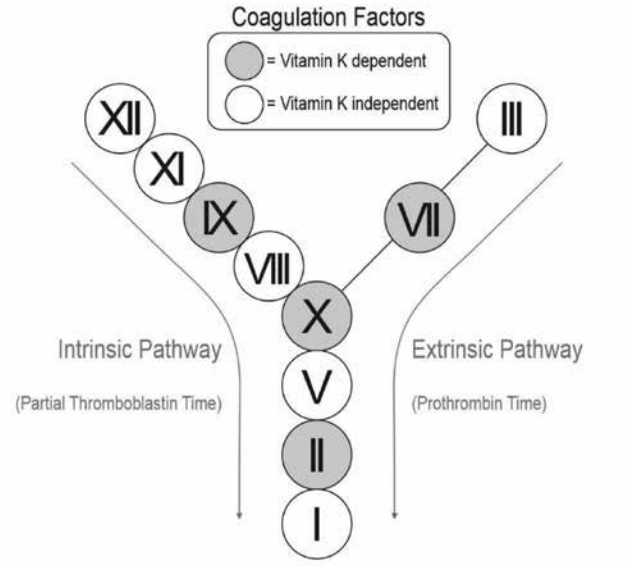


Figure 2. Coagulation cascade highlighting the vitamin K dependent factors.



mg of IV phytonadione (VK) in dextrose were administered which rapidly corrected his coagulation parameters. Electroencephalogram was abnormal and showed spikes and sharp waves noted in all four brain quadrants. Neurosurgical intervention was limited due to the concern of worsening the hemorrhage intraoperatively and the patient was managed medically instead. Patient was extubated on the sixth day of admission and sent home on day eight. Coagulation parameters remained stable for the duration of admission after administration of plasma and VK.

Discussion

This patient developed an intracranial bleed secondary to VKDB. Suspicious factors on presentation were new onset seizure activity in an otherwise healthy newborn coupled with parental refusal of intra-muscular of VK at birth. Once the diagnosis of intracranial hemorrhage was established, administration of VK reversed the deficiency in coagulation factors to achieve hemostasis.

VK is necessary for the proper function of the coagulation cascade. It is a cofactor involved in the carboxylation of coagulation factors II, VII, IX, and X as well as proteins S and C (Figure 2).[3] VK comes in two types with phylloquinone (VK1) being the form in circulation and menaquinone (VK2) residing in the liver.[4] Phylloquinone comes under the brand name Phytonadione which we will use interchangeably with "VK1." VKDB can be the result of reduced circulating levels of VK via deficient intake, impaired absorption, inherited deficiencies, and deficient production.

Newborns have low levels of VK and without exogenous VK they are at risk of VKDB events from birth up to 6 months of age. Both VK1 and VK2 levels in the newborn are almost undetectable at birth and take time to rise to adult levels during which time VKDB is a concern.[4] VK2 can also be produced by gut bacteria which are absent in the newborn leading to the "sterile gut" phenomenon.[5] Maternal medications that suppress VK synthesis can further hinder coagulation.[6] Even in utero, very little VK makes it across the placenta with a maternal to fetal cord blood VK ratio of 20:1 to 40:1.[4] There are low amounts of VK in breast milk with Greer et. al reporting that infants being fed mature breastmilk receive less than 1 ug of VK per day while formula fed infants typically get >45 ug per day.[7] Combined vitamin K-dependent clotting factor deficiency is the result of a genetic defect in either γ-glutamyl carboxylase or vitamin K 2,3-epoxide reductase complex.[8] Hereditary defects like these have a negligible effect on additional cases of VKDB as there are less than 30 cases worldwide due to it being an exceedingly rare autosomal dominant mutation.

There are three different types of VKDB categorized by the time of onset, all with unique characteristics. The early, classic, and late variants of VKDB were first classified by Lane and Hathaway in 1985.[6,9,10] Early VKDB onset occurs within the first 24 hours of life and is typically the result of maternal medication use that inhibits VK activity including antiepileptics, certain classes of antibiotics such as cephalosporins, and vitamin K antagonists like warfarin. In a similar fashion, the early variant can occur if maternal stores of VK are inadequate due to malnutrition or poor absorption. Early VKDB tends to have worse outcomes due to a high propensity for intracranial bleeding.[6] Classical VKDB presents between two and seven days. The classic variant is

mostly seen in infants that are exclusive breast fed due to the low VK content of breast milk. Contributing to the classic variant is a drop in coagulation factor II (prothrombin) levels after the first day of life.[11] Bleeding for classical VKDB tends to be slightly less severe with common sources arising from the gastrointestinal tract, umbilicus, or circumcision site. VK prophylaxis is effective at reducing the classic variant.[12]

The current case likely represents the late type of VKDB which can occur anywhere between eight days up to six months after delivery.[6] The overwhelming majority of late onset VKDB occurs in babies that have not been given VK at birth as was the case for the current patient. Similar to the early form, late VKDB tends to have worse outcomes due to most cases presenting with intracranial hemorrhage. A review of 131 cases showed that over half of late VKDB cases presented with IC hemorrhage with 14 percent of cases being fatal.[13] Mortality rates increase in low-income countries.[6] A primary diagnosis of VKDB should be suspected with any severe bleeding event in the newborn coupled with significant increases in prothrombin time, partial thromboplastin time, and INR ratio. Refusal of VK administration at birth should put the diagnosis high on the differential.[9]

Treating VKDB depends on the degree of bleeding. Non-life threatening bleeding can be managed with VK1 given intravenously or alternatively by subcutaneous injection at 250-300 ug/kg.[6] This dose of VK1 has been reported to reduce bleeding as soon as 20 minutes with correction of coagulation parameters within an hour.[14] Life threatening bleeding calls for treatment with fresh frozen plasma or prothrombin complex concentrate to quickly replete the coagulation factors in addition to VK1.[6] If there is any clinical suspicion that VKDB is responsible for blood loss, IV or subcutaneous VK1 administration should always be started immediately, even before coagulation lab results return. In the current case study, once coagulation labs returned abnormal, fresh frozen plasma and IV VK1 were administered. After treatments were initiated, coagulation labs had corrected 2 hours and 20 minutes later.

The AAP has recommended giving VK at birth since 1961 to prevent VKDB.[1] The original recommendation was "a parenteral dose of 0.5 to 1.0 mg or an oral dose of 1.0 to 2.0 mg" though it was noted that repeated doses may be necessary for treatment. This was revised in 2003 to "VK1 should be given to all newborns as a single IM dose of 0.5 to 1mg." Injection site reactions such as bleeding, dryness, and anaphylaxis are exceedingly rare even with millions of doses given a year.[15] Oral dosing of VK is used as the standard of care in multiple countries. As reviewed in Shearer et. al, most oral dosing prophylaxis regimens call for 2 or 3 doses of 1-2 mg though the data lack uniform timing and dosing.[6] While the oral route has been shown to reduce the incidence of VKDB, it is not as effective as a single IM dose at birth. The caveat to the superiority of IM over oral dosing might be from studies which showed that lower doses of daily or weekly VK by mouth have proven to be more effective at preventing VKDB than the 2 to 3 oral dose regimens.[4,9] The oral route also suffers from the potential for non-compliance involved with repeated dosing.[2,16] An additional obstacle of oral administration is occult cholestasis or liver disease in the newborn which can impair absorption of VK through the GI tract. While VK prophylaxis reduces the incidence of overall VKDB, a broader review shows it reduces the risk of the late type by approximately 97 percent.[12] Additionally, a study out of the British Isles showed a bleeding risk ratio of 0.01 for IM VK and 0.35 for the oral form.[17]

The hospital where the child was born followed the AAP guidelines on VK prophylaxis which are to offer an IM dose of VK1 at birth.[1,2] An additional hospital policy was to ask parents who refuse VK administration to sign a waiver saying that they had been informed of the risks of withholding VK prophylaxis which this family did sign. In 2002 the AAP released revised guidelines which note the uncertainty of the effectiveness of the oral forms and do not suggest oral VK1 as an alternative to the IM route.[2] Though it is not the stance of the AAP, Stanford has developed clinical guidelines on oral VK prophylaxis should parents refuse the IM form: 2-4 mg PO vitamin K after first feeding then 2 mg at 2-4 weeks and again at 6-8 weeks; OR 2-4 mg PO vitamin K after first feeding then 2 mg within first week and weekly while breastfeeding; OR 2 mg PO vitamin K after first feeding then 2 mg within first week followed by 25 mcg daily for 13 weeks.[15]

Some parental refusal of VK administration in their newborn stems from a 1990 study which corelated IM VK administration to childhood cancer.[18] After this publication there was an increase in the number of countries favoring the oral route over IM administration.[2] Multiple groups tried to confirm the correlation between cancer and IM VK, all of which failed to replicate the findings.[19-21] Additionally, an increase in parental refusal of IM VK has correlated with the trend of parental vaccination refusal. Zurynski et al. noted a significant increase in VKDB cases associated with parental VK refusal from 2006-2017 compared to 1993-2005.[16] A study out of New Zealand found a significant correlation with VK refusal and the refusal of other vaccines with a non-

vaccinated risk ratio of 14.11 (95 percent CI 7.75-25.68).[22] In the current case report, the patient had not received their first dose of the hepatitis B vaccine at birth due to parental refusal. As of the preparation of this manuscript the reported surviving patient had not received any of their scheduled vaccinations.

While it is tempting to attribute refusal of VK to negative views of prophylactic vaccines and medical treatment, a less explored possibility is a lack of parental information on VK. In a study out of Israel, four multiple choice questions were provided to expectant parents assessing their knowledge of IM VK in the newborn.[23] 61 to 74.5 percent of the respondents selected "I don't know" as their answer regarding the details of VK and the effect in the newborn. While this is a single study, these figures suggest that parents are not aware of how dangerous low VK levels can be in their child. A more targeted study would have to be carried out on a larger scale to draw causative relationships between parental knowledge of VK and its use at birth; however, the prospect that parents are not aware of the life-threatening problems VK prophylaxis prevents in their children is troubling.

Regardless of the reasons behind parents choosing to forego VK prophylaxis, providers must remain vigilant as the result of VK refusal will continue to be devastating for an unfortunate subset of children. In the U.S., legal challenges have gone so far as equating refusal to vaccinate with medical neglect of a child, though we are unaware of any cases involving refusal of VK prophylaxis.[24] These cases are almost always centered on the parent's reason for vaccine refusal in their child and existing vaccine exemptions in the state. This patchwork of laws at the state level makes it likely that vaccination and VK refusal will vary throughout the country.

Conclusion

We presented a case of a 6-week-old with intracranial bleeding secondary to VKDB. Critical factors in the VKDB diagnosis were an intracranial bleed in a child less than 6 months, abnormal/increased coagulation times, and parental refusal of VK at birth. Primary care physicians should consider VKDB with any bleeding event in a child ≤6 months, particularly if there is a history of parental VK refusal at birth. If VKDB is suspected, immediately start IV VK even before coagulation values are obtained. Though not infectious, this condition is on a growing list of highly preventable conditions that are making a resurgence with an increase in parental refusal of vaccinations. As always, educating your patients about the serious risk of VKDB is crucial. The CDC provides an informational sheet on VKDB which can be found at www.cdc.gov/ncbddd/vitamink/facts.html. Regardless of the cause of refusal, this case is a reminder of the serious consequences of children not receiving prophylactic VK at birth.

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About the Authors:

David H. Arendt, MD, PhD, University of South Dakota, Sanford School of Medicine, Sioux Falls, South Dakota.

Dane A. Hegdahl, MS IV, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota.

Benson S. Hsu, MD, MBA, FAAP, FCCM, Associate Professor, Department of Pediatrics, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota; The Miller Pediatric Critical Care Unit, Sanford Children's Hospital, Sioux Falls, South Dakota.

KayeLyn J. Wagner, MD, MME, Sanford Children's Hospital Sioux Falls, South Dakota; Assistant Professor, Department of Pediatrics, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota; Associate Program Director, Pediatrics Residency Program, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota.

Recurrent Epistaxis Throughout the Lifespan: A Clinical Review

Daniel C. Schmidtman, MS IV; Nathan A. Blaseg, MS IV; and Micah M. Likness, MD

Abstract

Epistaxis is a common otolaryngologic complaint experienced by 60 percent of the U.S. population and can be the result of either local or systemic disturbance. Most nosebleeds arise from an anastomotic region along the anterior nasal septum known as Kiesselbach's plexus. However, roughly ten percent of nosebleeds originate posteriorly from the sphenopalatine branch of the maxillary artery. Posterior nosebleeds can be more difficult to control and are frequently associated with systemic derangement. Patients presenting with a nosebleed should first be assessed for airway patency and hemodynamic stability. Once the patient is confirmed to be acutely stable, pre-existing clots should be cleared from the nasal cavity and the nasal alae should be compressed against the septum for ten to fifteen minutes. Application of a topical vasoconstricting agent can also be considered at this time. If the nosebleed persists and the location of the bleed can be visualized, chemical or electrical cautery can be used. If the site of the bleed cannot be identified, nasal packing materials in the form of lubricant-impregnated ribbon gauze or ready-made nasal packing devices can be placed to tamponade the bleed. Following failure of these conservative treatment modalities, otolaryngologist consultation should be sought. Next steps in management may include arterial ligation or embolization.

Introduction

Epistaxis, or nosebleed, is a common otolaryngologic complaint experienced by 60 percent of the U.S. population.[1] Prevalence throughout the lifespan shows a bimodal distribution: incidence is highest in children 10 years of age and younger and patients 70-79 years old.[2] Of those who experience epistaxis, recurrent episodes may occur in as many as 9 percent of children and 19 per cent of adults.[3-5] While a reasonable definition of "recurrent epistaxis" is epistaxis that occurs two or more times, no consensus exists to define the exact frequency or severity of recurrent epistaxis.[4] Although most cases can be managed without healthcare provider intervention, one in ten patients with a nosebleed requires medical or surgical management to control the bleeding.[1] Of those that require medical intervention, up to one-third of epistaxis incidents require otolaryngologist consultation and control measures.[6] Due to the common nature of recurrent epistaxis and the readily evolving understanding of etiologies, comorbidities, and effective management strategies, a review of this topic is warranted. The aim of this review is to provide a comprehensive evaluation of current literature surrounding the etiology, diagnosis, and management of recurrent epistaxis in adults and children.

Common Etiologies

Although most nosebleeds arise without identifiable cause, they can be the result of localized or systemic etiology (Table 1). Local insults include trauma (often digital in nature), dry mucosa (secondary to topical decongestants or corticosteroids, illicit drug use, or seasonal humidity fluctuations), septal perforations, rhinosinusitis, or malignancy.[7] Juvenile nasopharyngeal angiofibroma is a benign, locally invasive vascular tumor that arises in the lateral nasopharynx, most often in adolescent males, and can cause life-threatening epistaxis.[8] This rare tumor occurs in roughly 3.7 per 1 million adolescent males.[9]

Nosebleeds can also be the consequence of a systemic derangement, such as coagulopathy or anticoagulation therapy. Forty-five percent of patients hospitalized for a nosebleed have a contributory systemic condition of hepatic, renal, hematologic, genetic, or cardiovascular etiology.[10] One such condition is hereditary hemorrhagic telangiectasia (also known as Osler Weber Rendu), which is an autosomal dominant condition characterized by widespread mucocutaneous telangiectasias. A presenting feature is often recurrent epistaxis. The prevalence is between 1.5-2.0 per 10,000 individuals.[11] The presence of recurrent epistaxis

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Table 1. Common etiologies of recurrent epistaxis in adults and children.

Adults	Children
Rhinosinusitis	Environmental factors (cold, dry air)
Anticoagulation therapy	Local trauma
Inflammation	Foreign body
Vessel fibrosis (secondary to aging)	Inherited bleeding disorder
Irritants (illicit drugs or chemicals)	Hereditary hemorrhagic telangiectasia
Systemic disease (hepatic, renal, or cardiovascular)	Juvenile nasopharyngeal angiofibroma

along with other symptoms such as petechiae, purpura, recurrent ecchymoses, or blood in bodily fluids warrants further investigation for a potential bleeding diathesis. If no current medications or medical conditions can explain the increased bleeding, an extensive family history should be obtained for potential inherited disorders. The NEDS study, which included 1.2 million emergency department visits from 2009 to 2011, concluded that 15 percent of patients presenting to the emergency department with epistaxis are on long-term anticoagulation and 0.9 percent have an underlying coagulation disorder.[12] Although many patients with epistaxis have a history of hypertension, the causality of this relationship remains unclear.[13,14]

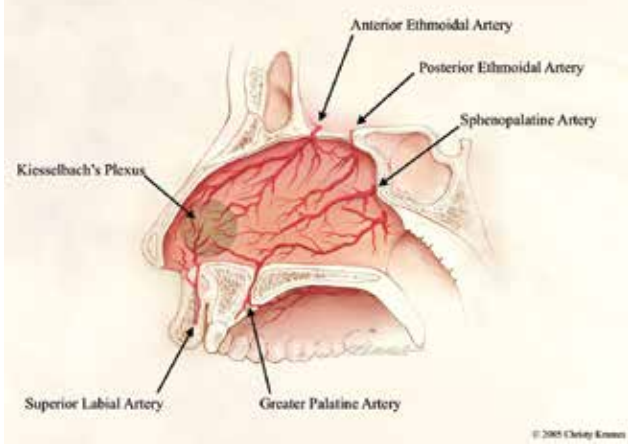
Relevant Anatomy

The vasculature of the nasal mucosa can be divided into an anterior and posterior supply (Figure 1). Anterior nosebleeds, which occur at a site known as Kiesselbach's plexus, account for approximately 90 percent of cases.[7] Kiesselbach's plexus comprises the anastomosis of five arteries in the anterior nasal septum. The arteries of this anastomosis are derived from the external carotid artery via the superior labial branch of the facial artery and the sphenopalatine branch of the internal maxillary artery, as well as the internal carotid artery through the anterior and posterior ethmoidal branches. Posterior nosebleeds constitute the remaining 10 percent of cases. These nosebleeds originate from the sphenopalatine artery.[7]

Clinical Work-Up and Triage

Initial work-up of a patient with epistaxis necessitates triaging the acuity of the bleed. While many nosebleeds can be managed in an ambulatory setting, severe nosebleeds can pose the risk of cardiovascular and/or airway compromise. Unfortunately, no unanimously accepted definition for severity of epistaxis exists. The World Health Organization, in an effort to categorize severity of epistaxis in cancer patients, proposed a three-level system for categorizing nosebleed severity. Those lasting less than 30 minutes in a single 24-hour period were designated Stage 1. Those lasting greater than 30 minutes in one 24-hour period were categorized as Stage 2. And, any nosebleeds requiring transfusion were designated as Stage 3.[15]

Figure 1. Vascular anatomy of nasal septal blood supply.



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Patient evaluation should include visualization via nasal speculum and continuous monitoring of vitals to ensure hemodynamic stability. In patients with recurrent severe epistaxis, further imaging via computed tomography (CT) may be warranted to assess for more insidious etiologies such as intracavernous carotid artery aneurysms or neoplastic causes.[16,17] However, no uniform guidelines exist for the utilization of imaging in the assessment of epistaxis, and CT imaging may only add marginal benefit, if any.[6,17] Therefore, the decision of whether or not to pursue further imaging must be made on a case-by-case basis. After assessing the nasal cavity for potential causes of the epistaxis, a management option may be pursued.

Management Options and Potential Complications

Compression and Clot Clearance

Initial management of nosebleeds includes clot clearance and nasal compression, which serve as simple and cost-conscious primary interventions. Pre-existing clots should be cleared by blowing the nose or aspirating the contents. The rationale for this intervention is that pre-existing blood clots can promote fibrinolysis and result in delayed hemostasis. Proper compression technique is accomplished by using the first and second digits to press the nasal ala against the nasal septum.[18] The patient should compress their nose while leaning forward, which will reduce symptoms of nausea and obstruction of the airway.

The application of a vasoconstricting agent (such as epinephrine, phenylephrine, oxymetazoline, and cocaine) or tranexamic acid (an antifibrinolytic agent) with a spray or

applicator can be considered as an adjunct to compression therapy. However, clinicians must also consider the impacts of systemic absorption in patients with hypertension, cardiovascular disease, or cerebrovascular disease. Nosebleeds that persist following 10-15 minutes of compression can be managed with cautery.

Cautery

Although highly effective, cautery is to be attempted only once the bleeding site can be visualized. Blind cauterization can result in excessive damage and ulceration of the nasal mucosa. Too much damage to the vascular supply can result in necrosis and perforation of the nasal septum. It is imperative to have good visualization with a headlight and suction with frazier tip ready.

Cautery comes in two forms: chemical cautery and electrocautery. Silver nitrate is the most commonly used form of chemical cautery and is often the next step in management of patients in whom compression and vasoconstrictor application have not resolved a nosebleed. One technique of silver nitrate application is to apply circumferentially, beginning just outside the focus of the bleed and working inward. The silver nitrate should be applied for 30 seconds before the applicator stick is removed. When silver nitrate comes in contact with the moisture of the nasal mucosa, it becomes activated and begins to work as a cautery agent. However, if the bleeding is too brisk, the silver nitrate can be washed away from the site of the bleed before it can achieve effective hemostatic control.[19] In the case of brisk bleeding, applying directly to the focus of the bleed and tracking the vessel proximally and distally may be the preferred technique. Thermal or electrical cautery can be used in the event that silver nitrate does not provide adequate control. Both forms of cautery have been found to be superior to controlling nosebleeds than nasal packing and electrical cautery has been found to be more effective than chemical cautery.[20]

Nasal Packing

When active bleeding persists despite nasal compression and a specific bleeding site is unable to be identified via rhinoscopy, clinicians should utilize nasal packing. Nasal packing alone may be sufficient to slow or stop active bleeding and, if not, may enable further evaluation and definitive management.

Many options for nasal packing materials exist, including the historically used lubricant-impregnated ribbon gauze as well as a wide array of ready-made nasal packing devices. Although ready-made devices may provide greater patient comfort and easier use for practitioners, studies do not suggest any difference in efficacy compared to lubricant-impregnated ribbon gauze, and current guidelines do not support one material over another for most cases.[19,21,22] Materials may include resorbable products such as oxidized regenerated cellulose (Surgicel), hemostatic gelatin thrombin matrices (Floseal, Surgiflo), and others such as Fibrillar, Nasopore, Hemopore, and Posisep. Nonresorbable products include ribbon gauze, polyvinyl acetate sponges (Merocel), or tamponade devices (Rapid Rhino), among others. Some products, such as Rapid Rhino, have different available lengths to customize the packing based upon the likely origin of the bleed. Resorbable packing is preferred in cases where packing removal may lead to mucosal trauma and further bleeding, including patients on coagulation or those with bleeding disorders. Additionally, resorbable packing should be considered in young children for whom nasal packing removal may be difficult.[22]

Anterior nasal packing does not usually require specialist consultation and may safely be performed in a variety of clinical settings, including the emergency department or outpatient clinics. Prior to packing, the nose should be inspected using a nasal specula and any present clot should be evacuated via suction. Packing materials may be lubricated prior to insertion to minimize mucosal trauma. Following anterior packing, most patients may be safely managed in the outpatient setting without otolaryngologist consultation.[22]

Posterior nasal packing should involve otolaryngology specialist consultation, as these patients often require more intensive monitoring and management. Compared to anterior epistaxis, posterior epistaxis is twice as likely to require nasal packing for control of active bleeding.[23] Due to the anatomic limitations of accessing the posterior nasopharynx in the acute setting, chemical cautery is often not possible as a specific bleeding source is rarely identified and flow rate of epistaxis is often higher.[24] Posterior nasal packing is often done using inflatable balloon catheters or polyvinyl acetate sponges. One example is the Epistat, a Y-shaped air filled catheter, which has a posterior "Lollipop" balloon to occlude the choana and then a longitudinal balloon along its length to compress the remaining nasal cavity. When performed by trained physicians, posterior epistaxis may be effectively controlled by these types of packing in up to 70 percent of cases.[25] Due to an increased association with major complications including stroke, myocardial infarction, arrhythmias, and death following posterior nasal packing, patients are often managed in an inpatient setting with telemetry monitoring.[26] While the etiology of these complications is likely multifactorial, some attribute their increased occurrence following posterior nasal packing to a "nasopulmonary reflex." However, the existence

and clinical relevance of such a reflex have been called into question.[27,28]

The management of patients following nasal packing varies widely, and current guidelines do not dictate any one specific care pathway.[22] Systemic antibiotic therapy following nasal packing is a common practice, theoretically meant to prevent sinusitis or staphylococcal-induced toxic shock syndrome. However, evidence is lacking to support this practice. Multiple meta-analyses and cohort studies on the topic have revealed no significant benefit to the use of antibiotics with nasal packing.[29–32] It should be noted, however, that these studies were underpowered to detect rare complications such as toxic shock syndrome. Therefore, the decision of whether or not to prescribe antibiotics following nasal packing should be made on an individual basis, weighing the pertinent risks and benefits for each patient.

Nonresorbable packing may be left in place for 24-96 hours, depending on the severity of bleeding. Usually, anterior packing is removed after 24 hours, depending upon specific patient characteristics. Unless removed in the operating room, posterior packing is typically left in place for 48-72 hours. Prior to removal a trial of deflating the catheter is often performed to ensure bleeding has resolved. If bleeding recurs, the pack is then reinflated. The British Rhinological Society consensus recommends that all nonresorbable packing be removed within 24 hours of insertion if there is no evidence of active bleeding, regardless of anticoagulation status.[33] One retrospective case series involving 147 patients with epistaxis treated with packing for a duration of three, four or five days found no significant difference in bleeding recurrence among the respective groups and an 85 percent successful treatment rate among patients who received packing for a duration of one to three days.[34] A prospective cohort study of 969 patients with epistaxis managed with nonresorbable packs found the most significant indicators of treatment failure were a packing duration less than 21 hours, comorbid ischemic heart disease, and no attempt at cautery following pack removal.[35]

Complications of nasal packing may include septal hematomas and abscesses, sinusitis, neurogenic syncope during packing, or airway obstruction. In instances of bilateral nasal packing, septal perforations may occur. Rarely, sepsis or toxic shock syndrome may develop, although there is a surprising scarcity of such reports given the frequent nasal carriage of *Staphylococcus aureas*.[36,37]

Arterial Ligation and Embolization

Following failure of more conservative treatment modalities, otolaryngologist consultation should be sought. While measures such as compression or nasal packing are usually effective in controlling epistaxis, approximately 8 percent of cases may require arterial ligation or embolization.[38] Several techniques for surgical arterial ligation in the treatment of epistaxis have existed throughout the years, with the most common current method being transnasal endoscopic sphenopalatine artery ligation (TESPAL). TESPAL has demonstrated success rates of up to 98 percent while maintaining relatively low rates of complication, with the rate of postoperative hemorrhage being 3.4 percent.[39,40] Given the high success rate, TESPAL may be an effective alternative to posterior nasal packing, as it has also demonstrated greater patient comfort and significant cost savings when employed as a first-line therapy.[41]

Endovascular embolization, utilizing embolic particles to control bleeding in the sphenopalatine or distal internal maxillary arteries, has demonstrated an average success rate of 87 percent.[40] The rate of serious complications, such as tissue necrosis, permanent facial nerve paralysis, monocular blindness, or stroke, may be as high as 2.1-3.8 percent.[40] Despite the risk of these serious complications in embolization, no difference in mortality has been demonstrated when compared to arterial ligation.[40] While TESPAL has been shown to be more cost effective than embolization in the treatment of intractable epistaxis, treatment choice should be determined by local resource availability and a shared decision making process after educating the patient on the risk-benefit profiles of each treatment modality.[42]

Conclusion

Epistaxis is a common complaint in the outpatient clinic and emergency department settings. Potential causes may range from minor trauma to major local and systemic pathologies. Effective treatment options abound, and these may include interventions as basic as continuous compression or as complex as endoscopic surgery or endovascular embolization. Understanding the current paradigms of epistaxis evaluation and treatment allows for successful management of this prevalent condition.

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About the Authors:

Daniel C. Schmidtman, MS IV, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota.

Nathan A. Blaseg, MS IV, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota.

Micah M. Likness, MD, Clinical Assistant Professor University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota.

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Tetralogy of Fallot Presenting as Severe Hypernatremic Dehydration: A Review of the Importance of Perinatal Care

Kaitlyn M. Dorn, MD; and Lauritz R. Meyer, MD

Abstract

We present a case of a female American Indian neonate born via a provider unattended home delivery. Her mother received limited prenatal care and the infant was not examined by a healthcare provider until day of life 10 when she presented to the emergency department for evaluation of a skin rash. She was found to have severe hypernatremic dehydration. She was subsequently diagnosed with tetralogy of Fallot, and this was the likely cause of her breastfeeding failure dehydration. The infant underwent careful correction of her electrolyte abnormalities and surgical repair of her cardiac defect on day of life 27. This case highlights the importance of comprehensive care during the prenatal and postpartum/newborn periods, especially in rural locations where access to care can be difficult.

Introduction

Tetralogy of Fallot (TOF) is the most common cyanotic congenital heart disease.[1] Advances in diagnostic testing have allowed many cases to be diagnosed during fetal life. Even when cases evade prenatal diagnosis, routine neonatal evaluation, including prompt examination by a medical provider, critical congenital heart defect (CCHD) screening, and subsequent echocardiogram, will reveal the diagnosis, allowing for proper management and treatment. The importance of perinatal care is often undermined, especially in rural settings where consistent access to care can be limited. We present a neonate born to an American Indian mother with limited prenatal care. She presented to the emergency department on day of life (DOL) 10 in critical condition with severe hypernatremic dehydration requiring significant medical intervention and was subsequently diagnosed with TOF requiring early repair. This case highlights the importance of comprehensive medical care during and after pregnancy.

Case Report

Our patient was born to a 19-year-old nulliparous American Indian mother who received intermittent prenatal care. She had planned for a midwife-attended home delivery; however, due to an unexpected winter storm, the delivery was unattended. She delivered a viable female at 38 weeks gestation assisted by family. The infant's reported birth weight was 3.6 kg.

On DOL 10, the mother brought the infant to the local emergency department due to an abnormal appearing leg, poor feeding, and only two wet diapers per day for the past two days. This was the infant's first examination by a medical provider. Her weight was down 1 kg from her reported birth weight. She was lethargic. Her skin appeared jaundiced and was dry with tenting. There was sloughing of skin in intertriginous areas of the groin and buttocks with yellow crusting. She had a grade III/VI harsh systolic murmur best heard at the left upper sternal border. Her resting heart rate was low, at 80 beats per minute, and she was started on supplemental oxygen of 2 L/min via nasal cannula due to oxygen saturations in the 80s.

Laboratory evaluation revealed severe hypernatremic dehydration with azotemia as well as hyperbilirubinemia. Her sodium was 190 meq/L (135-145 meq/L), chloride was 145 meq/L (99-109 meq/L), BUN was greater than 120 mg/dL (5-20 mg/dL), and creatinine was 1.4 mg/dL (0.2-0.6 mg/dL). Her bilirubin was 18.9 mg/dL on DOL 10, which is beyond the age range for the AAP bilirubin normogram used in the first week of life.[2] However, extrapolating the values for a baby at 146 hours of life or greater would place this level in the high-risk category (low risk less than 13 mg/dL, low intermediate risk 13-15.5 mg/dL, high intermediate risk 15.5-17.5 mg/dL, and high risk greater than 18.5 mg/dL at approximately 120 hours postnatal age). She was transported urgently to the neonatal intensive care unit (NICU) for management.

Upon admission to the NICU, chest X-ray showed a boot-shaped heart (Figure 1). An echocardiogram confirmed TOF with moderate sub-pulmonic and pulmonary valve stenosis, moderate to large ventricular septal defect, and hypoplastic

pulmonary arteries. Her head CT showed poor grey-white differentiation, concerning for mild cerebral edema felt secondary to her fluid and electrolyte abnormalities. An abdominal ultrasound demonstrated gallbladder sludge but was otherwise unremarkable. Nasal cannula was continued on admission to the NICU, but was weaned off on DOL 12. Genetic testing was negative for DiGeorge syndrome.

The infant underwent careful correction of her free water and solute fluid deficit over many days with the assistance of pediatric nephrology. Hypertonic fluids (3 percent saline, D5NS) were initially used to correct her free water deficit while maintaining a hypernatremic state. Once rehydrated, the hypertonic solutions were slowly weaned in efforts to reduce her serum sodium by no more than 10 meq/L per 24 hours (Figure 2). Her sodium was successfully normalized without the infant developing signs or symptoms of worsening cerebral edema or seizure activity. She received phototherapy for her hyperbilirubinemia.

She was started on propranolol once her hypernatremia had been corrected to treat her sub-pulmonic stenosis. On DOL 18 she began having hypercyanotic spells. These hypercyanotic spells continued to increase in frequency and severity, with saturations dropping as low as 50 percent and improved with volume, knee to chest maneuvers, and comforting. Additionally, on DOL 22 she required supplemental oxygen of at least 2 L via nasal cannula to maintain adequate saturations. Ultimately, she required referral to a pediatric cardiothoracic surgery center and underwent surgical correction of her TOF on DOL 27. She did well post-operatively and was seen multiple times in the first year of life by pediatric cardiology. Unfortunately, she has since been lost to follow up.

Discussion

This case highlights the importance of perinatal care, and how quickly a baby can develop life threatening complications if a problem is not identified early. Assessment of maternal and fetal wellbeing, including ultrasound, would likely have identified this patient's cardiac defect prenatally. Educational opportunities at prenatal visits could have highlighted the importance of newborn evaluation at birth and in the first days of life. This mother planned a midwife-assisted home delivery; however, it was apparent no plan of care for after birth was discussed. If the infant's TOF was not revealed during obstetric visits, physical examination and routine cardiovascular screening after birth would have revealed the diagnosis. This could have prevented much of the morbidity the infant experienced.

Figure 1. Chest X-ray revealing an elongated cardiac apex, or boot-shaped heart.

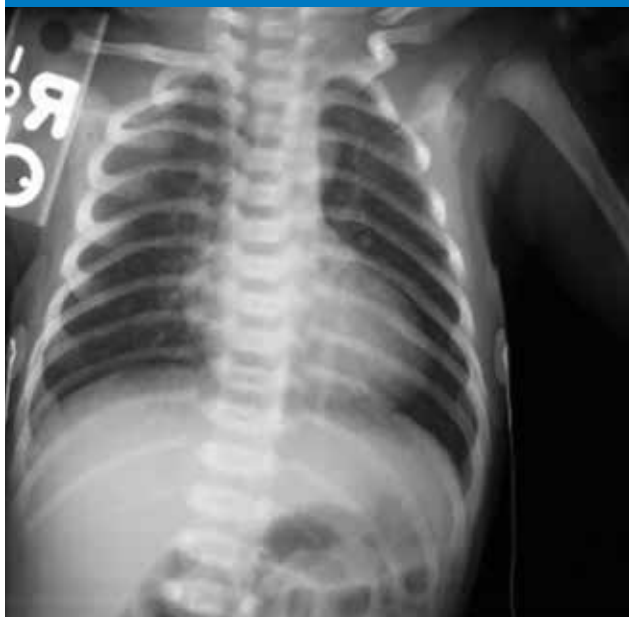
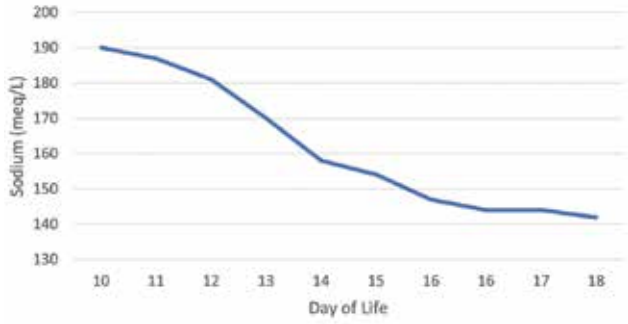


Figure 2. Sodium correction. Graph demonstrating careful correction of hypernatremia during hospitalization.



Current prenatal care guidelines for an uncomplicated pregnancy recommend examination every four weeks for the first 28 weeks gestation, every two weeks from 28 to 36 weeks gestation, and then weekly until delivery.[3] Pregnancies complicated by medical or obstetric risks require closer surveillance, often with the perinatology team. These visits allow for assessment of maternal and fetal wellbeing, provision of relevant prenatal education, completion of recommended prenatal health screening (i.e. routine laboratory testing, ultrasonography, antepartum immunizations, genetic screening), and detection of medical and psychosocial issues to allow for proper intervention. A detailed ultrasound at approximately 20 weeks gestation may have revealed the cardiac defect in our patient, prompting fetal echocardiogram.[1] Knowing the presence of a congenital anomaly prior to delivery allows for proper evaluation and

management by specialists. Perinatal care planning can include discussions of fetal surgery to improve the long-term outcome of infants with specific, repairable defects, including spina bifida, congenital cystic adenomatoid malformation, congenital diaphragmatic hernia, and twin-twin transfusion syndrome. Delivery planning can include scheduling a delivery date at the gestational age best suited for the condition, prenatal consultation with the appropriate specialists and maternal and neonatal care team, and planning for delivery at a facility prepared to care for the neonate after delivery.

Even with recommended prenatal care, some conditions may go undiagnosed until after delivery, pointing towards the importance of regular care of the newborn. A detailed clinical examination of the infant should be performed soon after birth, ideally within the first 24 hours of life. During hospitalization, the infant is monitored for signs of illness, including temperature instability, unusual skin coloration, abnormalities in cardiac or respiratory rate or rhythm, lethargy, hyper or hypotonicity, delayed stooling (more than 24 hours), or excessive weight change.[3] Newborn screening programs involve pre-symptomatic testing to establish necessary care for various medical conditions that may have little to no clinical findings at birth. Screening modalities include newborn blood spot, hearing screening, evaluation of glucose homeostasis, monitoring for jaundice/hyperbilirubinemia, screening for developmental dysplasia of the hip, and CCHD screening (i.e. TOF). Of these, newborn blood spot, hearing screening, and CCHD screening are mandated by law. Newborn screening dates back to the 1960s when Robert Guthrie developed large-scale testing procedures for phenylketonuria that were quickly adopted by many countries.[3] Blood spot screening was required in South Dakota in 1973 (Table 1), universal newborn hearing screening was enacted in the U.S. in 1999, and CCHD screening was mandated in South Dakota in 2013.[5-7] Anticipatory guidance on topics including car-seat safety, safe sleep position, sudden infant death syndrome, lactation support, and postpartum depression screening are paramount for proper neonatal and maternal care.

After initial evaluation, screening, and safety instruction, a follow-up care plan should be established. Follow-up care performed by a trained provider allows for proper assessment of the physical and psychosocial status of both mother and

Table 1. Newborn blood spot screen. Table of conditions tested for in the South Dakota newborn screen.

Amino Acidemias and Urea Cycle Disorders	Organic Acidemias
(ASA) Argininosuccinic aciduria	(GA-1) Glutaric acidemia type I
(CIT) Citrullinemia, type 1 or ASA Synthetase Deficiency	(HMG) 3-Hydroxy 3-methylglutaric aciduria
(HCY) Homocytinuria (cystathionine beta synthetase)	(IVA) Isovaleric acidemia
(MSUD) Maple Syrup Urine Disease	(3-MCC) 3-Methylcrotonyl-CoA carboxylase
(PKU) Classic Phenylketomuria	(Cbl-A,B) Methylmalonic acidemia (cobalamin and vitamin B12 disorders)
(TYR-1) Tyrosinemia, type I	(ßKT) Beta-Ketothiolase
(ARG) Argininemia	(MUT) Methylmalonic Acidemia (methylmalonyl-CoA mutase)
(BIOPT-BS) Defects in biopterin cofactor biosynthesis	(PROP) Propionic acidemia
(CIT-II) Citrullinemia, Type II	(MCD) Holocarboxylase synthetase
(BIOPT-REG) Defects of biopterin cofactor regeneration	(2M3HBA) 2-Methyl-3-hydroxybutyric aciduria
(H-PHE) Benign hyperphenylalaninemia	(2MBG) 2-Methylbutyrylglycinuria
(MET) Hypermothioninemia	(3MGA) 3-Methylglutaconic aciduria
(TYR II) Tyrosinemia, type II	(Cbl-C, D) Methylmalonic acidemia with homocystinuria
(TYR III) Tyrosinemia, type III	(MAL) Malonic acidemia
Fatty Acid Oxidation Disorders	**Endocrine**
(CUD) Carnitine uptake defect (Carnitine transport defect)	(CAH) Congenital adrenal hyperplasia
(LCHAD) Long-chain L-3 hydroxyacyl-CoA dehydrogenase	(CH) Primary Congenital hypothyroidism
(MCAD) Medium chain acyl-CoA dehydrogenase	**Hemoglobinopathies**
(TFP) Trifunctional protein deficiency	(Hb SS) S, S Disease (Sickle Cell Anemia)
(VLCAD) Very long-chain acyl-CoA dehydrogenase	(Hb S/C) S, C Disease
(CACT) Carnitine acylcarnitine translocase	HB S/ßTH) S, ßeta-thalassemia
(CPT-Ia) Carnitine palmoitoyltransferase type I	(Var Hb) Variant hemoglobinopathies
(CPT-II) Carnitine palmitoyltransferase type II	**Other Disorders**
(GA2) Glutaric acidemia type II	(BIOT) Biotinidase deficiency
(MCKAT) Medium-chain ketoacyl-CoA thiolase	(CF) Cystic Fibrosis
(M/SCHAD) Medium/Short chain L-3-hydroxyacyl-CoA dehydrogenase	(SCID) Severe Combined Immunodeficiency
	(GALT) Classic Galactosemia

infant (i.e. postpartum depression, infant weight, feeding and diapering patterns, mother-infant attachment, neonatal behaviors).[3] These visits also allow for further educational opportunities (i.e. immunizations, medical emergencies, safe sleeping habits).

Also readily apparent in this case are the health disparities faced by individuals living in rural locations, especially American Indian/Alaskan Native (AIAN) women. The 2010 Census identified 38 percent of the AIAN population as residing in rural settings; however, the First Nations Development Institute identified 54 percent as living in rural areas.[8,9] Our patient and her mother lived on a reservation in the rural Northern Plains, subjecting them to the healthcare disparities and barriers faced by the AIAN population. American Indians experience disproportionately high rates of infant mortality and adverse perinatal outcomes; some of the worst health disparities in the American Indian population are seen in the Northern Plains.[10]

While Indian Health Services and other tribal health programs have shown improvements in perinatal and infant health, there remain persistent health gaps between white and AIAN populations, many of which are related to barriers to healthcare.[11,12] Numerous barriers to care of the AIAN population have been identified, including communication difficulties, lack of trust in physicians and the healthcare system, transportation issues, and interpersonal problems (i.e. poverty, current or past sexual or physical abuse, substance use).[13] Understanding these barriers to care can aid in development of resources to increase prenatal care in our AIAN population, especially those in rural locations. Increasing prenatal care can improve both maternal and neonatal morbidity and mortality via increased utilization of necessary resources and interventions.

Current perinatal care guidelines have greatly enhanced our abilities to diagnose congenital anomalies before or shortly after birth, greatly improving the management and outcome for affected infants. However, as above, many barriers to perinatal care exist, especially within rural and AIAN populations. Efforts should be aimed to improve access to resources and provide education on the importance of close maternal and neonatal care in at-risk rural and AIAN populations. By advancing the level of care provided to all populations, the health of the community will continue to improve, helping to decrease morbidity experienced by patients such as ours.

Written informed consent was not obtained, as the patient was lost to follow-up. An IRB waiver was obtained.

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About the Authors:

Kaitlyn M. Dorn, MD, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota.

Lauritz R. Meyer, MD, Department of Pediatrics, University of South Dakota Sanford School of Medicine, Sioux Falls, Southy Dakota; Sanford Children's Specialty Clinic, Sanford USD Medical Center, Sioux Falls, South Dakota.

Clinical Evidence of Medical Marijuana: Reviewing the Highs and Lows

Jeremy Daniel, PharmD, BCPS, BCPP

In 2020, South Dakota voters passed Initiated Measure 26, which created a medical marijuana program within the state. Since that time, the South Dakota Department of Health (SDDOH) and lawmakers have been working to fine-tune the program and pass laws to close loopholes within the broad voter initiative. SDCL 34-20G contains the laws that regulate medical marijuana. Within South Dakota, providers (including midlevel practitioners with the passage of Senate Bill 26) are able to certify patients for the medical marijuana program if they have a debilitating medical condition. Per the codified law, certain conditions and symptoms are listed for certification, though the law also states the SDDOH can adjust this list. These conditions/symptoms include cachexia or wasting syndrome; severe, debilitating pain; severe nausea; seizures; or severe and persistent muscle spasms, including those characteristic of multiple sclerosis. In addition to these conditions/symptoms, marijuana is commonly used in other states for conditions such as glaucoma, post-traumatic stress disorder (PTSD), appetite stimulation, and Crohn's disease. Table 1 shows a list of these conditions/symptoms and the overall level of evidence of benefit for treatment. However, before reviewing the literature, some additional background may be helpful.

Marijuana Background

Marijuana is made up of 113 cannabinoids and over 300 other chemicals. Within the cannabinoids, tetrahydrocannabinol (THC) and cannabidiol (CBD) are the most common in marijuana plants and synthetic strains. THC is responsible for the psychoactive effect while CBD is generally responsible for the medical benefit (and can down-regulate the effects of THC). The primary targets for cannabinoids are CB1 and CB2 receptors found throughout the body. Marijuana can be smoked, vaped, eaten, or applied topically.

Predicting pharmacokinetic and pharmacodynamic changes can be challenging. Smoked and vaped marijuana have predictable onset and duration, though oral products have unpredictable bioavailability and onset. Oral bioavailability can range between 20-40 percent and onset can range between 30-120 minutes, even within the same batch consumed by the same person on different days. This can lead to unintentional overdoses when the user feels suboptimal effects. THC and CBD have metabolism inhibition properties and can increase levels of medications metabolized by CYP 1A2, 1B1, 2B6, 2C9, 2C19, 2D6, 2J2, and 3A4/5/7. This includes medications such as clozapine (1A2), methadone (2B6, 2C19), warfarin (2C9), most beta blockers (2D6), and numerous antiepileptic agents and DOACs (3A4). Degree of inhibition depends on the potency of the product and amount used. Smoking (i.e. burned hydrocarbon) can induce CYP 1A2, and this induction normally overrides the inhibition by the cannabinoids discussed above. However, with high-potency marijuana (i.e. dabbing) use, inhibition overrides induction. Caution should be used when combining marijuana with products that have a narrow therapeutic index or in complex/hard to control patients.

The sections below provide a brief overview of the evidence of marijuana use in treating the conditions/symptoms listed in Table 1.

Table 1. Evidence of benefit for conditions/symptoms treated with medical marijuana.

Condition/symptom	Evidence of Benefit
Nausea/vomiting	Low
Appetite stimulation	Low/moderate
Glaucoma	Low
Epilepsy	Whole plant – low/moderate CBD – high
Pain management	High
PTSD	Short term, as needed use – moderate/high Daily/chronic use – low (may cause harm)
Crohn's disease	Moderate
Multiple sclerosis	Pain, spasticity, and spasms – high Other symptoms - low

Nausea/Vomiting

Studies reviewing the antiemetic efficacy of marijuana are complicated by variations in patient population, dose administered, route of administration, and THC/CBD content of the chosen product. Additionally, most studies with marijuana for nausea are open-label and enroll small sample sizes. There are no well-powered studies that compare marijuana to traditional antiemetics (e.g. 5HT3 antagonists, olanzapine). When looking closer at chemotherapy-induced nausea/vomiting (CINV), the 2017 American Society of Clinical Oncology antiemetic guidelines state evidence remains "insufficient" to recommend marijuana for prevention or treatment of CINV. It is important to mention that there are two FDA-approved products for CINV – dronabinol and nabilone. These agents should be trialed prior the use of marijuana. In several small studies investigating marijuana benefit after dronabinol failure, marijuana did not produce significant results. Overall evidence of benefit for marijuana remains low for nausea/vomiting.

Appetite Stimulation

Similar to nausea/vomiting above, study design of marijuana appetite stimulation studies are highly heterogeneous. Anecdotally, marijuana gives users "the munchies" and older studies of marijuana for increasing appetite show promise. However, as studies become well-controlled, that benefit wanes. An active control study with megestrol demonstrated inferior performance of marijuana. Though people may temporarily increase food intake, there appears to be no effect on weight and long-term outcomes. This includes both inhaled and oral cannabis. Dronabinol is also FDA-approved to treat loss of appetite in AIDS patients. Overall evidence of benefit for marijuana remains low/moderate for appetite stimulation.

Glaucoma

The treatment of glaucoma with marijuana is the most commonly approved indication in medical marijuana states across the U.S. Physiologically, agonism of CB1 receptors in the eye can open the Canal of Schlemm and decrease intraocular pressure (IOP). However, a commonly cited 1980 study demonstrated a drop in IOP from 28 to 22 mmHg. It is important to note this is still above the goal IOP in glaucoma. Also, duration of action is only 3.5 hours, necessitating 6-8 doses per day. Newer studies confirm these results. Overall evidence of benefit for marijuana remains low for glaucoma.

Epilepsy

Multiple studies demonstrate a decrease in seizure frequency with CBD administration. This is true in both children and adults. When considering quality of life as a clinically significant outcome, CBD does yield benefit even without total seizure control. Whole-plant marijuana studies do not demonstrate the same clinical benefit, though high-CBD containing strains appear to be slightly more efficacious than high-THC strains. An FDA-approved product (cannabidiol) is approved for adjunct treatment of seizures associated with Lennox-Gastaut syndrome (LGS), Dravet syndrome, and tuberous sclerosis complex (TSC). Overall evidence of benefit for CBD appears to be high for CBD, though whole-plant marijuana remains low for seizure control.

Pain Management

Agonism of CB1 receptors in the CNS and CB1/CB2 receptors in peripheral tissues creates analgesia. Multiple studies show efficacy with whole plant marijuana, THC, and CBD administration. A dose-finding study equated approximately 10 mg of THC with 60 mg of codeine, though variability exists in other studies. Efficacy has been shown with both musculoskeletal pain and neuropathic pain, including HIV-induced neuropathy. Marijuana administration has also led to a decrease in use of other non-opioid pain medications such as NSAIDs. Overall evidence of benefit for marijuana appears to be high for pain management.

PTSD

Agonism of CB1 receptors in the CNS produces downregulation of the hypothalamic-pituitary-adrenal (HPA) axis, thus producing a decrease in release of catecholamines and cortisol. With infrequent, short term use, this can produce anxiolysis. Multiple studies that are shorter than three months in duration correlate as-needed marijuana use to decreases in anxiety scores in PTSD patients. However, this effect is not durable with continued use. Since cortisol provides negative feedback for the HPA axis, chronic inhibition of cortisol release can strengthen the HPA axis and increase anxiety leading to possible treatment-resistance with commonly used anxiolytic medications (including antidepressants). Long term studies in PTSD show worsening of PTSD symptoms and an increase in violent behavior with chronic marijuana use. Overall evidence of benefit for marijuana appears to be moderate/high for short-term infrequent use, though long-term marijuana use evidence remains low and may cause harm in PTSD.

Crohn's Disease

Many studies demonstrate benefit for pain and nausea relief in Crohn's disease with similar evidence to the above sections. A white paper from the Crohn's and Colitis Foundation (CCF) highlights improvement in symptoms and quality of life per patient report, though also notes no disease-modifying benefit confirmed on endoscopy. CCF's position statement supports policy changes that advances research, but calls the evidence "conflicting." Overall evidence of benefit for marijuana appears to be moderate for Crohn's disease.

Multiple Sclerosis (MS)

Multiple studies demonstrate benefit with pain, muscle spasms, and spasticity symptoms in MS, including a systematic review of 11 systematic reviews. Evidence for smoking marijuana appears to be lower than with edibles. While benefit for these symptoms is robust, evidence for relief of other MS-related symptoms is lacking. Overall evidence of benefit for marijuana appears to be high for pain, muscle spasms, and spasticity, though evidence remains low for other symptoms in MS.

There is still much to learn about the possible benefits of marijuana for the management of medical conditions. A March 31, 2022 episode of On Call with The Prairie Doc aimed to answer questions for residents of South Dakota on this issue. Evidence is always changing, which is why it is so important to remain up to date in this area of medicine.

REFERENCES

Please note: Due to limited space, we are unable to list all references. You may contact South Dakota Medicine at ereiss@sdsma.org for a complete listing.

About the Author:
Jeremy Daniel, PharmD, BCPS, BCPP, Associate Professor, College of Pharmacy and Allied Health Professions, South Dakota State University, Brookings, South Dakota; Psychiatric Clinical Pharmacist, Avera Behavioral Health, Sioux Falls, South Dakota.

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For more information, visit sdstate.edu/pharmacy-and-allied-health-professions/pharmacy-practice.

Member News

Visit www.sdsma.org for the latest news and information.

For Your Benefit:

Fighting for You and Your Patients

The SDSMA serves as your vehicle for advocacy for your patients and the art and science of medicine through lobbying at the state and federal levels, grassroots activity, and legal initiatives.

SDSMA PAC is your grassroots avenue that works to impact public policy decisions through bipartisan political participation. SDSMA PAC supports and elects pro-medicine candidates on the state level. Members of the SDSMA and their spouses can join SDSMA PAC.

The SDSMA's motto is "Values, Ethics, Advocacy." We take our advocacy role to heart. With your help, SDSMA and SDSMA PAC have the opportunity to dramatically impact the political and legislative process to create meaningful changes in South Dakota's current health care system:

- Improving health and access to care in rural areas;
- Increasing Medicaid reimbursement;
- Promoting Medicare physician payment reform and stopping reimbursement cuts;
- Working to improve clinical quality and patient safety;
- Partnering with state agencies to tackle regulatory, socioeconomic, public health and scientific policy issues;
- Advocating for immunizations;
- Promoting adequate funding for medical education;
- Stopping inappropriate expansion of non-physician scope of practice;
- Defending the patient-physician relationship; and
- Reforming medical liability.

If you would like to become involved in any of our advocacy programs, visit sdsma.org to learn more.

Join Us for the 2022 SDSMA Annual Leadership Conference!

Make sure to reserve your spot and join us for the 2022 SDSMA Annual Leadership Conference on Friday, June 3 at the Hilton Garden Inn Downtown Sioux Falls. For registration, tickets and the full schedule with details, visit sdsma.org.

This event brings together physicians, residents, and medical students to connect and discuss the most important issues impacting healthcare. This year's theme is the Social Determinants of Health. Whether a seasoned physician or just beginning your medical training, this conference will provide you with the opportunity to learn more and weigh in on issues affecting physicians, the SDSMA, and the practice of medicine.

In the evening, join us for a membership mixer followed by dinner where we will honor physicians who have made significant achievements, inaugurate the incoming president, Dr. Lucio Margallo II, and recognize medical student scholarship recipients. You won't want to miss it!

The conference is a benefit of your SDSMA membership. There is no conference registration fee. Tickets for the SDSMA PAC Lunch ($40) and the Awards Banquet & Scholarship Recognition ($65) are available for purchase.

Membership Mixer is Networking Opportunity

Members are invited to the SDSMA's Membership Mixer from 6:30-7 pm Friday, June 3 at the Hilton Garden Inn Downtown Sioux Falls during the 2022 SDSMA Annual Leadership Conference.

Enjoy an opportunity to meet SDSMA leaders and network with your peers. Meet other physicians in the state to expand your professional network. The event is sure to be an all-around great time! Spouses are welcome to attend. The mixer is free of charge. Tickets are required (available at sdsma.org) for the Awards Banquet and Scholarship Recognition following the mixer. Please purchase tickets and register by May 23.

Awards Banquet & Scholarship Recognition

Enjoy a fun-filled evening of celebration Friday, June 3 at the Hilton Garden Inn Downtown Sioux Falls!

Start the evening with the Membership Mixer at 6:30 p.m. and continue the celebration at the Awards Banquet, Scholarship Recognition and Presidential Inauguration at 7 p.m. where Lucio Margallo II, MD, will be sworn in as SDSMA president, awards will be bestowed upon fellow colleagues, outgoing and incoming officers will be celebrated and welcomed, and medical student scholarship recipients will be recognized.

The mixer is free of charge; banquet tickets must be purchased in advance. Buy tickets and register for other annual meeting activities by May 23 at sdsma.org.

SDSMA PAC Lunch: Being an Effective Advocate

The SDSMA Political Action Committee (PAC) will welcome Kai Sternstein, vice president of the American Medical Association's State Advocacy Resource Center, at 12 noon on Friday, June 3 for the SDSMA PAC Lunch at the Hilton Garden Inn Downtown Sioux Falls. The lunch is part of the SDSMA 2022 Annual Leadership Conference. Sternstein will give the presentation, "Being an Effective Advocate for Medicine." The AMA's State Advocacy Resource Center works with state and national medical societies on state-level issues important to physicians and patients.

Join us for just the lunch, or consider participating in the additional activities the SDSMA Annual Conference has to offer throughout the day. Register by May 23. **The full schedule of the day's events is available at sdsma.org.**

Announcing the South Dakota Physician Well-Being Program

South Dakota physicians seeking support for their health and well-being now have a confidential and professional resource. The South Dakota Physician Well-Being Program is a responsive, high-quality program for physicians and residents that offers confidential, individualized support services and resources. Learn more and get confidential support at www.mwhms.com/pwbp.

The South Dakota State Medical Association, with funding assistance from Avera Health, Monument Health and Sanford Health, has developed this program as a resource for all South Dakota physicians.

The SDSMA and its Committee on Physician Wellness have spent the last two years tackling the goal of improving physician wellness and reducing burnout in recognition that physician well-being is essential for high-quality patient care. Burnout among physicians continues to be a major issue that has only been compounded by the COVID-19 pandemic.

The SDSMA has contracted with an external vendor, Midwest Health Management Services (MWHMS) to offer the South Dakota Physician Well-Being Program. The staff of MWHMS have extensive expertise in providing support for South Dakota's health care professionals and physicians. The program is confidential and independent of the licensing board, state government and employers. The program is committed to supporting the well-being and health of physicians, enabling them to continue to provide high-quality patient care.

The South Dakota Physician Well-Being Program offers confidential, supportive services and seeks to empower physicians to move beyond burnout and lead more satisfying lives.

- Confidential
- No insurance billing
- No medical record

The program is offered via in-person and remote access. Individualized services may include:

- Well-being resources
- Career fatigue
- Grief and loss
- Financial stressors
- Stress and anxiety
- Depression
- Substance abuse
- Behavioral concerns
- Work/family balance
- Personal and family stressors

SDSMA PAC Board Urges "No" Vote on Amendment C

At its meeting last month, the SDSMA PAC Board of Directors voted to oppose Amendment C. The PAC Board asks SDSMA members to join them on **June 7 in South Dakota's Primary Election** in voting "NO" on C.

South Dakotans for Fair Elections, the campaign formed to oppose Amendment C, is comprised of a broad coalition of individuals and organizations that spans industries and partisan politics, working to ensure that South Dakota's ballot initiative, constitutional amendment, and referred measure process stay intact.

Amendment C would permanently change our constitution to end majority rule for ballot measures. Additionally, Amendment C gives power to special interests while undermining the will of South Dakota voters. If the amendment passes, it will take just 41 percent of voters to block funding for important programs, including Medicaid expansion and would profoundly impact South Dakota's long history of voter engagement at the ballot box since creating the ballot initiative process in 1898. Since then, South Dakotans have regularly been asked to play a role in policymaking. For more than 124 years, South Dakotan voices have been heard with a simple majority.

SDSMA PAC Membership 2022

South Dakota State Medical Association Political Action Committee

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Your SDSMA PAC membership is very important in order to elect political candidates who understand and embrace the SDSMA's philosophy and vision for the future of healthcare in South Dakota. To contribute to SDSMA PAC, visit sdsma.org.

Recognizing PTSD

By Jill Kruse, DO

Post-traumatic stress disorder, or PTSD, was first listed as a medical diagnosis in 1980. However, it has been recognized and called by many different names throughout history. The first recorded description of PTSD is in the *Epic of Gilgamesh* which dates back to 2100 B.C. In *The Iliad and The Odyssey*, Homer wrote about Trojan War soldiers exhibiting the symptoms of PTSD. Shakespeare described a character in *King Henry IV* who suffered from post-traumatic nightmares.

During the Civil War, the terms "irritable heart" and "soldier's heart" were used to describe PTSD symptoms. In World War I it was called "combat stress" or "shell-shock." In World War II it became "battle fatigue" and "combat exhaustion." PTSD is not limited to soldiers, as the terms "concentration camp syndrome," "survivor syndrome," "battered child syndrome," and "rape trauma syndrome" were all recognized as conditions in the aftermath of WWII.

PTSD is a mental health condition resulting from experiencing trauma firsthand or from witnessing others undergoing a severely traumatic event. It can also result from repeated exposure to distressing details of an event. For example, many firefighters and other rescue personnel who searched for survivors after the 9/11 attacks suffer from PTSD.

The traumatic experience can lead to flashbacks or nightmares which can progress to physical reactions such as rapid heart rate or shaking when reminded of the event. Individuals with PTSD will often avoid any person, place, activity, or object that could trigger memories of the event. As a result, they may feel detached from others, or have persistent negative thoughts of themselves or others. They may have difficulty experiencing positive emotions like joy and happiness.

Another common symptom of PTSD is hyper vigilance and always feeling "on guard." This in turn can cause problems such as excessive sleeping, irritability, aggressive behavior, heightened startle response, or difficulty concentrating. If these symptoms last more than one month and interfere with multiple areas of a person's life, then they meet criteria for the diagnosis of PTSD.

PTSD is best treated by psychiatrists and psychotherapists with special training in this condition. Treatment often involves a combination of medication and therapy. Support groups, exercise, and mindfulness practices are also healthy coping strategies. And, as with any sickness, compassion from family and friends is crucial.

While the name for this illness may have changed, PTSD has been acknowledged for centuries. If you or someone you know is suffering from PTSD, don't wait. Talk to your doctor, counselor, or spiritual leader. For more information, call the Substance Abuse and Mental Health Services Administration National Helpline at 1-800-662-HELP (4357) or text HELP4U (435748).

Jill Kruse, DO, is part of The Prairie Doc® team of physicians and currently practices as a hospitalist in Brookings, South Dakota. Follow The Prairie Doc® at www.prairiedoc.org and on Facebook featuring On Call with the Prairie Doc®, a medical Q&A show celebrating its 20th season of truthful, tested, and timely medical information, broadcast on SDPB and streaming live on Facebook most Thursdays at 7 p.m. CT.

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