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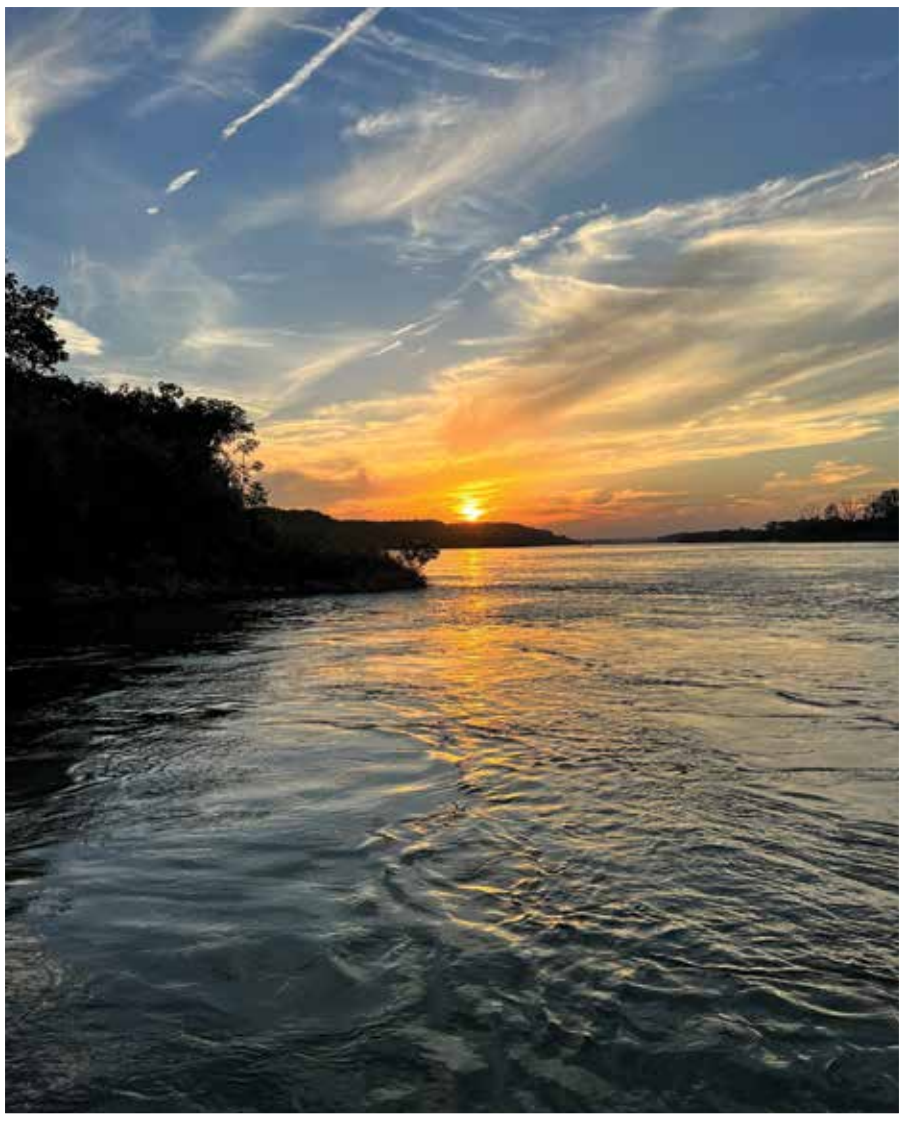

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I was chatting with an extended family member a few weeks ago, and he told me that October was the worst month for new car sales at his dealership in over ten years. I asked what was driving that statistic, and he suspected higher interest rates were creating sticker shock at new car payments. In fact, only about 10% of car buyers that month were electing to lease new vehicles and typically, leasing is less expensive than buying. What's going on here? Let's jump into the deep end on vehicle leases!

It turns out that existing customers nearing the end of their typical three-year leases were facing new lease payments that were 30-40% higher than their current leases due to much higher, 6-8%, interest rates. This led many of them to purchase their lease vehicles outright for the residual value. What's the residual value? It's time to review the typical terms of a lease agreement.

A lease is like a long-term rental. Just as in car purchase negotiations, begin with the price of the car. The lower you can negotiate the price, the lower your payment. Yes, you can negotiate the price on a leased vehicle. During your use of the car, you will also pay the related sales tax, dealer fees, and car registration fees. Ignoring one-time lease payment structures for the moment, you always have a monthly payment under the terms of the lease agreement, and it's based on the difference between the capitalized cost, beginning amount, and the residual value, which is the value of the car after depreciation for the lease term.

The car manufacturer determines the residual value, calculated as a percentage of the beginning value. So, if the capitalized cost is $40,000 and the residual value is 60%, this means that the customer can purchase the car for $24,000 at the lease end. The manufacturer also sets the "money factor," which is car-speak for the implied interest rate applied during the lease. A typical money factor is a very small number, like .0031. To get the interest rate, multiply this number by 2400. The result is 7.5%.

The car companies change both the residual values and the money factors monthly, to manage inventory levels. If they wish to move more cars, they can apply greater incentives, which could mean higher residual values, lower interest rates and cash rebates off the Manufacturer's Suggested Retail Price (MSRP).

From the consumer's perspective, leasing a vehicle means that you are usually under the manufacturer's warranty, so maintenance costs are low, you get to enjoy the latest safety equipment and technology (e.g. 360° backup cameras, adaptive cruise control, etc.), and you can trade your vehicle every three years or so. The downside is that you are restricted to a mileage maximum, and going over could mean paying a 'per mile' charge. Note: if you buy the car at the lease-end, excess miles will not be a factor. You also have a car payment that never stops so if your goal is to pay off your car, that just doesn't happen with a lease. Finally, the dealership expects you to return the car in good condition, meaning you could be charged for excess "wear and tear".

From a financial perspective, many lease "deals" suggest something like $509/month with $3,999 down. However, if you total the vehicle in the 14th month of your lease, the $3,999 you put down is lost. There is no recovering it, because you used it to "buy down" your monthly payment. If you can afford a higher lease payment, it's better to put $0 down and just pay as you go. Also, in some cases, as long as you exchange your vehicle for a new lease vehicle with the same dealer, they may ignore the excess miles so that they can obtain your vehicle for resale. In some cases, it could be less expensive for the dealer to buy back in an imperfect vehicle (from the customer) than to let the vehicle go to auction and compete with other car dealers to buy it back.

If you desire to learn more about leasing, one great resource is to read the articles posted on Edmunds.com. They actively moderate their "forums" area, and you can obtain current monthly lease data on a variety of vehicle types. They also have updated sales data that will allow you to evaluate your lease offer.

Leasing a car is potentially one way to help manage your monthly cash flow. Rather than take $50,000 or more from your investment portfolio to buy a car at an inopportune time, you could leave your money invested and just tap enough to make the lease payment. If you're already a Foster Group client, consult your advisor to discuss the pros and cons of leasing. It's not for everyone. If you're looking for a new advisory relationship, we'd be happy to design a financial and investment plan that incorporates all your financial decisions—even acquiring a new car.

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The Humanities: A Guide to Understanding the Human Condition

Benjamin Limburg, MS I; Nicholas Kendall, MS I; and Parker Owen, MS I

"The first year (Pillar 1) students at USD Sanford School of Medicine received a series of lectures that highlight humanities and ethics issues. The students were challenged to create a manuscript reflecting the important role that humanities can play in clinical practice."
- Jerome W. Freeman, MD and Ann Cook, PhD

"Doctors are men who prescribe medicines of which they know little, to cure diseases of which they know less, in human beings of whom they know nothing."[1] This quote is one of many written by M. de Voltaire, harshly critiquing the medical field in the 18th century. Over the next few centuries, modern science would thankfully prove Voltaire wrong. Scientists and doctors would work to learn the cause of diseases, where pathogens originate, and even how to use this information for novel medications. The medical field has proudly triumphed over many vectors of disease. However, Voltaire's statement may still hold one stinging truth. How well do clinicians know and connect with the people? Innovation often focuses on the condition and forgets about the effects the illness has on the human who harbors it. In many cases, patients enter the clinic or hospital in fear, only to become exasperated by being stripped of their clothes, costumed in thin hospital gowns, scrutinized under cold exam lights, and subjected to the many invasive interventions characteristic of modern medicine. In this contemporary age of progress, it is easy to forget the human connection that underlies the basis of every patient interaction. Long shifts, administrative pressure, and a myriad of other stressors can unfortunately lead physicians to adopt a calloused outlook towards the humanistic side of medicine.

The desperate need for human connection in medicine is not a new topic. Hippocrates, often regarded as the pioneer of modern medicine, transitioned medicine from being grounded in religion to focused on treatments driven by reason and proven by experiential knowledge.[2] Despite insisting on treating patients rationally, the innovative Hippocrates also knew there was more to being a physician than the ability to gather and apply evidence. Hippocrates said, "Wherever the art of medicine is loved, there is also love for humanity."[3] Hippocrates' statement is equal parts focused on the scientific and the emotional side (a love of humanity) of medicine. What does it mean to love patients? Medical care is love in action. Being inspired to cry tears of joy with a mother after the delivery of a healthy baby, or tears of sorrow with a different mother after a stillbirth, only comes from a place of deep emotion, even love.

How do we cultivate these human connections? Dr. William Osler, another seminal figure in medical history, believed that a great physician must be informed by the humanities. Known for having an extensive "bedside library" containing a broad swath of philosophical literature, Osler is known to have considered Sir Thomas Browne's *Religio Medici* the book which had the "most enduring influence" on his life.[4] *Religio Medici,* translated literally from Latin as "the religion of a doctor," features themes not of empirical science and medical practice but of religious tolerance and the interplay between science and medicine. Learning medicine for Osler went beyond physiology and pharmacology. We'd be wise to follow suit.

As Osler knew, the needed awareness of human hopes, dreams, and fears is not gleaned from the pages of science texts. Rather, it is the humanities in which people have expressed the visceral feelings entwined in the human condition throughout history. At times, the humanities aren't prioritized when it comes to medical education. However, the mark of a great physician is the ability to make patients feel comfortable and heard in their presence. Being humanities-informed provides physicians a deeper awareness of patients' journeys and thus the wisdom to better minister to their trials and tribulations. Following Osler's example allows us to have a practical way to cultivate the "love of humanity" that Hippocrates taught.

Samuel Beckett's play *Waiting for Godot* is a powerful example of what can be learned within literature and applied to medical practice: the importance of being present. "Nothing happens. Nobody comes, nobody goes. It's awful."[5] The two main characters fruitlessly wait the entire play for Godot, even though he never appears. The only thing giving the characters on the stage some tether to sanity is each other. *Waiting for Godot* can parallel a physician's relationship with the patient. Sometimes, patients enjoy a physician's presence

in hopeless conditions, regardless of the outcome. Everyone is unbearably waiting for their own Godot. Having somebody to wait with makes it tolerable. We can tether each other to sanity by being present, even when "it's awful." This presence does more than create comfort. It connects the physician to the patient. It shows love.

Such a profound expression of love finds its essence throughout the arts, and perhaps no artist has better captured the essence of humanity than Shakespeare. Shakespeare's works have influenced generations of people across cultures, prompting deep reflection on the human experience. It is only natural for physicians to likewise draw on these stories as they labor to understand the intense emotions that accompany life's trials. In Shakespeare's "King Lear," we see the deep emotional deterioration experienced as we age. Despite the play's tragic conclusion, the audience is left with a valuable lesson from Shakespeare's character Edgar: "Men must endure their going hence, even as their coming hither."[6] Like Lear, we are all destined to go through the trials of life's decline, and we must find the strength to endure them. A great physician can ensure that a patient never bears the emotional burden of "Their going hence" alone. Physicians are meant to guide patients hand in hand as they navigate the often uncharted waters of sickness, aging, cognitive impairment, and ultimately, death.

The forgoing examples are meant to illustrate how the humanities deepen our comprehension of a patient's emotions. Delving into these narratives undoubtedly enhances our understanding of the human condition. Art, literature, philosophy, and other humanities disciplines offer a plethora of perspectives that can effectively bridge the emotional gap between doctor and patient. The only limit to what can be gained from such ideas is our willingness to search and learn. As medical students at the University of South Dakota Sanford School of Medicine, we hope to maintain sight of the emotions and experiences of the individual patient as we learn the scientific side of medicine over the next four years. We believe that the Sanford School of Medicine can continuously provide a space for students and physicians to investigate the human side of medical practice. By dedicating ourselves to a lifelong study of the humanities, our generation of medical students will amass our own "bedside libraries" and personify the physicians Voltaire sought.

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AI in Medicine

Denise Hanisch, MD
President, South Dakota State Medical Association

The integration of artificial intelligence (AI) into the realm of medicine has brought about transformative advancements in healthcare. However, alongside the potential benefits, there exist valid concerns regarding the ethical, social, and practical implications of AI in this field.

One primary concern is the ethical dilemmas surrounding AI algorithms in healthcare. The opacity and complexity of AI decision-making processes raise questions about accountability and bias. To mitigate these concerns, transparency in AI systems must be prioritized.

Implementing explainable AI techniques can help healthcare professionals understand how AI arrives at its conclusions, enabling them to interpret and validate its recommendations.

Another pressing issue is data privacy and security. As AI relies heavily on vast amounts of patient data for training and decision-making, safeguarding this information is paramount. Institutions must adhere to stringent data protection regulations, ensuring that patient confidentiality is maintained. Implementing robust encryption methods, access controls, and regular security audits can enhance data security in AI-driven healthcare systems.

Furthermore, the potential impact of AI on the healthcare workforce raises concerns about job displacement and the redistribution of roles. While AI has the capacity to streamline operations and improve diagnostic accuracy, healthcare professionals may fear redundancy. To address this, investing in reskilling and upskilling programs for healthcare workers can equip them with the necessary skills to collaborate effectively with AI technologies, thereby enhancing patient care outcomes.

The concerns surrounding AI in medicine necessitate a proactive and multidisciplinary approach to ensure ethical AI deployment. By emphasizing transparency, data privacy, and workforce development, the healthcare industry can harness the full potential of AI while mitigating associated risks. Collaborative efforts between policymakers, healthcare providers, technologists, and ethicists are essential to navigate the evolving landscape of AI in medicine responsibly and ethically, ultimately benefiting patients and society at large.

The word "transparency" is used frequently when discussing the use of AI in medicine and needs to be applied to both patients and physicians. So, in full transparency, I used ChatGPT to write the first four paragraphs of this article. It was my first experience using this technology and it was mildly frightening how easy it was. After downloading the program and typing in four key words, the text was generated in less than 2 seconds. It was exciting and concerning at the same time, which is how the majority of physicians feel about using AI in their practice. The AMA conducted a recent survey of 1081 physicians (420 primary care providers and 661 specialists) and found that 70% are either, more concerned than excited, or equally concerned and excited about a future with AI.

The American Medical Association recently published the survey findings and recommendations in a report that can be found on the AMA website. I know very little about technology, and am especially naive regarding the subject of AI but read the report, "Future of Health: The Emerging Landscape of Augmented Intelligence in Health Care" and strongly encourage every physician to familiarize themselves with the rapidly expanding future of AI.

The AMA has adopted terminology that they feel is important when discussing "augmented intelligence." Describing the technology as "augmented," as opposed to "artificial," makes it clear that technology should be used to support, not replace, decisions made by physicians.

I learned several new terms and definitions while reading the report. Most interesting was the explanation of machine learning and deep learning. Machine learning occurs when systems "learn from data without being explicitly programmed." Machine learning is a subtype of AI and deep learning is a subtype of machine learning and occurs when a systems trains itself based on data it receives. Machines learn by three different models, supervised learning, unsupervised learning and reinforcement training in which an algorithm "receives a reward when its action and output align with the goals of the programmer." Depending on the data, the output could be accurate or biased in any of these forms of learning.

It may be hard to imagine how a machine could produce bias but a perfect, real world example was provided. An algorithm used health care costs as an indicator of health care needs. The output assumed that White people had more medical illnesses than Black patients and therefore would benefit more from a care management program. AI did not take into account that Black people often have a disadvantage in accessing care and therefore were not represented in a system that focused on costs as opposed to needs.

I feel it will be hard to predict how AI will affect us as physicians and as individuals, but ignoring it's existence will only be a detriment. We need to be informed, aware and educated in the potential and flaws of this tool. The amazing thing about humans is that we have experiences that are truly unique to each one us. My history cannot be replicated. We all have our own individual story that provides us with the human ability to care for other humans.

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A Rare Case of Axillary Extramammary Paget's Disease with an Underlying Adenocarcinoma

Colby Felts, MD; Victoria Durkin, MD; and Amy Kerkvliet, MD

Abstract

Extramammary Paget's disease (EMPD) is an uncommon cutaneous neoplasm almost exclusively located in the vulvar, perianal, and male genitalia regions. Evaluation and management are complicated given the average delay in diagnosis is two years and approximately 30% of cases are associated with underlying malignancies. The axilla is a unique location for EMPD. We report a rare case of a 78-year-old male with axillary EMPD associated with an underlying adenocarcinoma. A 1-cm tender and pruritic erythematous plaque with surrounding erythema appeared in the patient's axilla. An irritated seborrheic keratosis secondarily impetiginized along with irritant contact dermatitis was suspected. Treatment of cefdinir and topical hydrocortisone failed and a biopsy was taken. Microscopic and immunohistochemical examination showed ulceration with an underlying proliferation of atypical glands (Figure 2A) and a nested intraepidermal proliferation with pagetoid spread (Figure 2B). The atypical cells were positive for gross cystic disease fluid protein 15 (Figure 2C), epithelial membrane antigen (Figure 2D), cytokeratin 5/6, and cytokeratin 7. These findings were supportive of an apocrine adenocarcinoma arising in association with EMPD. Wide location excision was performed. Screening for associated malignancies or lymphatic spread is the primary goal during evaluation. Outcomes are favorable when the primary neoplasm is of limited distribution. The accepted treatment for primary lesions is wide local excision, although anatomic tissue constraints necessitate further research into other treatment modalities. To our knowledge, this is the 14th reported case of axillary EMPD with an underlying adenocarcinoma which may help with identification and management of future cases.

Introduction

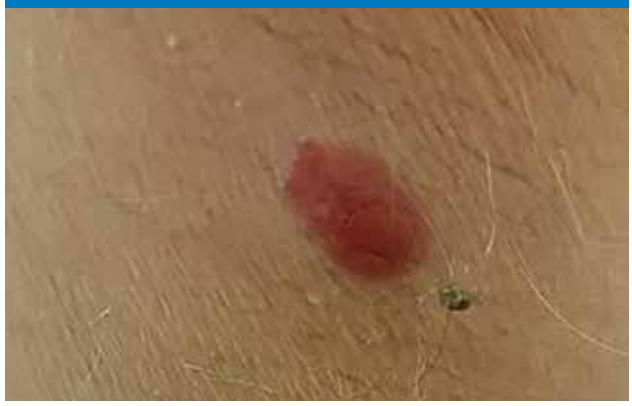
Extramammary Paget's disease (EMPD) is an uncommon cutaneous neoplasm almost exclusively (>98%)[1] located in the vulvar, perianal, and male genitalia regions.[2] Given the similarity of EMPD to other cutaneous lesions, it is difficult to identify and the average delay in diagnosis is around 2 years.[2,3] Approximately 30% of cases are associated with underlying malignancies which emphasizes the importance of appropriate identification and subsequent screening.[2] The axilla is an unusual location for EMPD, with even fewer cases being reported in the literature of axillary EMPD with an underlying malignancy.[1]

Here, we examine an extremely rare case of axillary EMPD with an underlying adenocarcinoma and evaluate the proper workup, diagnosis, and management.

Case

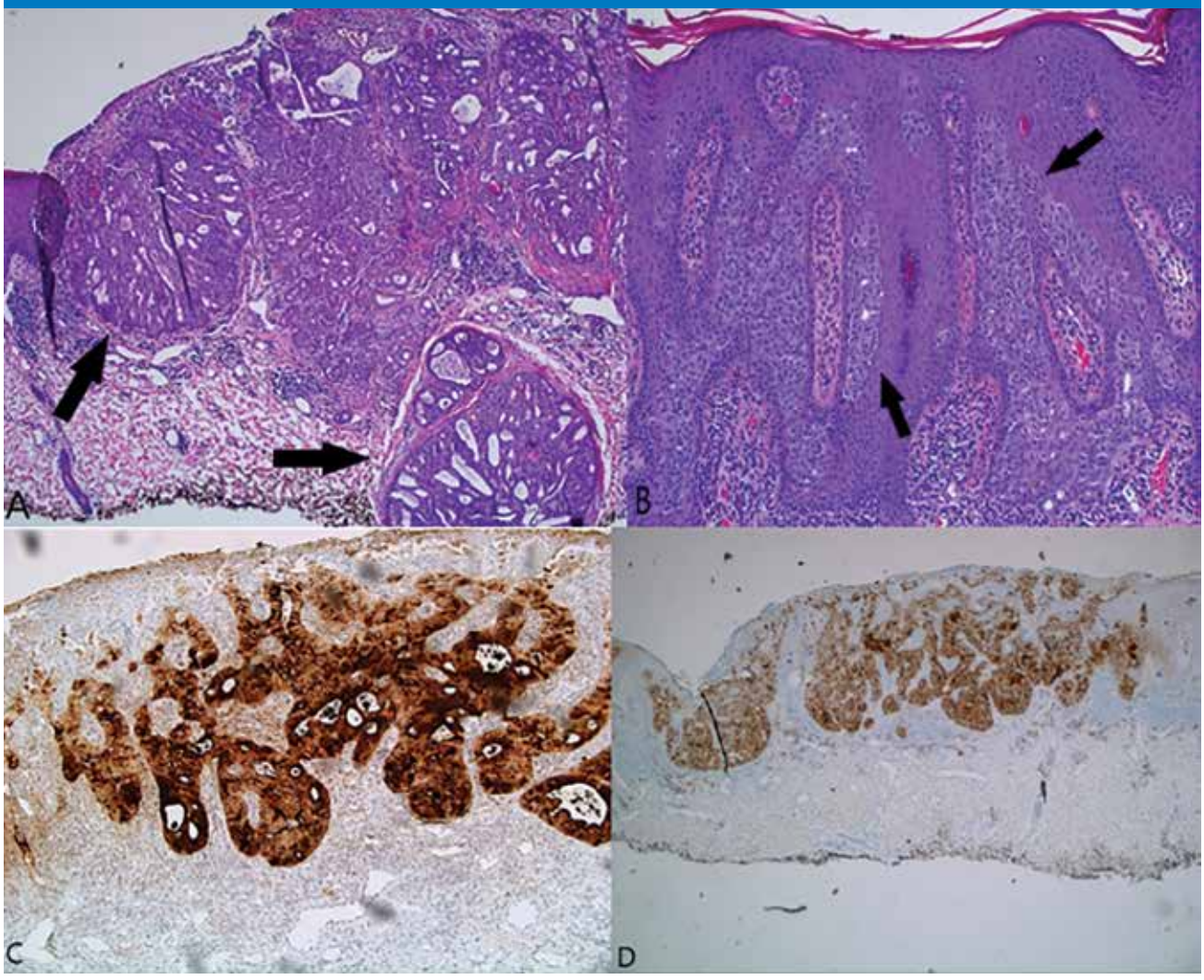
A 78-year-old Caucasian male presented to his primary care provider for a left axillary skin lesion which appeared 5 months ago. The patient's history included significant sun damage and multiple non-melanoma skin cancers, but no other malignancies. Physical exam showed a 1-centimeter (cm) mildly tender and pruritic erythematous plaque with surrounding erythema extending into the armpit (Figure 1). The patient denied deodorant use or trauma to the area. He declined biopsy and elected to see his dermatologist.

Figure 1. Clinical photograph showing a well-demarcated erythematous plaque with faint surrounding erythema in the axilla.



The dermatologist suspected an irritated seborrheic keratosis

Figure 2. (A) Ulceration with underlying proliferation of atypical glands (see black arrows); H&E 4X. (B) Nested intraepidermal proliferation with pagetoid spread (see black arrows); H&E 10X (C) GCDFP-15 positivity; 10X. (D) EMA positivity; 4X.



secondarily impetiginized along with mild irritant contact dermatitis vs intertrigo for the surrounding erythema. The patient was given cefdinir and recommended to use hydrocortisone cream. Dermatology saw the patient six months later and the lesion had not changed. Physical exam showed an erythematous and crusted oval plaque.

A shave biopsy of the 0.8 x 0.7-cm lesion showed ulceration and proliferation of atypical glands with apocrine features and a high degree of mitotic activity extending deep into the dermis (Figure 2A). Another aspect showed a nested intraepidermal proliferation of cells with abundant vacuolated cytoplasm and large, atypical nuclei arrayed in pagetoid fashion within the surface epithelium (Figure 2B). The atypical cells were positive for gross cystic disease fluid protein 15 (GCDFP-15), epithelial membrane antigen (EMA), and cytokeratin (CK) 5/6 (Figure 2C-D). Factor XIIIa and preferentially expressed antigen in melanoma (PRAME) also showed positivity, suggesting a sebaceous component. Melanoma antigen recognized by T cells 1 (MART-1) was negative. A second institution evaluated the case where further immunohistochemical (IHC) stains were completed. The atypical cells were strongly positive for CK7 and CAM 5.2. The microscopic and immunohistochemical findings were supportive of an apocrine adenocarcinoma arising in association with EMPD, extending to both peripheral and deep margins.

The patient was referred to hematology-oncology. Routine lab work including prostate specific antigen and

lactate dehydrogenase was within normal limits. The carcinoembryonic antigen (CEA) level was slightly elevated at 5.8 ng/mL. A computed tomography (CT) scan of the chest, abdomen, and pelvis with intravenous contrast showed non-specific thickening within the colon. Mammography and an ultrasound for lymphadenopathy were negative. With no systemic symptoms, hematology-oncology believed the malignancy to be a primary neoplasm.

Wide local excision (WLE) with 2-cm margins (total excision size 5.0 x 15.0-cm) was completed which was negative for residual adenocarcinoma or EMPD. Sentinel lymph node biopsy and a subsequent positron emission tomography (PET) scan were negative. He continues to follow with hematology-oncology and was asymptomatic one month following the WLE. He was encouraged to schedule a colonoscopy due to a history of colon polyps, CT with colonic thickening, slightly elevated CEA levels. and his last colonoscopy performed over 10 years ago. However, the patient declined due to his age.

Discussion

The uncommon cutaneous neoplasm of EMPD was first described by Radcliffe Croker in 1889.[4] Croker's description came from a case in which EMPD was found on the penis and scrotum with the patient also having an underlying bladder cancer.[2]

Epidemiology

The exact incidence of EMPD is unknown[2], although studies in China (0.4 per 1,000,000 people)[5] and Europe (0.6 per 1,000,000 people)[6] suggest a rare disease. This cutaneous malignancy tends to occur in individuals between 60 to 80-years old.[3] Interestingly, gender predominance depends on race with a female predominance in Caucasians and male predominance in Asians.[2,3]

Clinical Presentation

EMPD commonly presents as a well demarcated erythematous plaque with pruritis, burning, or tenderness, although some (10%) are asymptomatic.[3] Less often, EMPD may appear as a hypopigmented macule or patch, which is seen more frequently in Asians.[2] Although slow growing, later stages can present as nodules or deep ulcers.[3] Many clinicians empirically treat with corticosteroids or anti-fungal medications given the similarity to eczema, psoriasis, and fungal infections.[2,3] Given the relatively mild symptoms and frequent failed treatment strategies, diagnosis is delayed two years on average.[2]

Body areas rich in apocrine glands are the most common location of EMPD with the vulva, perianal, and male genitalia regions comprising 65%, 20%, and 14% of lesions respectively.[2,3] With only 1-2% of lesions not in the vulva, perianal, and male genitalia regions, axillary EMPD is a rare finding.[1]

Secondary Malignancy

An estimated 30% or more of EMPD cases have an underlying malignancy.[2] The underlying malignancy is most often in close anatomical location to the EMPD but does not show a predilection for a specific organ or classification of malignancy.[2] Only 13 cases of axillary EMPD with an underlying adenocarcinoma have been reported in the literature[1,7-13] and this case would be the 14th reported instance. Rates of secondary malignancies in axillary EMPD range from 14-50%[1,7] based on a limited data available given the rare nature of axillary EMPD.

EMPD is classified as a primary or secondary malignancy. Primary is defined as a primary intraepithelial neoplasm which can have invasion or an underlying primary adenocarcinoma of a skin appendage (this case). Secondary is caused from spread from an internal malignancy.[14]

Histology

Microscopic analysis of EMPD under hematoxylin and eosin shows epidermal Paget cells.[3] These large, atypical cells have abundant pale-staining (also considered 'clear' or 'vacuolated') cytoplasm with prominent nuclei.[2] The epidermis frequently shows acanthosis with parakeratosis, hyperkeratosis, or ulcerations.[3] IHC stains are essential to exclude other pathologies such as Langerhans cell histiocytosis, squamous cell carcinoma in-situ (Bowen's disease), amelanotic melanoma, and mycosis fungoides.[2] The vacuoles of Paget cells contain large amounts of mucin which stain Periodic acid-Schiff (PAS) positive.[2] Primary lesions show strong positivity to CEA and GCDFP-15.[2,3] S-100 or MART-1 are used to evaluate for melanoma while p63 will show positivity in Bowen's disease.[3]

CK7 and CK20 are also important markers for evaluating EMPD. Primary lesions are usually CK7+/CK20- while secondary lesions tend to be CK7-/CK20+ (although urothelial carcinoma is frequently CK7+/CK20+).[3] CAM5.2 can be used to identify glandular epithelium.[9] Evaluating the margins is a challenge due to the multifocal growth of the neoplasm with extension into normal skin without overlying clinical changes.[2]

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Evaluation and Treatment

Evidence for EMPD evaluation and treatment is unclear and does not have a defined protocol or timeline.[3] Various strategies, like CT and PET scan in this case report, have been used to screen for associated malignancies.[9,12] The exact screening process is per provider preference but is typically localized to evaluating regions in anatomical proximity to the EMPD.[2] Apocrine and mammary tumors are extremely similar histologically.[9] Thus, an underlying apocrine adenocarcinoma should prompt a breast work-up including a mammography, which was completed in this case.[11,12] The role of sentinel lymph node biopsy is unclear although it is a option for axillary EMPD[12,15] and may help with predicting survival.[2] Lymph node dissection and scouting biopsies have also been discussed.[2]

The current accepted treatment for a primary lesion is WLE although exact margins are not defined (ranging from 1-5 cm).[3] Axillary EMPD has favorable anatomy for WLE compared to the tissue constraints of more common areas.[2,11] Every report of axillary EMPD with an underlying adenocarcinoma was treated with WLE.[1,7-13] Mohs micrographic surgery is an excellent therapeutic option for the anatomic and cosmetic challenges of EMPD in sensitive areas and may be superior to WLE.[2,3] However, the uncommon nature of EMPD makes it difficult to become comfortable with this procedure.

Non-surgical treatment options include radiation, topical imiquimod, photodynamic therapy and chemotherapy.[3] No clear guidelines exist for these therapies,[2] although some consider radiation the first alternative to surgical treatment while saving chemotherapy for distant metastasis.[3] Common chemotherapeutics include docetaxel or low dose combination 5-fluoruracil and cisplatin.[3] In cases of axillary EMPD with an underlying adenocarcinoma, one patient received radiation[12] while another received docetaxel and cyclophosphamide.[13] Other options include anti-HER2 antibody, hormonal, and immune checkpoint therapy[3] while genetic analysis for markers such as HER2, Ki-67, Cyclin D1, and MUC5AC are also being evaluated.[2]

Outcomes

EMPD is typically slow growing and has favorable outcomes when of limited distribution.[3] One study noted five-year survival rates of >80% with spread to 0 or 1 lymph node. However once two or more lymph nodes were positive, five-year survival rates dropped to 40%.[16] Like other malignancies, depth of invasion and extracutaneous involvement are predictors of a poor prognosis. Long term follow-up is required due to the risk of secondary malignancy.[2] Only one case of axillary EMPD with an underlying adenocarcinoma reported a recurrence (eight months later) which was removed with WLE and had clear margins.[9] As treatments continue to improve, rates of secondary malignancies will climb due to increased rates of survival from EMPD.[4]

Conclusion

In conclusion, we presented a rare case of axillary EMPD with an underlying adenocarcinoma and evaluated the workup, diagnosis, and management. Given the difficulty diagnosing this pathology in addition to the risk for secondary malignancies, it is important to keep EMPD in mind when considering other more common dermatologic diseases.

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Extraosseous Ewing Sarcoma Manifesting as an Acute Abdomen in a Young Adult Male: a Case Report

Mamoon Ahmed, MBBS; Swaminathan Perinkulam Sathyanarayanan, MD; Kayla Hoerschgen, MD; and Randall Lamfers, MD, FACP

Abstract

Ewing sarcoma is a tumor primarily affecting children and young adults, and usually affects long bones. Extraosseous Ewing sarcoma (EES) is a rare primary tumor of soft tissues. We present a case of abdominal EES with metastasis to thoracic cavity, which presented as abdominal pain and vomiting in a 21-year-old previously healthy gentleman.

Introduction

Extraosseous Ewing sarcoma (EES) is a rare tumor belonging to Ewing sarcoma (ES) family of tumors.[1] ES is a type of neuroendocrine tumor mainly affecting children and young adults with 70% of the cases occurring at less than 20 years of age.[2] Incidence of EES is 0.4 per million and has a bimodal distribution peaking at age less than 5 and more than 35.[3,4]

Tumor cells in ES have reciprocal translocation which creates an abnormal rearrangement of two genes. The EWSR1 gene on chromosome 22 fuses together with FLI1 gene on chromosome 11. EWSR1 gene encodes a protein that is involved in various cellular processes, including cell signaling, gene expression, and RNA processing and transport while FLI1 gene is a protein-coding gene that provides instructions for making the FLI protein, which controls the transcription of genes. It is a somatic mutation hence it is only found in tumor cells and is not inherited. In ES, PAS stain is usually positive for cytoplasmic glycogen. Over 95% of tumor cells express cell-surface glycoprotein CD99. CD99 expression is highly reliable and characteristic marker for ES. Almost 80% cases have t (11; 22) (q24; q12) balanced translocation.[5] Histologically, EES is indistinguishable from ES.[1]

EES can occur at various sites including Papilla of Vater,[6] cervical esophagus,[7] pancreas, kidneys, gallbladder, and thoracic spine[8-11] but to our knowledge, EES has not yet been reported as an epigastric mass with metastasis to thoracic cavity. Here we present a case of EES in a young healthy gentleman who presented with abdominal pain and intractable vomiting.

Case Presentation

A 21-year-old previously healthy gentleman presented to the emergency department with complaints of sudden onset of severe epigastric abdominal pain associated with nausea and vomiting. His vital signs were unremarkable except for tachycardia. Physical examination demonstrated significant epigastric tenderness without palpable mass. Testicular exam was unremarkable. Ultrasound abdomen was done which showed an ill-defined mass adjacent to the liver and stomach. A subsequent CT chest/abdomen demonstrated a 6.5 x 8 x 7.4 cm mass (Figure 1A) along the lesser curvature of stomach and a large mass (Figure 1B) in the left side of the chest adjacent to the heart measuring 12.3 x 11.6 cm, along with multiple nodular masses in lungs bilaterally. There was some irregular attenuation in the scrotum concerning for a testicular mass. His lab work was unremarkable except for elevated LDH of 414. Ultrasound of the scrotum was negative for testicular mass and AFP and beta-HCG were negative.

He then underwent a CT guided biopsy of his left thoracic and the epigastric mass which demonstrated small round blue tumor cells with positive EWSR 1 gene rearrangement.

To further characterize the neoplastic cells, immunohistochemical stains including synaptophysin, CD56, CD3, TdT, CD99, WT1, desmin, myogenin, CD45, CD7, CD34, Pax-5, OSCAR, pankeratin, and BCL-2 were attempted. The neoplastic cells were positive for CD99 and BCL-2, weakly positive for TdT and synaptophysin, and negative for CD56, CD3, WT1, desmin, myogenin, CD45, Pax-5, CD34, OSCAR, and pankeratin. The neoplastic cells also showed nonspecific weak staining with CD7.

Findings were consistent with ES. Work-up for other primary bone neoplasms was negative. Oncology was consulted. The patient decided to leave and follow up with oncology on an outpatient basis. Unfortunately patient was lost to follow-up until he presented two months later with severe left sided chest pain, shortness of breath, and abdominal pain.

Figure 1A. CT chest/abdomen. (A) 6.5 x 8 x 7.4 cm mass along the lesser curvature of stomach.

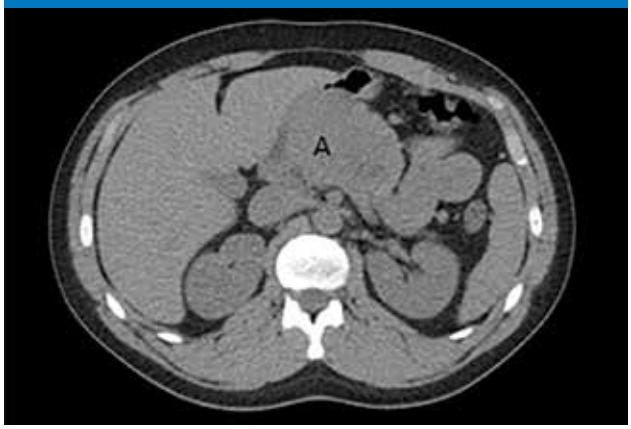
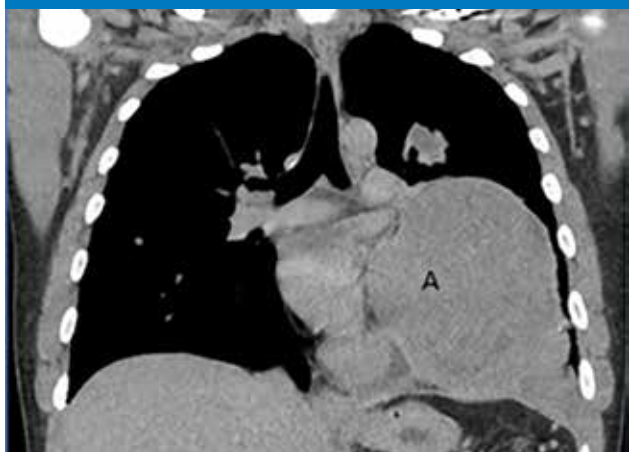


Figure 1B. CT chest/abdomen. (A) 12.3 x 11.6 cm in left side of chest.



Repeat CT chest performed at that time showed interval worsening of the left sided chest mass which occupied 3/4th of the thoracic cavity, multiple small bilateral lung masses with left sided pleural effusion and the abdominal mass now measuring 9.3 cm in its greatest diameter. An ultrasound guided thoracentesis yielded 800 cc of blood-tinged serous pleural fluid. Cytology showed mesothelial cells and chronic inflammation but was negative for malignancy.

Oncology re-evaluated the patient and even with chemotherapy, his chance of survival for the next several months was thought to be <10%. Thus, he opted for hospice care. He passed away after 2 months of his initial presentation.

Discussion

This is a case of abdominal EES with metastases to the thoracic cavity.

EES is a small blue round tumor derived from neural crest, which differentiates along neuroendocrine lineage. Small blue round tumors have numerous subcategories including Ewing sarcoma, rhabdomyosarcoma neuroblastoma, synovial sarcoma, and desmoplastic small round blue tumor. It is called small blue round tumor because of large hyperchromatic nuclei and a thin rim of cytoplasm.[1] Amongst these, desmoplastic small round blue tumor characteristically manifests in young males in abdomen. But it has a translocation t (11;22) and co-expresses neural markers including Desmin, cytokeratin, epithelial membrane antigen. MRI is the test of choice for initial diagnosis on which they are seen as well circumscribed masses with low intensity while FDGPET imaging is used to detect metastasis.[12] It is mostly found in females.[12] Core-needle biopsy with pathological testing is used to obtain a definitive diagnosis. Risk factors associated with worse prognosis in EES include older age, pelvic involvement, high WBC, elevated LDH and low Hb at the time of diagnosis. Initial tumor size is also a risk factor and is considered a strong prognostic factor in localized disease. Five-year survival rate as per Surveillance, Epidemiology, and End Results (SEER) stage is localized 82%, regional 71%, distant 39%, all SEER stages combined 63%.[14] Metastatic disease is a bad prognostic factor, with a five-year overall survival rate <30%. Recurrent ES is almost always fatal.[1] In our case, the pathology sample was negative for desmin, and the biopsy was labeled as ES per FISH.[3]

EES is difficult to diagnose as it might present with nonspecific symptoms.[13] Abdominal EES has also previously been reported as asymptomatic, heterogeneous, partially necrotic lower mid-intraabdominal mass also involving root of the small bowel mesentery.[13]

The current chemotherapy regimen of alternating vincristinedoxorubicin, cyclophosphamide and ifosfamideetoposide along with surgery and/or radiation has increased five-year survival rate for localized Ewing sarcoma up to 73% but chemotherapy without radiation and/or surgery is insufficient in effective treatment.[15] Overall survival at five years might be less than 30% in metastatic cases.[13] Our patient decided to move forward with comfort measures and hence no treatment was given. He passed away within two months of initial diagnosis.

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Influenza Cerebellitis in a 3-Year-Old Male

Katherine Nielson, MS IV; Meaghan Sievers, MS IV; Connie Taylor, MD; and Peter Paul Lim, MD

Abstract

Acute cerebellitis (AC) is often a para-infectious inflammatory process that usually presents with a variable clinical picture; often with fever, nausea, headache, altered mental status, gait abnormalities, and coordination defects. It is usually a complication of an infectious process or as a result of post-infectious autoimmune mechanisms. We report a case of a 3 year old male with influenza A who presented with an acute encephalitic picture whose course and radiologic studies demonstrate cerebellar changes strongly compatible with AC.

Introduction

Acute cerebellitis (AC) is reported to be one of the most common causes of acute cerebellar dysfunction in the pediatric population.[1] Fortunately, in most cases, complete recovery is observed.[2] AC is often a post-infectious inflammatory process that usually presents with cerebellar symptoms, the most prominent being progressive broad-based gait disturbance, balance disturbance, dysarthria, and dysmetria.[2] AC is also generally associated with fever, nausea, vomiting, headache, and altered mental status. It has been implicated in infections with varicella zoster, mumps, epstein-barr virus, enterovirus, cytomegalovirus, measles, rubella, herpes simplex, rotavirus, and echovirus.[2-5] Bacterial infections such as *Salmonella typhi, Bordetella pertussis, Borrelia burgdorferi, Mycoplasma, Coxiella burnetii, group A Streptococcus,* and *Orientia tsutsugumushi* have also been implicated.[3] An unclear link to the production of autoantibodies resulting from post-infectious autoimmune mechanisms has been postulated.[6] Influenza is a single stranded enveloped RNA virus often implicated in viral pneumonia. Very few clinic cases of AC from Influenza have been reported. To date, there have only been 11 cases of AC from influenza published in relevant literature. Eight of these cases were reported in pediatric patients.[3,5] In this article, we present a case of a three-year old male with influenza AC who was treated with IVIG and steroids resulting in a favorable outcome.

Case

A 3-year-old completely unvaccinated male with global developmental delay and a remote history of a febrile seizure presented to the emergency department (ED) for fever (Tmax 102) and abnormal movement preceded by a 2-day history of anorexia. His mother described him to have difficulty with purposeful movement including walking, feeding, or sitting upright. Until the morning of his presentation, the patient was conversant and interactive but suddenly became unresponsive to questions and unable to follow instructions. He also had some seizure-like activity described as the patient tensing up for a few seconds and falling limp with his head falling backwards.

Initial evaluation revealed a child that was drowsy and aphasic. He was hypotonic but moved extremities equally to stimulation. Movement was non-purposeful, and he was unable to sit or stand independently. He had normal cranial nerve function and deep tendon reflexes. A comprehensive viral panel was positive for influenza A. His chest X-ray was suggestive of viral bronchiolitis with no evidence of focal pneumonia. Complete blood cell count and basic metabolic panel were unremarkable aside from a mild metabolic acidosis and hyponatremia (Table 1). Computed tomography of the head with contrast demonstrated no acute intracranial abnormalities but showed opacification of the paranasal sinuses and left middle ear cavity that are compatible with his influenza infection.

Upon admission, the patient was empirically started on treatment dosing of oseltamivir, meningitic dosing of ceftriaxone, high dose methylprednisolone (2.0 mg/kg IV), and maintenance fluids. Electroencephalogram (EEG) showed a slowing post-ictal state that quickly resolved. Uric acid levels fluctuated during hospitalization and later normalized. This was felt to be due to the initial illness. Additional metabolic and baseline labs were also obtained and demonstrated overall reassuring values (Table 1).

Brain MRI with and without contrast was eventually obtained showing leptomeningeal enhancement throughout the cerebellum consistent with cerebellitis (Figure 1A). Abnormal DWI signals in the splenium and genu of the

Table 1. Summary of patient's initial laboratory results showing unremarkable values.

Labs	Value	Reference
Acylcarnitine and Carnitine Profiles	Acylcarnitine and Carnitine profiles were normal	Normal
Amino Acid Quantitative	In this sample, the concentrations of several amino acids were elevated. This pattern is not specific of a particular metabolic disorder and is of uncertain clinical significance.	
Complete Blood Cell Count (CBC)	WBC 10.6 K/uL	5.0-15.5 K/uL
	Neutrophil % 68.2	29.5-36.5%
	Lymphocyte % 19.7	52.7-65.3%
	Monocytes % 11.7	4.5-5.5%
	Eosinophils 0.0	2.7-3.3%
Creatinine Kinase (CK)	34 U/L	20-180 U/L
Inflammatory Markers	CRP 0.8 mg/Dl	<0.5 mg/dL
Metabolic Chemistries	Na 132 mmol/L (Day 1) 136 mmol/L (Day 3)	134-147 mmol/L
	CO2 13 mmol/L (Day 1) 19 mmol/L (Day 2)	14-24 mmol/L
	Anion Gap 18 mmol/L (Day 1) 11 mmol/L (Day 2)	3-15 mmol/L
	Uric Acid 8.9 mg/dL (Day 1) 2.6 mg/dL (Day 9)	1.9-4.9 mg/dL
Serology/Viral Panel	Influenza A (H1N1/09) Detected	Not Detected
	CMV IgG Ab 5.6 (Day 10)	<0.9 AI
	CMV IgM Ab 1.0 (Day 10)	<0.9 AI
Thyroid Stimulating Hormone (TSH)	1.754 uIU/mL	0.7-4.170 uIU/mL
Urine Organic Acids	*In this sample, the excretions of 3-hydroxy butyric acidand acetoacetic acid were markedly elevated. In addition,metabolites of ibuprofen and acetaminophen were detected.There were no other unusual organic acids. This profile isconsistent with ketosis due to intercurrent illness and/orprolonged fasting; however, be aware that it could also bethe only biochemical manifestation of two disorders ofketone bodies utilization: succinyl-CoA:3-ketoacid CoAtransferase deficiency (with persistent hyperketonemia andketoaciduria) and cytosolic acetoacetyl-CoA thiolasedeficiency. (Day 1) *In this sample, metabolites of ibuprofen were detected.There were no other unusual organic acids. (Day 10)	
Venous Blood Gas (VBG)	pH 7.36	7.31-7.41
	pCO2 26 mm Hg	40-50 mm Hg
	pO2 78 mm Hg	35-42 mm Hg
	HCO3 15 mmol/L Total	22-28 mmol/L
	CO2 15 mmol/L Venous	25-29 mmol/L
	O2 Saturation 95%	60-85%

corpus callosum and in the midbrain were also noted (Figure 2A). This is a nonspecific finding, although it can be a reversible finding observed with viral infections including influenza A. There was no evidence of intracranial abscess, hemorrhage, hydrocephalus or herniation. Cerebrospinal fluid (CSF) studies were promptly recommended, but the patient's mother vehemently declined to a lumbar puncture. Eventually, a CSF analysis was performed with parental consent on hospital day 8 which was found to be normal.

Surveillance brain and spinal cord MRI with and without contrast on hospital day 8 showed abnormal T2 hyperintensities in the cerebellar hemispheres with

Figure 1. Axial 3D T1 FS PG cranial MRI day 2 (1A) vs day 8 (1B) demonstrating resolved leptomeningeal enhancement in the cerebellum.

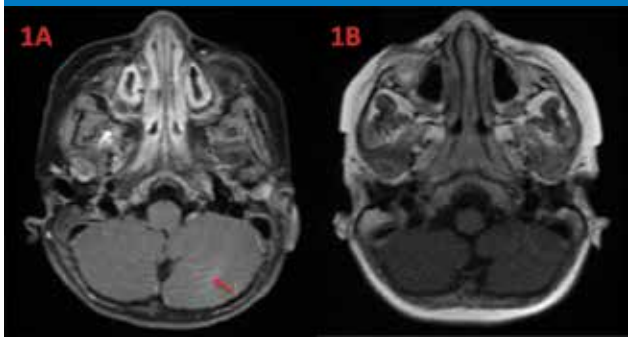
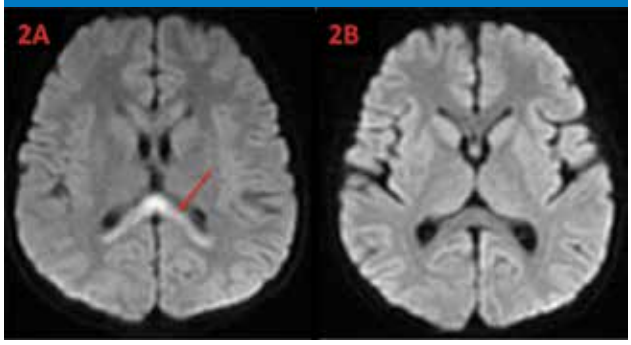


Figure 2. Axial DWI cranial MRI day 2 (2A) vs day 8 (2B) demonstrating resolved restricted diffusion in the splenium and the corpus callosum.



resolution of the cerebellar leptomeningeal enhancement (Figure 1B) and restricted diffusion in the corpus callosum (Figure 2B) seen on the previous MRI. Due to persistent weakness, intravenous immunoglobulin (IVIg) was added to his treatment regimen on Day 9. He completed a course of IVIG (2g/kg divided over 5 days).

He made gradual improvements in strength and tone with physical, occupational, and speech therapy over the course of his hospitalization. His hospital course was unfortunately complicated by a skin abscess on hospital day 20 near one of his intravenous sites for which he was initially given a course of clindamycin 10 mg/kg q6h for 24 hours and underwent an incision and drainage with culture collection. Following the culture resulting positive for *Staphylococcus aureus*, he was prescribed 500 mg cephalexin 3 times a day for 10 days. The patient was discharged on hospital day 30. Currently, the patient continues to have minimal restricted verbal communication and gait abnormalities which the authors suspect to have been part of his baseline, pre-AC neurologic impairment. He continues to follow with ancillary rehabilitation therapy with perpetual protracted progress.

Discussion

Acute cerebellar dysfunction is a rare but serious clinical syndrome in the pediatric population. One of the most common causes of acute cerebellar dysfunction in the pediatric population is AC. A retrospective study of AC in the pediatric population by Lancella et.al. showed that the most frequent clinical features of AC are broad-based gait disturbance (92%), balance disturbances (68%), vomiting (42%), fever (34%), headache (30%), and slurred speech (27%). Pleocytosis was the most common pathological finding in CSF studies. The majority of CT imaging showed no pathological findings for AC. Although, in the cases involving a definite diagnosis of AC, MRI results showed pathological findings.[3] According to the *American Journal of Neuroradiology* (AJNR), typical diagnostic features include bilateral hemispheric cerebellar swelling with cortical and white matter T2 hyperintensities and leptomeningeal enhancement. Although, cases have been reported where MRI findings included obstructive hydrocephalus, unilateral involvement, and normal T2 signal. Atypical features of MRI results would include cortical enhancement. AJNR also states that the CSF may show elevated protein and leukocytes, with lymphocytic predominance and normal glucose.[7] It is important to note that not all confirmed and documented cases of AC have pathological findings on MRI and diagnosis in these cases were based on clinical findings alone.[3]

Our case describes a pediatric patient with a clinical course compatible with AC related to Influenza A infection. Our patient presented with fever, encephalopathy, ataxia, hypotonia, febrile seizure, and weakness. The imaging results included a brain CT showing almost complete opacification of the paranasal sinuses and a left middle ear effusion. A brain MRI was also collected and described abnormal signaling in the splenium and genu of the corpus callosum and in the midbrain along with leptomeningeal enhancement of the cerebellum. A delayed CSF analysis was normal. The brain MRI, along with clinical features, was the basis of the diagnosis._

It is essential to differentiate AC from other possible causes of acute cerebellar dysfunction including but not limited to tumor, abscess, metabolic disease, meningitis, encephalitis, vasculitis, drug intoxication, and hereditary degenerative disorders.[3,7] Because there are very few reported cases of influenza cerebellitis in the literature, there is no consensus for a diagnostic approach to date. Due to the varied presentation for this diagnosis, a comprehensive workup is often performed including examination of CSF and MRI. While examination of CSF is not required for diagnosis of influenza-associated AC, a lumbar puncture should be

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Table 2. Summary table of reported cases of influenza-associated cerebellitis in literature. The table was adapted from Gökçe Ş, Kurugol Z, Aslan A and modified.3 Current case report is bolded.

Year	Age/Gender	Symptoms	Brain Imaging	CSF Analysis	Treatment	Outcome
1997 (Hayase, Y and Tobita, K)	31/F	Fever, myalgia, arthralgia, ataxia, dysarthria, truncal titubation, and hypotonia.	Normal	Normal	NA	Symptoms self-resolved in 3 months.
2004 (De Bruecker et al.)	4/F	Headache, fever, and neck stiffness.	MRI showed abnormalities in both cerebellar hemispheres and the vermis.	Elevated protein concentration and leukocyte cell.	NA	NA
2006 (Tlili-Graiess et al.)	4 patients 2-7/F-M	Headache, fever, vomiting, and ataxia.	In two cases, initial MRI demonstrated increased intensity on T2W and flair sequences of the cerebellar gray matter.	High lymphocytes and proteins in three patient samples. Normal values in one patient sample.	Prednisone (All patients)	Complete resolution of symptoms in 3 cases; persistent mild right upper limb paresis in 1 case.
2006 (Ishikawa et al.)	25/F	Fever, headache, ataxia, scanning slurred-speech, and dysarthria.	T2-weighted brain MRI demonstrated a high signal lesion in the cerebellar cortex.	Pleocytosis	Oseltamivir	Truncal ataxia normalized after 3 months.
2010 (Apok, V, Alamri, A, Qureshi, A)	14/F	Ataxia and drop in consciousness	Hydrocephalus	NA	External ventricular drain placed due to hydrocephalus development.	Residual left-sided ataxia after 3 months.
2013 (Hackett et al.)[4]	6/F	Headache, worsening dysarthria, nystagmus, and ataxia.	MRI of the brain confirmed findings consistent with cerebellitis.	Normal	Oseltamivir	All symptoms fully resolved after 1 week.
2013 (Sfeir, MM and Najem, CE)[5]	37/F	Fever, headache, ataxia, dysarthria, vomiting, fatigue, broad-based ataxic gait.	Brain MRI revealed enlarged bilateral cerebellar hemispheres and evidence of hypointensities.	Pleocytosis	Oseltamivir	All symptoms fully resolved after 2 months.
2017 (Gökçe Ş, Kurugol Z, Aslan A)[3]		Weakness, hypotonia, ataxia, intermittent hallucinations, vomiting, broad-based ataxic gait, dysmetria, and dysarthria.	Brain CT was normal. Brain MRI was normal.	Normal	Oseltamivir *1 g/kg IVIG started on day 4 due to intermittent hallucination and ataxia continuing.	All symptoms resolved by 13 days.
2023 (Nielson, K, Sievers, M, Taylor, C, Lim, P)[3/M]		**Fever, ataxia, hypotonia, febrile seizure, and weakness.**	**Brain CT was normal. Brain MRI showed abnormal signaling in the splenium and genu of the corpus callosum and in the midbrain. Brain MRI also showed leptomeningeal enhancement.**	**Normal**	**Oseltamivir, 100 mg/kg of Rocephin, methylprednisolone, and IVIG.**	**Patient continued to have restricted verbal communication and gait abnormalities at 2 months.**

performed in patients with findings of central nervous system infection alongside ataxia. CSF analysis has shown viral RNA in some previously reported cases. Thus, CSF findings and PCR evaluation of CSF studies could perhaps aid in confirmation of a diagnosis. It is important to note though that CSF Influenza PCR is only done in reference institutions. There have also been reported cases of AC with no viral RNA in the CSF but a positive nasopharyngeal swab specimen as in our case.[3]

Due to limited reported cases of influenza-associated cerebellitis, there is no defined treatment plan.[3] A previous literature review done by Gökçe Ş, Kurugol Z, Aslan A, found a total of 11 reported cases, including their own, from 1997-2016 (Table 2). In those reported cases, 4 (36%) used oseltamivir, 4 (36%) used methylprednisolone, 1 (9%) used IVIg, and 3 (27%) did not report a treatment.[3] Our patient was treated with a combination of 100 mg/kg Ceftriaxone (meningitic coverage), oseltamivir, methylprednisolone, and a delayed addition of IVIg due to protracted weakness. Ceftriaxone was discontinued once cultures were negative.

There is limited information regarding clinical outcomes for patients with influenza-associated cerebellitis. However, reports demonstrate a favorable course.[3] In the case of our patient, residual symptoms were improving but not resolved 2 months after initial diagnosis. Although, residual neurologic impairment could have been part of his baseline neurologic functioning. As highlighted in our case, continued multidisciplinary approach and protracted clinical follow-up is essential to optimizing outcomes in patients with cerebellitis.

Conclusion

Suspicion for AC should be considered in a patient exhibiting cerebellar symptoms and encephalopathy in the setting of a concomitant infectious process. AC is a significant cause of acute cerebellar dysfunction in the pediatric population and diagnosis of this pathology requires more sensitive imaging such as brain MRI. Influenza infection has been rarely implicated in AC. Due to the paucity of influenza-related AC cases, scarce evidence guides treatment approaches for this clinical syndrome. In our index case, similar treatment modalities were used which include methylprednisolone, oseltamivir, and IVIg concomitant with rehabilitative therapy. This management approach demonstrates a protracted but favorable clinical outcome.

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Pericardial Effusion as a Complication of Severe Primary Hypothyroidism

Andrii Maryniak, MD; Patrick Biskupski, MD; Filip Oleszak, MD; and Adam Stys, MD, FACC, FASA, FSCAI, FACP

Abstract

Large pericardial effusions with associated cardiac tamponade are a rare manifestation of hypothyroidism. We present the case of a 63-year-old female with chronic heart failure and newly diagnosed hypothyroidism, who presented to her primary care physician complaining of progressively worsening dyspnea. Chest radiography showed cardiomegaly and transthoracic echocardiography (TTE) revealed a large pericardial effusion with tamponade physiology. An emergent pericardial window was performed, resulting in an improvement in left ventricular systolic function. Pericardial tissue biopsy was normal. Thyroid function tests were consistent with severe primary hypothyroidism. After inpatient treatment with intravenous levothyroxine and interval resolution of symptoms without recurrence of effusion, the patient was discharged home on oral levothyroxine therapy. Close follow up with surveillance echocardiography was planned. While metabolic disorders are seldom thought of as an etiology, it is imperative for clinicians to recognize hypothyroidism as a cause of the pericardial effusion. It is one of the few reversible causes and delay in treatment can result in fatal sequelae.

Introduction

Hypothyroidism is a prevalent endocrine disease. Manifestations are variable and include cold intolerance, weight gain, fatigue, and menstrual irregularities among others. A rare complication is pericardial effusion. Etiologies of pericardial effusion commonly include trauma, malignancy, iatrogenic causes, pericarditis, connective tissue disorders, and malignancy, but rarely metabolic disorders like hypothyroidism. If left untreated expanding pericardial effusions can impair cardiac hemodynamics, causing tamponade. We present the case of an elderly female recently diagnosed with hypothyroidism whose symptoms of dyspnea and exertional intolerance were attributed to cardiac tamponade, a rare consequence of severe hypothyroidism.

Case Presentation

A 63-year-old female with a past medical history of hypertension, chronic systolic heart failure, and dyslipidemia presented to her primary care physician for follow-up for newly diagnosed hypothyroidism. She reported progressive dyspnea and exertional intolerance associated with worsening pedal edema. Initial evaluation included a chest X-ray which showed an enlarged cardiac silhouette. The level of thyroid stimulating hormone (TSH) was also measured and found to be >100 μIU/L. An electrocardiogram (ECG) showed normal sinus rhythm with low voltage in the precordial leads (Figure 1). She was referred to cardiology clinic for further workup. Transthoracic echocardiography in the ambulatory setting showed a large circumferential pericardial effusion with right ventricular diastolic collapse (Figure 2), and reduced LV systolic function, EF 25%. This was consistent with tamponade physiology and prompted referral to the nearest emergency department for consideration of pericardial drainage.

On arrival to the emergency department, the patient was hemodynamically stable. Blood pressure was 141/80 mmHg, heart rate was 61, respiratory rate was 18, and oxygen saturation on ambient air was 99%. The patient was seated

Figure 1. Initial electrocardiogram showing normal sinus rhythm and low voltage in the precordial leads.

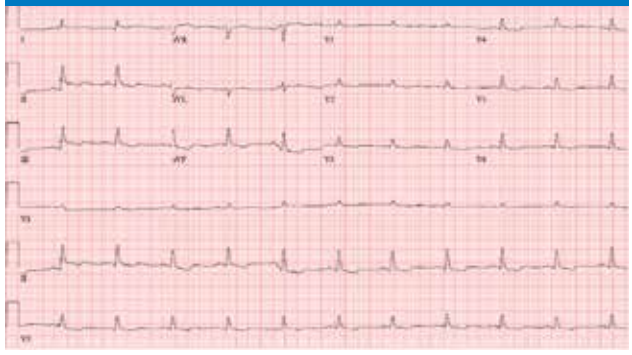

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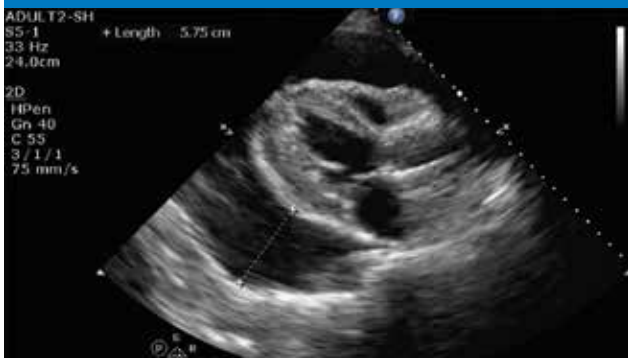
Figure 2. Parasternal long axis view showing a large circumferential pericardial effusion measuring 5.75 cm at its maximal depth (anechoic separation of pericardial layers).



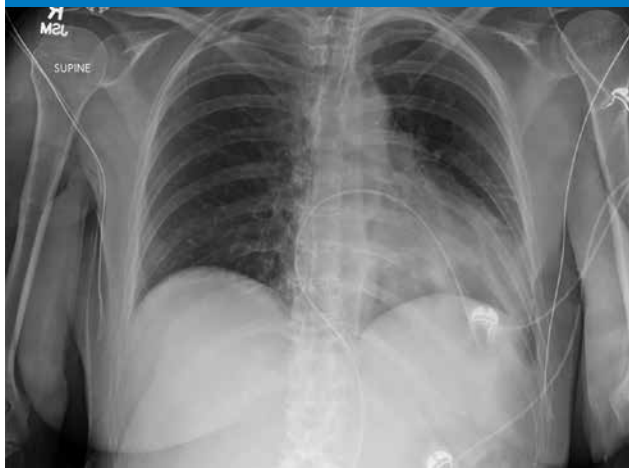
in fowler's position due to orthopnea and increased work of breathing. Cardiac auscultation revealed distant heart sounds, a regular rate and rhythm, and no apparent murmurs. Lungs were clear to auscultation with bronchovesicular breath sounds present. Jugular venous distension was appreciated to the angle of the mandible. 2+ non-pitting pedal edema was identified on examination of the lower extremities.

After initial triage, cardiothoracic surgery was consulted for consideration of pericardial drainage. Endocrinology was also consulted for assistance in the management of severe hypothyroidism and recommended treatment with intravenous levothyroxine 75 µg daily and workup for adrenal insufficiency (AI). Baseline cortisol level was 9.4 µg/dL. 30 minutes after cortisol stimulation testing, the level was 15.2 µg/dL, and after a subsequent 30 minutes 17.4 µg/dL. Adrenal insufficiency was excluded because a minimum cortisol level of 16-18 µg/dL was achieved.

Surgical drainage was performed. A 3 cm incision was made over the xiphoid, developing a sub xiphoidal plane. The pericardium was identified and incised. A very large bilious pericardial effusion was drained, approximately 2000 cc in volume. A 2x2 cm window of the pericardium was excised, and a pericardial biopsy was taken. This window was then extended into the right pleural space. A 24 French Blake chest tube was placed along the base of the diaphragm and secured to the skin (Figure 3). The drain was clamped and removed after no re-accumulation for 48 hours.

Repeat TSH while hospitalized was 144 µIU/L. Pericardial tissue biopsy was normal. Cytology was negative for malignancy. Pericardial fluid analysis revealed normal cell counts, protein, glucose, amylase, and absence of bacterial or fungal growth. Post-operative TTE showed resolution of the large effusion and improvement of left ventricular systolic

Figure 3. Anteroposterior chest X-ray after pericardial window and drain placement.



function, EF 45-50%. The patient was discharged on oral levothyroxine 100 µg/day and was instructed to follow up with her cardiologist.

Discussion

Hypothyroidism is a prevalent endocrine disease. Manifestations are variable depending on age, acuity and severity. Symptoms include cold intolerance, weight gain, fatigue, myxedema, and menstrual irregularities among others. On physical examination, hypothyroid patients may display goiter, xeroderma, non-pitting edema, bradycardia, diastolic hypertension, and delayed relaxation phase of deep tendon reflexes. Our patient presented in the months prior with symptoms of progressive dyspnea, fatigue, hair loss and examination identified increased peripheral edema, weight gain and severe skin dryness. Diagnosis is established by serologic assessment of TSH and thyroxine (T4) levels. Primary hypothyroidism which accounts for most cases of hypothyroidism, is characterized by an elevated serum TSH and low serum T4 concentration. Treatment is with hormone replacement, usually oral and less commonly parenteral levothyroxine.

Physiologically thyroid hormones effect cardiac myocytes via the regulation of genes influencing cardiac contraction, relaxation, and oxygen consumption. This affects cardiac output (CO), heart rate (HR), and system vascular resistance (SVR). Hypothyroid states decrease CO by 30-50%, decrease HR, and increase SVR.[1] Hypothyroidism also has an influence on vascular pathology by precipitating atherosclerosis via endothelial dysfunction, low-grade inflammation and dyslipidemia, which ultimately predisposes affected patients to coronary artery disease. A

rare complication is a pericardial effusion with progression to cardiac tamponade, a life-threatening condition. Effusion may occur as a result of increased capillary permeability and reduced lymphatic drainage.[1] Most consequences from hypothyroidism are reversible through treatment with levothyroxine however large pericardial effusions may require emergent drainage. AI should also be considered in young individuals with pericardial fluid accumulation and autoimmune comorbidities. In patients with AI, autoimmune mediated inflammation of the pericardium can cause acute pericarditis, and eventually lead to cardiac tamponade.[2,3] Adrenal insufficiency is primarily evaluated with cosyntropin stimulation whereby cortisol levels >16-18 μg/dL rule out the diagnosis.

Our patient's ECG met criteria for low voltage which is commonly associated with pericardial effusion and cardiac tamponade. This occurs due to fluid accumulation which dampens electrical signal reception by precordial and limb leads, as well as impaired hemodynamics.[4] Some studies have only shown an association between cardiac tamponade and low precordial lead voltage, suggesting that until enough pericardial fluid accumulates to impart hemodynamic compromise, dampening of electrical reception is not observed.[5] Contrastingly, low voltage has also been reported in severe hypothyroidism, without effusion.[6] Kerber et al. concluded that low ECG voltage was not a reliable indicator of pericardial effusion.[7]

In our case, pericardial window via a subxiphoid approach provided therapeutic relief and aided in diagnosis. Extension of the window into the right pleural space helped prevent re-accumulation and allowed for continuous drainage. Pericardiocentesis was not performed due to high risk of recurrence.[8] The optimal window has yet to be established with two approaches available: subxiphoid, as in our case, and left anterior mini-thoracotomy. A study by Langdon et al. evaluated the differences between these techniques. Postoperatively there was no difference in volume drained. There was a reduction in time to extubation and less analgesia with a subxiphoid approach. However, patients treated with the subxiphoid approach had a higher probability of re-accumulation and repeat procedures compared to mini-thoracotomy.[9]

Hypothyroidism-related pericardial effusion can be treated medically with levothyroxine, pericardiocentesis and/or pericardial window. In myxedema coma (severe hypothyroidism), ICU supervised administration of liothyronine sodium may be required at the discretion of an endocrinologist. Surgical drainage is the standard of care for hemodynamically significant cardiac tamponade. Long-term prevention of recurrent effusion relies on treatment with levothyroxine and maintenance of euthyroid state.

Conclusion

Pericardial effusions have a myriad of aetiologies, but metabolic causes are often overlooked.

Recognizing cardiac tamponade as a rare manifestation of hypothyroidism is critical for management and prevention of one of the few fully reversible causes of effusion.

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Antidepressant Medication Use During Lactation: A Review for Providers

Andrew Reuter, MS III; Andrew Nerland, MS III; Deborah Pritchett, PharmD; and Maria Skorey, MD

Abstract

This article presents a summary of information found within the existing medical literature on the pharmacological treatment options for maternal depression during lactation and the concurrent effects on the breastfeeding infant. Existing data on safety and efficacy varies by treatment modality. Medications used to treat depression are all secreted in breast milk to some extent; however, most antidepressants are considered relatively safe to use during breastfeeding. The selective serotonin reuptake inhibitors (SSRIs) sertraline and paroxetine are present in low levels and are considered preferred agents. Safety data for other antidepressants varies, however. monoamine oxidase inhibitors (MAOIs) should generally be avoided. Available references and resources can help providers optimize treatment of maternal depression while mitigating risk to the infant. Optimizing treatment of maternal depression is a complicated undertaking, which should be made in conjunction with the provider through shared decision making with the patient. Specific properties of any proposed medication, such as the relative infant dose and side effect profile, should always be taken into account during the decision-making process.

Introduction

The Center for Disease Control (CDC) provides an estimate that 1 in 8 mothers will experience postpartum depression.[1] More specifically, the CDC's Pregnancy Risk Assessment Monitoring System found 12.6% of South Dakota mothers had self-reported postpartum depressive symptoms in the year 2020.[1] It also reports that 83% of infants nationally are breastfed to some extent.[2] The most recent statistic available (2019) for infants born in South Dakota having ever been breastfed is 88.9%.[2] The benefits of breastfeeding are numerous. Exclusive breastfeeding for at least the first 6 months of a newborn's life, with continuation to one to two years of age or longer if mutually desired, is recommended by the American College of Obstetricians and Gynecologists (ACOG) and the American Academy of Pediatrics (AAP). Thus, many women could benefit from antidepressant medication use during the period in which they are breastfeeding. Unfortunately, the existing data regarding antidepressant use during lactation is not comprehensive and there are no widely accepted standards established for the use of these medications in this period.

The picture is further obscured by the lack of consensus on what values will serve as a marker of drug safety, largely due to the difficult nature of analyzing levels of psychotropic drugs in breast milk.[3] One of the most used markers is the relative infant dose (RID). This information may also be stated as weight adjusted percentage of the maternal dose. Both terms describe the percentage of maternal medication dose that is ingested by a child who is exclusively breastfed by that mother. They are generally thought to be safest when lower than 10%.[4] This paper will utilize both terms interchangeably, as they represent the same value.

While this paper will mainly focus on the risks associated with antidepressant use in breastfeeding, one must also consider the risks of lactating people *not* taking antidepressants when they are indicated. Untreated depression can be devastating to both mother and infant. It has been found that women who discontinue their antidepressant medication during the pre- or postpartum period are three times more likely to develop another episode of depression.[5] In a report from the Maternal Mortality Review Committees from 36 states, 22.7% of pregnancy-related deaths between 2017-2019 were from mental health conditions.[6] When considering antidepressant use in a breastfeeding mother, a shared decision-making approach must be utilized to evaluate the risks and benefits of treatment in light of the lack of data available to guide clinical decision making.

Selective Serotonin Reuptake Inhibitors (SSRIs)

SSRIs are among the most studied classes of medications for treating depression during lactation. These drugs are

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excreted in breast milk in varying proportions, but they have a strong safety profile, as adverse effects on the infant are most often limited to irritability, poor feeding, or uneasy sleep.[7] Specifically, sertraline and paroxetine are generally viewed as the safest options for use during breastfeeding due to their low passage into the breast milk and their large base of evidence relative to other medications. Both of these medications have RIDs at or below 1%.[8] Ram and Gandotra's 2015 systematic review of psychiatric drugs in pre- and postpartum women showed that the infant serum levels of sertraline were most often undetectable when the lactating mother was taking sertraline. These studies also reported either no adverse effects or benign sleep disruptions. This was also true for paroxetine, as infant serum levels were either low or undetectable, and adverse effects were either absent or limited to irritability.[9] Due to these factors, sertraline and paroxetine are first line treatment options for depression in lactating mothers.

In contrast, citalopram and fluoxetine are passed to the infant much more readily and are associated with a wider range of adverse effects. Ram and Gandotra reported maternal weight adjusted doses of citalopram as high as 6%.[9] Birnbaum et al. found detectable serum levels of fluoxetine in 78% of exposed infants and Kristensen et al. found maternal weight adjusted doses to be as high as 12%.[10,11] While most studies still do not report any adverse effects for infants, irritability and sleep disturbances are noted in a small number of studies. Brent and Wisner's 1998 case report described seizure-like activity and peripheral cyanosis in an infant exposed to fluoxetine, although the mother was also taking carbamazepine and buspirone.[12] More recent literature has not expanded meaningfully on this adverse effect profile. Additionally, Chambers et al. found evidence of reduced growth in infants exposed to fluoxetine.[13] While these reported adverse effects do not contraindicate fluoxetine in breastfeeding mothers, they drive the preference for sertraline and paroxetine.

Escitalopram, the S-isomer of citalopram, is another commonly prescribed SSRI. A variety of studies have found breast fed infants receive a maternal weight adjusted dose of 1-5%, on average.[14] There are few adverse effects reported with use of escitalopram, with some reports of behavioral or sleep disturbances, such as drowsiness, restlessness, agitation, poor feeding, and poor weight gain.[14] There is one report of necrotizing enterocolitis in an infant whose mother was taking escitalopram, although no causality was established.[15] Escitalopram prescribing information recommends that infants should be monitored for adverse reactions, such as those mentioned above, when the medication is given to breastfeeding mothers.[16] Infant caretakers should be counseled to report these symptoms to their child's provider.

Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)

The use of SNRIs during breastfeeding has not been formally studied as extensively as SSRIs; therefore, SNRIs are generally not regarded as first-line treatment for depression in lactation. However, the existing research on the effects and safety of venlafaxine and duloxetine during breastfeeding can be used to guide decision-making for treatment when indicated.

Venlafaxine has been found to have an RID around 7-8%, which is below the generally acceptable threshold of 10%.[17,18] The adverse effect profile of venlafaxine for a breastfeeding infant tends to be minimal. Bellantuono et. al. described no short-term adverse effects in 30 newborns across a review of 7 studies of breastfeeding mothers taking venlafaxine.[17] A review by Ram and Gandotra included 41 newborns across 8 studies and found no adverse events reported except for one case of postnatal adaptation syndrome, which can include such symptoms as jitteriness, irritability, feeding and sleeping difficulties in an infant exposed to SSRIs or SNRIs. The infant's symptoms subsequently subsided after a week of breastfeeding without alteration of maternal medication use. Other findings were mixed, with one study in the review reporting the adverse outcome of decreased body weight percentiles among ten venlafaxine-exposed infants while another study reported no neurobehavioral abnormalities upon follow-up of 27 venlafaxine-exposed infants.[18] Guille et. al. found no developmental abnormalities among two venlafaxine-exposed infants at one year of age.[19] According to the National Institutes of Health (NIH) Drugs and Lactation Database (LactMed), side effects of venlafaxine are rare for the breastfed infant, and the LactMed safety scoring system finds it is possible to use the drug while breastfeeding; however, the drug is found in the plasma of most breastfed infants, and there is disagreement regarding the extent of its safety during breastfeeding.[20]

While exposure to duloxetine in breastmilk has been shown to be significantly lower than venlafaxine with an RID of around 1%, less data exists surrounding its effects on the infant.[17,18] It is estimated that an infant's daily dosage of duloxetine would be approximately 10,000 times lower than the breastfeeding mother's dosage, and a maternal weight adjusted infant dose of duloxetine was found to be 0.14% (maximum 0.25%) compared to venlafaxine at 3.2% (maximum 5.9%).[21,22] Additionally, duloxetine does not

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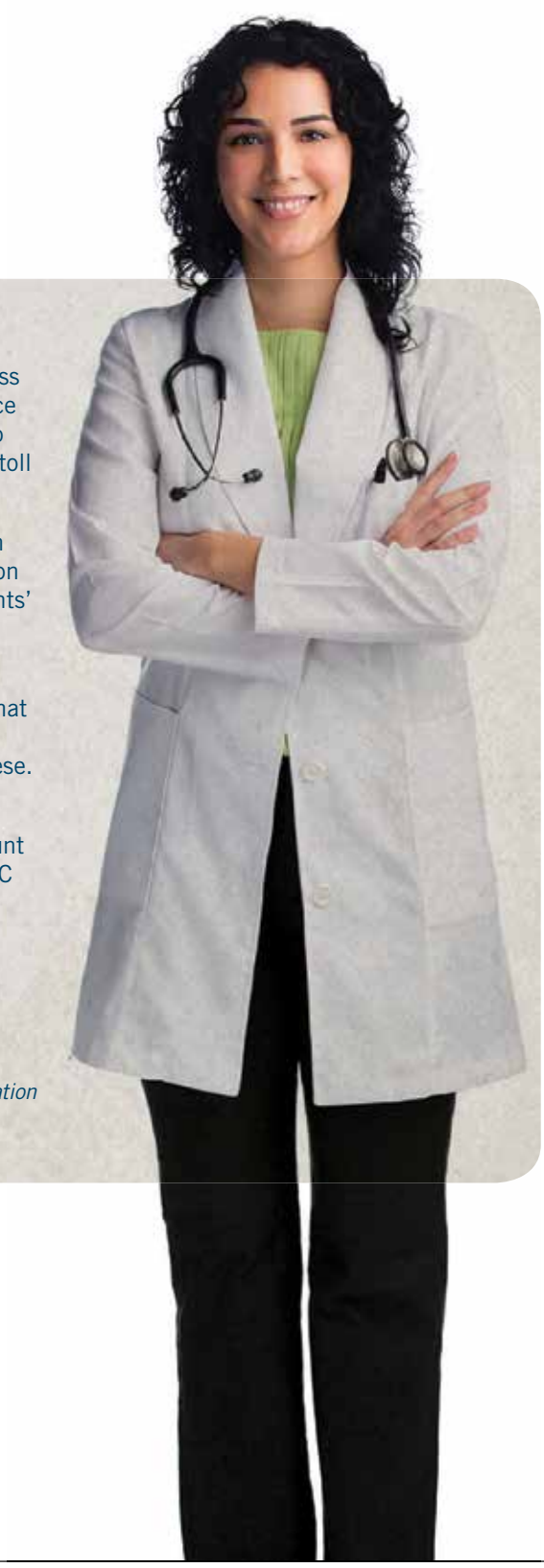

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have any circulating active metabolites whereas venlafaxine does, potentially causing even less exposure for the breastfed infant. LactMed reports that duloxetine is acceptable to use cautiously during breastfeeding if it is required by the mother.[23]

Generally, venlafaxine and duloxetine are not suggested as first-line options during breastfeeding as there is very little evidence surrounding them in comparison to SSRIs. If a breastfeeding mother has failed first-line treatments and has had past success being treated with venlafaxine or duloxetine, these drugs may be acceptable alternatives.

Atypical Antidepressants

Similar to the SNRIs (and all following classes of drugs in this paper), evidence regarding the use of atypical antidepressant medication in pregnancy is lacking. Bupropion has been shown to have an RID as low as 1.4%. While reported infant adverse effects of bupropion are also scarce, there have been case reports indicating that infants of mothers being treated with bupropion developed seizures which resolved with supportive measures.[24] In this particular study, the diagnostic workup was negative, although the mother was concurrently taking escitalopram, which may have contributed. While it is difficult to know how directly bupropion use contributed to this instance, this potential side effect should be taken into account in infants at high risk of seizures.

Mirtazapine also has some evidence supporting its use in lactation, albeit limited. RID of mirtazapine has been found to be 1.5%.[25] Various studies have monitored for adverse effects on breastfed infants exposed to mirtazapine, but the majority of these studies reported no effects. There was one report of restlessness, but this could not be solely attributed to mirtazapine use, as the mother was concurrently taking paroxetine.[26] Overall, bupropion and mirtazapine are not first-line drugs during lactation due to their lack of evidence relative to other medications. Both should be considered safe if other therapies are not effective, however.

Tricyclic Antidepressants

Tricyclic antidepressant medications have been shown to have low passage into the breast milk, with RIDs ranging between 1-2%.[10] Among these medications, nortriptyline is regarded as the safest option. LactMed states that at least 44 infants have been reported as being exposed to nortriptyline in varying maternal doses, with none of these infants showing any adverse effects. Twenty-seven of these infants were formally tested and found to have unaffected growth and development patterns.[27] Nortriptyline's strong safety profile makes it a good alternative in the event of failure of SSRI therapy.

Amitriptyline is not as favorable as nortriptyline. Although it also has low passage into breastmilk, there have been reports of sedation in neonates whose mothers are taking the medication.[28] Specifically, a 15-day old infant was found to have severe sedation and reduced feeding that correlated temporally with initiation and discontinuation of amitriptyline.[29] Because of this, amitriptyline should be used with caution in neonates. However, LactMed states that infants over the age of 2 months are unlikely to experience adverse effects.[28]

Monoamine Oxidase-Inhibitors

Monoamine Oxidase Inhibitors are no longer commonly used pharmacotherapies in patients with unipolar depression due to extensive side effects, drug interactions, food interactions, overdose potential, and the emergence of more targeted and specific depression treatments. As a result of their limited use in the modern era, there is scarce data on use during pregnancy. One case study of a breastfeeding mother on selegilene reported undetectable levels in the infant's serum, and no developmental abnormalities were seen after 5 months.[30] The minimal lactation information available for isocarboxazid, phenelzine, and tranylcypromine indicates alternative agents are preferred.

Multiple Medications

Other factors may complicate the evaluation of medication safety during breastfeeding. The need for multiple antidepressant medications in mothers who are lactating may increase the risk for adverse effects, especially if the drugs being used share similar side-effect profiles. Premature and newborn infants, or infants with medical conditions that may decrease metabolism and excretion may be more likely to exhibit side effects from medications in breast milk. In these scenarios, communication should be established between maternal and infant provider to discuss treatment decisions. Further, the resources listed below can inform these discussions and help providers guide their patients.

Resources for Providers

There are several evidence-based and peer-reviewed resources available to assist providers in facilitating the best treatment options for their lactating patients.

The LactMed database presented by the National Institutes of Health contains an alphabetized list of medications and summarizes the safety and efficacy profile of each medication

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during lactation and breastfeeding.[31] Its use is recommended by professional societies such as the American College of Obstetricians and Gynecologists (ACOG) and the American Academy of Pediatrics (AAP).

The InfantRisk Center at Texas Tech University Health Sciences Center is a call center and online resource (www.infantrisk.com) which can be utilized by healthcare providers and patients alike for questions and concerns regarding breastfeeding and infant exposure to drugs. The InfantRisk Center can be reached by the number 1-(806)-352-2519 between the hours of 8:00am-3:00pm Central Standard Time.

MotherToBaby (www.mothertobaby.org) is a leading source of evidence-based information on maternal and infant exposure to medications and other potential hazards during breastfeeding with backing by the Centers for Disease Control and Prevention and the Food and Drug Administration's Office of Women's Health. MotherToBaby provides online resources, including over 250 fact sheets on exposure topics, for both patients and providers. A MotherToBaby representative can be contacted toll free by phone at (866) 626-6847, by text via the number (855) 999-3525, and online live chat is available.

Conclusion

The decision to use antidepressant medication during lactation is multifaceted and should be a joint decision-making process between patient and provider, taking into account the benefits of breastfeeding to both mother and baby, the risks of untreated maternal depression, patient preferences, available treatment options, and known and unknown effects of medication exposure to the infant. Overall, sertraline and paroxetine are preferred medications for treatment of depression while breastfeeding, as they are present in low levels in breast milk, have favorable evidence surrounding their use and have few reports of adverse effects. However, some mothers may have previously failed therapy with sertraline or paroxetine or are well-controlled on other antidepressant medications. While these other classes may not enjoy the same depth of research as sertraline and paroxetine, most are not absolutely contraindicated in the lactation period. Generally, it is not recommended to switch antidepressant therapies in the lactation period, as this puts the mother at risk of relapse.[32] In these instances, providers may find helpful information in online databases, such as LactMed, to help guide patient centered and evidence-based discussions.

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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.

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Congenital Sucking Blisters

Peter Paul C. Lim, MD; Kate Boos, MD; and Maria Talavera-Barber, DO

A 2-day old female baby born by spontaneous vaginal delivery at 39 weeks presented with congenital vesicles. Pregnancy complications include well-controlled gestational diabetes and a history of vaginal herpes simplex II (HSV-2) infection. Prenatal imaging did not show any abnormalities. Prior to this pregnancy, the mother had two episodes of vaginal lesions requiring valacyclovir prophylaxis at 36 weeks of gestation with reported faithful compliance. The father also had a history of genital HSV-2 infection and placed on suppressive valacyclovir therapy. The mother did not have active lesions during delivery. The baby was born vigorous. On physical exam, two vesicles in the left dorsal wrist (Figure A and B) were noted with erythematous base and mild peripheral scaling. The vesicles were unroofed and sent for HSV-1 and HSV-2 PCR and bacterial culture, which were all negative. HSV-1 and -2 surface and blood PCR were also negative. The scab healed uneventfully without further treatment. Infant was diagnosed with a congenital sucking blister. Congenital sucking blister (CSB) occurs in about 1:250 live births although the true incidence is unknown and may be lower than this.[1] While a benign condition, it usually mimics other blistering conditions that may be associated with infectious or a primary dermatologic condition, prompting a thorough but directed work up. The most common infectious conditions presenting very similar to CSB include HSV, varicella zoster, bullous impetigo, syphilis and candidiasis. Primary dermatologic conditions mimicking CSB include neonatal lupus, hereditary bullous disorders and epidermolysis bullosa.[2] CSB is a wastebasket diagnosis that requires a spectrum of clinical diagnostics that can be guided by prenatal history and maternal risk factors.

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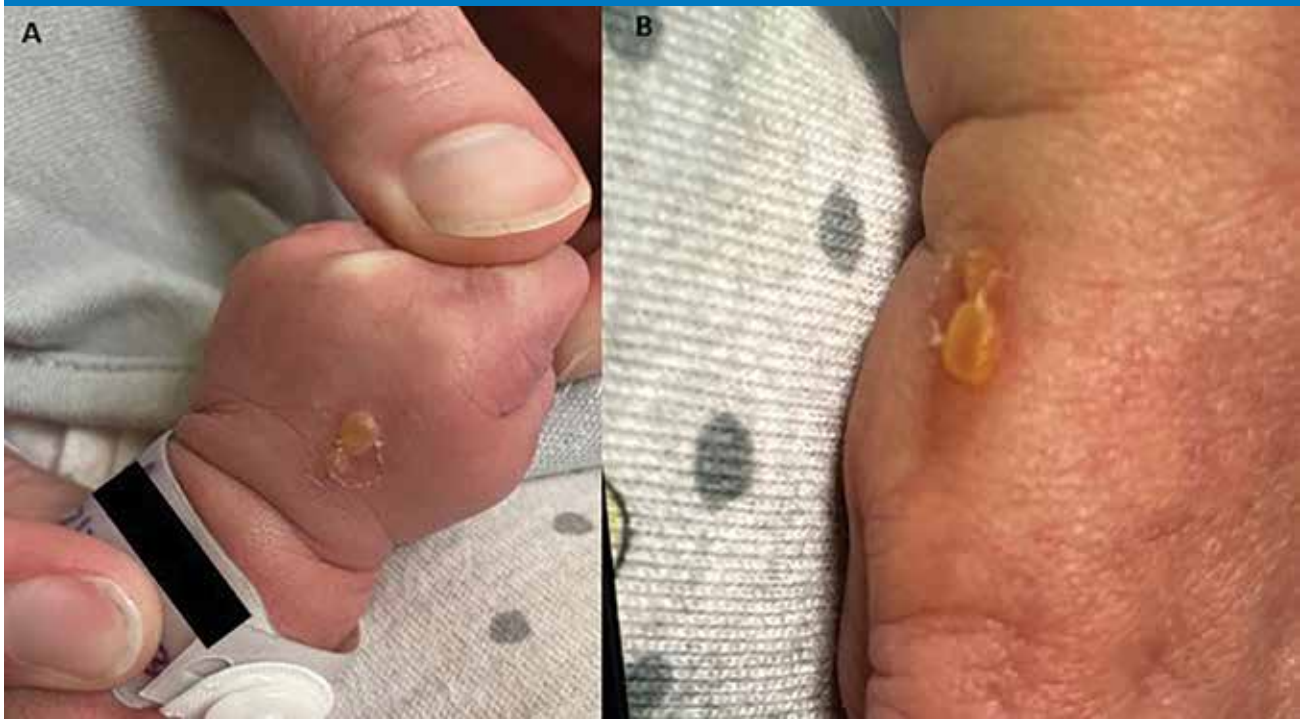
Figure 1. On physical exam, two vesicles in the left dorsal wrist (A,B) were noted with erythematous base and mild peripheral scaling.



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TRIBAL HEALTH

Interventricular Mechanical Dyssynchrony Due to Leadless RV Septal Pacing Culminating in Cardiogenic Shock

Muhammad Hamza Saad Shaukat, MBBS; Luke Merrill, MS IV; Matt Pohlmann, MS IV; and Orvar Jonsson, MD

Introduction

A 69-year-old woman with ischemic cardiomyopathy and improved heart failure with reduced ejection fraction (HFrEF) underwent leadless pacemaker implantation for complete heart block. Persistent RV septal pacing led to interventricular mechanical dyssynchrony-mediated decompensation to cardiogenic shock.

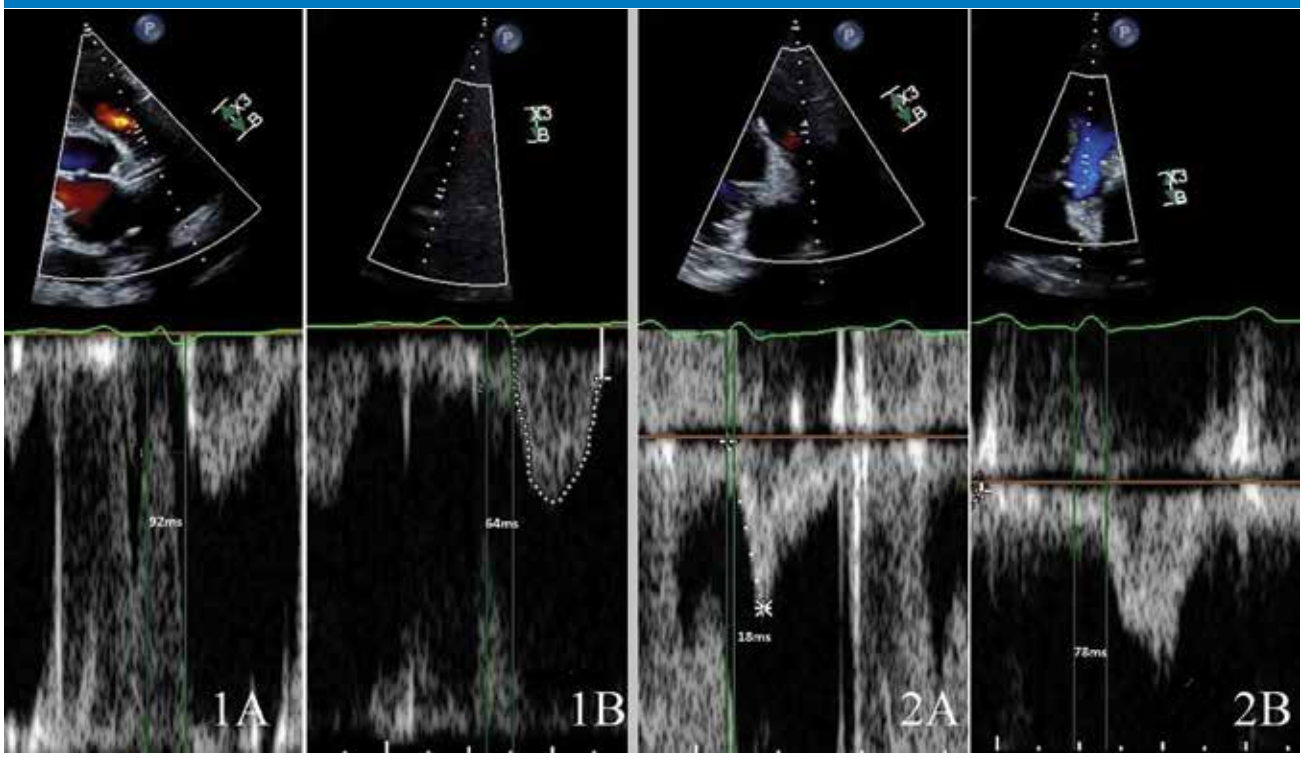
Although guidelines recommend cardiac resynchronization therapy-pacing (CRT-P) in ambulatory patients with high-degree AV block and baseline LVEF = <50%, hemodynamic severity of LV dyssynchrony is difficult to predict.[1]

Among patients with LVEF 36-50% and no indication for cardioverter-defibrillator, echocardiographic interventricular mechanical dyssynchrony index* (interventricular difference in time to onset of systole) may help identify patients at risk for hemodynamically significant ventricular dyssynchrony requiring cardiac resynchronization therapy for pacing.

Case Description

A 69-year-old woman with type 1 diabetes mellitus was admitted for new HFrEF (EF 20%). Invasive coronary angiogram showed severe ostial left main, critical proximal LAD and circumflex disease. High surgical-risk for CABG (frailty & deconditioning), she underwent Impella-supported/ intravascular ultrasound-guided percutaneous coronary intervention to ostial left main, proximal LAD & circumflex. The patient was discharged on guideline-directed medical therapy and EF improved to 40-45% on follow-up. Later she had complete heart block treated with a leadless

Figure 1. No interventricular mechanical dyssynchrony before PPM. Pulse wave doppler: onset of systole in RV (panel 1A) is 28ms after that in LV (panel 2B). Interventricular mechanical dyssynchrony after PPM implantation. Pulse wave doppler: onset of systole in RV (panel 2A) is 60ms before that in LV (panel 2B).



permanent pacemaker (PPM). On three-month clinic visit, EF was stable at 40-45% with 97% RV pacing.

Five months after leadless PPM implantation, the patient was admitted with cardiogenic shock. LVEF was 20-25% with moderate mitral regurgitation & pacing-related paradoxical septal motion. Interval increase in inter-ventricular mechanical dyssynchrony index from ~28ms to 60ms (reference: <40ms; Figure 1) after leadless PPM implantation suggests the etiology of cardiogenic shock despite initial improvement in ischemic cardiomyopathy/ LVEF was ventricular dyssynchrony from high RV septal pacing burden.

Interventricular mechanical dyssynchrony index on echocardiography may help identify patients at risk for hemodynamically significant ventricular dyssynchrony.

Compared to endocardial lead pacemakers, leadless pacing is less invasive but cannot be upgraded to cardiac resynchronization therapy. In this case, despite an improving EF after percutaneous coronary intervention, endocardial pacemaker with cardiac resynchronization therapy would have been preferable to leadless pacing.

* Interventricular mechanical dyssynchrony index = [Time to onset of systole in left ventricle] – [Time to onset of systole in right ventricle.]

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Match Day 2024!

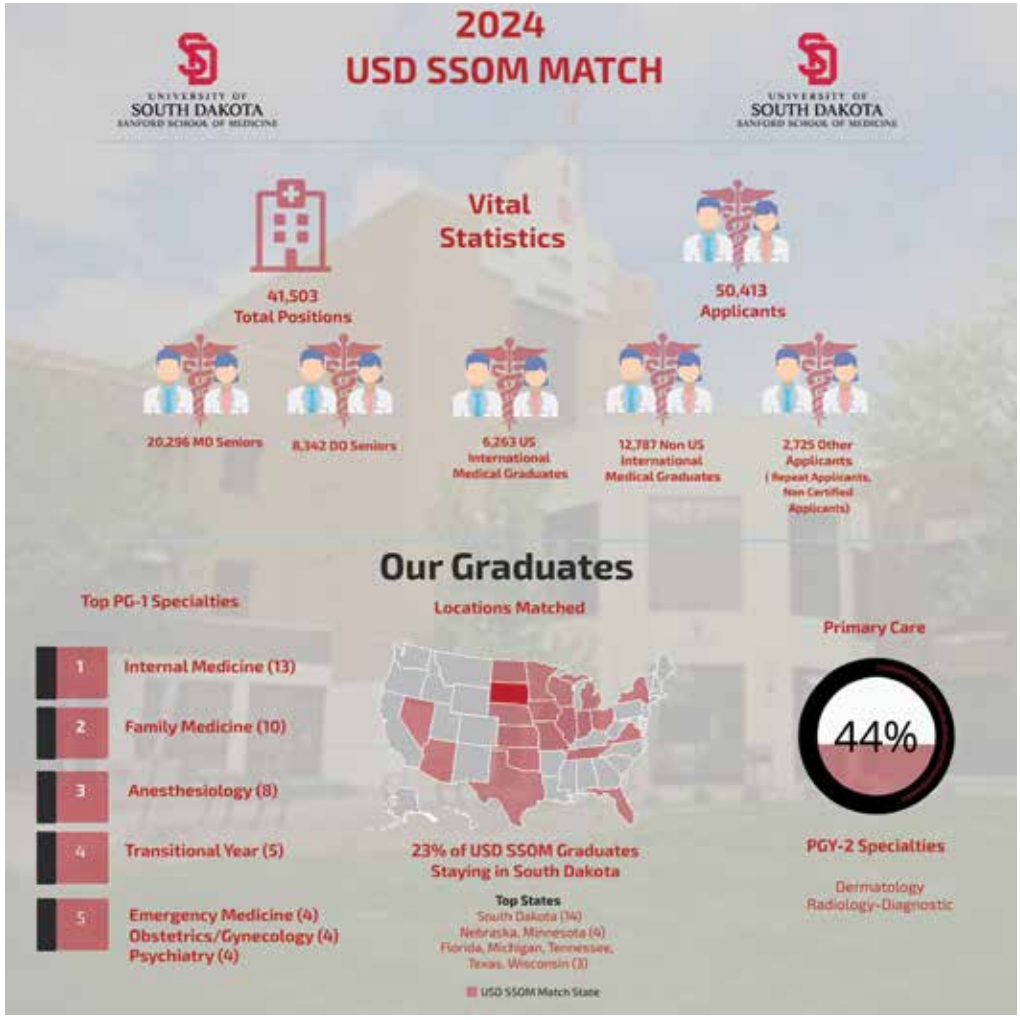
Suzanne Reuter, MD MPH

Congratulations to the Class of 2024 on a very successful match! Match Day is recognized each year as that momentous day when aspiring doctors learn where they will complete their post-medical school training. Students have spent countless hours applying to and interviewing with residency programs. There was a record high 50,413 applicants in the 2024 residency Match.

The 2024 Match offered 19,423 primary care positions, which totaled 46.8 percent of all residency positions offered in the Match. Forty-four percent of students from the University of South Dakota Sanford School of Medicine (SSOM) matched into a primary care specialty. SSOM graduates will be training at programs across the U.S. in a wide range of specialties and twenty-three percent will be training in South Dakota for their residency in family medicine, internal medicine, psychiatry, and transitional year.

Match Day celebrations were held at SSOM clinical campuses in Sioux Falls, Rapid City, and Yankton. We are so very proud of the hard work and dedication of our students and wish them well in their educational journey. We look forward to their return to South Dakota to practice medicine in the future.

About the Author:
Suzanne Reuter, MD, MPH, Interim Associate Dean, Medical Student Affairs; Professor, Department of Pediatrics, University of South Dakota Sanford School of Medicine.



University of South Dakota Sanford School of Medicine 2024 Residency Match Listing

Last Name	First Name	PG1 Inst Name	PG1 Pgm Name	PG1 Location	PG2 Inst Name	PG2 Pgm Name	PG2 Location
Anderson	Lucas	Lakeland Regional Health	Transitional Year	LAKELAND, FL			
Bamberg	Brittany	University of Nebraska Medical Center	Psychiatry	OMAHA, NE			
Behrend	Christopher	Hennepin County Medical Center	Internal Medicine	MINNEAPOLIS, MN			
Blankespoor	Thomas	Mayo Clinic School of Graduate Medical Education	Anesthesiology	ROCHESTER, MN			
Boeckholt	Tayt	Ascension St. John Hospital	General Surgery	DETROIT, MI			
Boleyn	Jennifer	Vanderbilt University Medical Center	Anesthesiology	NASHVILLE, TN			
Bormann	Sydney	University of Kansas School of Medicine	Plastic Surgery (Integrated)	KANSAS CITY, KS			
Brown	Ethan	Center for Family Medicine	Family Medicine	SIOUX FALLS, SD			
Buchanan	Jamuna	University of Nebraska Medical Center	Pediatrics	OMAHA, NE			
Buchholz	Alaire	University of Iowa Hospitals and Clinics	Obstetrics-Gynecology/Rural	IOWA CITY, IA			
Dirks	Shouri	State University of New York Health Science Center	Neurology	BROOKLYN, NY			
Eastman	Benjamin	Children's Mercy Hospital	Child Neurology	KANSAS CITY, MO			
Edwards	Cole	Kirk Kerkorian School of Medicine at University of Nevada	Psychiatry	LAS VEGAS, NV			
Fiegen	Noah	University of Tennessee College of Medicine	Family Medicine	CHATTANOOGA, TN			
Forest	Kennedy	University of South Dakota	Internal Medicine	SIOUX FALLS, SD			
Gates	Steven	Monument Health Rapid City Hospital	Family Medicine	RAPID CITY, SD			
Grosdidier	Morgan	HCA Medical City Healthcare	Internal Medicine	ARLINGTON, TX			
Gubbrud	Jonathan	University of Nebraska Medical Center	Emergency Medicine	OMAHA, NE			
Haskell-Hanisch	Brianne	University of South Dakota	Transitional Year	SIOUX FALLS, SD	Marshfield Clinic	Dermatology	MARSHFIELD, WI
Hemmer	Allison	University of Oklahoma College of Medicine	Internal Medicine	OKLAHOMA CITY, OK			
Hohn	Layne	University of Tennessee Graduate School of Medicine	Anesthesiology	KNOXVILLE, TN			
Hollinsworth	Troy	Orlando Health	Orthopaedic Surgery	ORLANDO, FL			
Holmes	Andrew	University of South Dakota	Transitional Year	SIOUX FALLS, SD	University Michigan Hospitals	Radiology-Diagnostic	ANN ARBOR, MI
Hurd	Autumn	University of Minnesota Medical School	Family Medicine	DULUTH, MN			
Jaton	Eric	Rush University Medical Center	Anesthesiology	CHICAGO, IL			
Jensen	David	University of Nebraska Medical Center	Medicine-Pediatrics	OMAHA, NE			
Johnke	Logan	University of South Dakota	Internal Medicine	SIOUX FALLS, SD			
Jones	Marlee	University of Arizona	Opthalmology	TUCSON, AZ			
Kennedy	Carolyn	University of Nebraska Medical Center	Emergency Medicine	OMAHA, NE			
Kim Sawtelle	Kirsten	University of Rochester/Strong Memorial	Pediatrics	ROCHESTER, NY			
King	Ryan	University of Florida College of Medicine-Shands Hospital	Anesthesiology	GAINESVILLE, FL			
La Nasa	Anthony	University of South Dakota	Transitional Year	SIOUX FALLS, SD	University of Nebraska Medical Center	Radiology-Diagnostic	OMAHA, NE
Lanier	Ross	Indiana University School of Medicine	Medicine-Pediatrics	INDIANAPOLIS, IN			
Larsen	Autumn	University of Kansas School of Medicine	Obstetrics-Gynecology	KANSAS CITY, KS			
McLaury	Madison	University of Michigan Hospitals	Anesthesiology	ANN ARBOR, MI			

University of South Dakota Sanford School of Medicine 2024 Residency Match Listing

Last Name	First Name	PG1 Inst Name	PG1 Pgm Name	PG1 Location	PG2 Inst Name	PG2 Pgm Name	PG2 Location
Merrill	Lucas	Center for Family Medicine	Family Medicine	SIOUX FALLS, SD			
Mohr-Eymer	Conrad	Gundersen Lutheran Medical Foundation	Internal Medicine	LA CROSSE, WI			
Morris	Kahlen	Mayo Clinic School of Graduate Medical Education	Urology	ROCHESTER, MN			
Mutsch	Kailyn	MercyOne North Iowa Medical Center	Internal Medicine	MASON CITY, IA			
Myrmoe	Anna	University of South Dakota	Internal Medicine	SIOUX FALLS, SD			
Nielson	Katherine	HealthPartners Institute	Emergency Medicine	BLOOMINGTON, MN			
O'Connor	Hunter	University of Nebraska Medical Center	Orthopaedic Surgery	OMAHA, NE			
Ochoa	Lauren	University of North Dakota School of Medicine	Psychiatry	FARGO, ND			
Orozco	Brenda	Center for Family Medicine	Family Medicine	SIOUX FALLS, SD			
Pohlmann	Matthew	University of Michigan Hospitals	Anesthesiology	ANN ARBOR, MI			
Pond	Kristi	University of Toledo	Obstetrics-Gynecology	TOLEDO, OH			
Quinn	Garrett	University of Texas at Austin Dell Medical School	Obstetrics-Gyneology	AUSTIN, TX			
Rath	Joseph	University of Oklahoma College of Medicine	Orthopaedic Surgery	OKLAHOMA CITY, OK			
Redlin	Tanner	University of South Dakota	Transitional Year	SIOUX FALLS, SD	University of Wisconsin Hospital and Clinics	Radiology-Diagnostic	MADISON, WI
Ricke	Amanda	ProHealth Waukesha Memorial Hospital	Family Medicine	WAUKESHA, WI			
Risinger	Casey	University of Texas Medical Branch	Anesthesiology	GALVESTON, TX			
Rumrill	Christopher	Virginia Commonwealth University Health Systems	Internal Medicine	RICHMOND, VA			
Rupe	Eric	University of South Dakota	Internal Medicine	SIOUX FALLS, SD			
Schulte	Lillian	Gundersen Lutheran Medical Foundation	Family Medicine	LA CROSSE, WI			
Schulz	Carter	University of Nebraska Medical Center	Internal Medicine	OMAHA, NE			
Sievers	Meaghan	Mayo Clinic School of Graduate Medical Education	Emergency Medicine	ROCHESTER, MN			
Slunecka	John	University of Minnesota Medical School	Internal Medicine	MINNEAPOLIS, MN			
Trierweiler	Hannah	Center for Famliy Medicine	Family Medicine	SIOUX FALLS, SD			
Van Der Werff	Brenden	University of Louisville School of Medicine	Family Medicine	GLASGOW, KY			
Van Kalsbeek	Mitchell	University of Arizona College of Medicine	Internal Medicine	TUCSON, AZ			
Wei	Henry	University of South Dakota	Psychiatry	SIOUX FALLS, SD			

Comprehensive Cardiac Care

Across Nebraska, the Region and Beyond

In the Dr. C.C. & Mabel L. Criss Heart Center at Children's Nebraska, pediatric cardiology and heart surgery teams specialize in treating a range of congenital heart defects and offer comprehensive cardiac care. From the Fetal Heart to Adult Congenital Heart Disease (ACHD) programs, Children's has the expertise to provide exceptional cardiac care in all stages of life. In addition to providing care in Omaha, Children's cardiologists conduct pediatric and congenital heart disease outreach clinics in 11 locations, providing the same standard of specialty care closer to home.

CUTTING-EDGE CARE

Children's is dedicated to staying at the forefront of medical innovations, investing in state-of-the-art equipment and expert providers.

One such investment is to offer comprehensive interventional and diagnostic cardiac catheterization procedures. Our state-of-the-art cardiac catheterization suites double as full-service operating rooms if and when surgery is needed. The suites house ARTIS pheno, a robotic C-arm X-ray that provides swift, 360-degree images of even the tiniest hearts with limited exposure to radiation for patients. Children's was the first in the world to adopt ARTIS pheno in a pediatric setting.

Children's also houses a first-in-the-region Cardiac Care Unit (CCU), a floor exclusively dedicated to caring for the full spectrum of pediatric heart patients. Working alongside Children's pediatric specialists, the CCU team includes highly skilled nurses and advanced practice providers specially trained in providing care to pediatric patients with cardiovascular conditions.

EXTENDING EXCELLENCE ACROSS THE REGION

Understanding the challenges that geographic distance can pose to families, Children's has established outreach clinics across Nebraska, Iowa and South Dakota. The outreach clinics bring the expertise and innovation of Children's pediatric cardiac care right to the communities we serve. Children's cardiology outreach clinics are offered in:

Nebraska: Columbus, Grand Island, Kearney, Hastings, Lincoln, Norfolk and North Platte

Iowa: Atlantic and Sioux City

South Dakota: Rapid City and Sioux Falls

When visits to Children's main campus are necessary, patients and families traveling from more than 90 miles outside of Omaha can access the Rainbow House, a 56-room overnight guest house for a patient's immediate family.

OUR PROGRAMS & SERVICES

Children's offers a range of cardiac programs and services to meet the needs of our patients and families. Our providers use a patient-centered approach to care, meaning each patient receives an individualized care plan tailored to their specific condition. Cardiac programs offered at Children's include:

- Adult Congenital Heart Disease
- Aortopathy Program
- Cardiac Rehabilitation
- Cardiothoracic Surgery
- Cardiovascular Genetics
- Diagnostic Testing & Advanced Cardiac Imaging
- Electrophysiology
- Fetal Cardiology
- Fontan Program, in partnership with Children's Adolescent Medicine and Gastroenterology, Hepatology & Nutrition
- Interventional Cardiology
- Pediatric Cardiology
- Pulmonary Hypertension Program, in partnership with Children's Pulmonology
- Single Ventricle Program
- 3D Visualization Lab

Scan the QR code to learn more about Children's Criss Heart Center and how to make a referral. For immediate consult or transport, call (855) 850-KIDS (5437).

Children's NEBRASKA

Member News

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

2024 SDSMA Annual Leadership Conference

Register Now!

Join us for the 2024 SDSMA Annual Leadership Conference on Friday, May 31 at the Holiday Inn Rapid City Downtown! This conference is a benefit of your SDSMA membership – there is no registration fee for members (ticket purchase required for some events and meals). Registration, details and the schedule are posted sdsma.org.

Presentations Will Focus on Native American Healthcare

Join us for a day of learning and engagement as we address Native American healthcare issues and challenges. Native American communities face a complex set of issues and concerns regarding healthcare, resulting in significant disparities compared to the general population.

Medical Student Poster Session

Be sure to join us for the Medical Student Poster Session at 1 pm followed by a presentation given by the #1 abstract recipient. This opportunity helps USD SSOM students improve their CVs and their competitiveness for medical residencies.

Submit a Policy Issue & Participate in the Open Forum

Do you have a policy issue you'd like to bring to the SDSMA's attention? Make plans to address the SDSMA Policy Council. Policy issues submission forms are available at sdsma.org. Submissions are being accepted until May 10. The open forum will be held at the Holiday Inn Downtown Rapid City during the conference.

Events and Activities

- **University of South Dakota Sanford School of Medicine Update** – Tim Ridgway, MD – Dean, USD SSOM
- **Physician advocacy update from the American Medical Association** – Bruce Scott, MD – President-elect, AMA
- **Syphilis and measles in South Dakota** – Melissa Magstadt – Secretary, Department of Health
- **Panel discussion on access to care**
- **Membership open forum** – submit an issue at sdsma.org
- **SDSMA PAC lunch** – Walking Forward Program
- **Medical student poster session and oral presentation of #1 abstract**
- **Policy Council meeting**
- **Membership mixer**
- **Awards banquet & scholarship recognition**

Register at sdsma.org

FRIDAY, MAY 31
HOLIDAY INN DOWNTOWN
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South Dakota State Medical Association

LEGISLATIVE ACCOMPLISHMENTS

2024 South Dakota Legislature

Overview

South Dakota's 2024 Legislative Session opened January 9 and continued through March 7, with the 38th legislative day held on March 25. Of the 504 pieces of legislation brought forward, 54 had the potential to impact health care in South Dakota. The SDSMA and its legislative team began preparations and outreach to legislators prior to the first legislative day, which is critical to establishing and developing relationships necessary to successfully advocate during South Dakota's brief 38-day legislative session. In addition, the SDSMA Board of Directors meets with the legislative team on a regular basis during the session to provide direction on specific pieces of legislation.

The session got off to a fast start and kept that pace throughout its run. During the nine-week session, the SDSMA worked on a wide range of issues to protect the practice of medicine and to enhance the delivery of medical care. Some highlights include:

Promoting the art and science of medicine

The South Dakota State Legislature began its 2024 session with Governor Kristi Noem's State of the State address in which she spoke on several issues of interest to the SDSMA including overdose deaths due to fentanyl and xylazine, telemedicine and emergency medical services in rural areas, and care coordination for pregnant mothers enrolled in Medicaid. The governor also voiced her support for workforce development initiatives including multiple interstate licensure compacts that would seek legislative approval.

HB 1168 sought to revise state statute regarding pharmacists who refuse to dispense drugs for an off-label use during a public health emergency. The bill was brought in response to the debate over the use of ivermectin during the COVID-19 pandemic. The SDSMA opposed the bill, which was defeated 12-0 by the House Health and Human Services Committee.

SB 43 permits DOH to promulgate rules establishing procedures for the imposition of fines or the probation, suspension, and termination of the registration certificate of a medical cannabis establishment that commits multiple or serious violations. Consistent with its position supporting strict state regulation of medical cannabis, SDSMA supported the bill, which passed the Senate 22-11 and the House of Representatives 59-10.

SB 100 would have restricted any school, early childhood program, state agency, elected official, or state employee from adding new immunization requirements to state statute. Proponent testimony focused on the COVID-19 vaccine. The SDSMA opposed the bill, which was defeated in the Senate Health and Human Services Committee on a 5-1 vote.

Protecting and improving public health

HB 1028 classifies xylazine as a Schedule III controlled substance and establishes permissible uses. The SDSMA testified in support during committee hearings and the bill received unanimous, bipartisan support of the legislature for passage.

HB 1166 attempted to create a legal defense in statute for any individual who refused to follow employer requirements or policy regarding wearing facemasks in a public or private setting. The bill would have allowed an individual to sue his or her employer for enforcement of a workplace policy in violation of the proposed change in statute. The SDSMA was among many opponents who testified against the bill in committee, where it was defeated by a vote of 12-0.

HB 1167 was another attempt for a vaccine exemption bill that would have permitted individuals to make all decisions whether to receive the COVID-19 vaccine without consequences from an employer. The SDSMA was one of many opponents of the legislation, which was ultimately withdrawn by the sponsor for lack of support prior to its committee hearing.

SB 42 modifies several administrative provisions related to medical cannabis. Notably, the bill increases the number of days allowed to renew a registration certificate, increases testing requirements for retail cannabis products, limits dispensaries to sales of no more than 3 ounces within a 14-day period, and requires DOH to submit the name and date of birth of a qualifying patient who receives a registry ID card to the Prescription Drug Monitoring Program. The SDSMA supported the bill for its notification requirement that aids in comprehensive patient care, and the bill was signed by the governor after passing the Senate 29-4 and the House of Representatives 57-12.

Ensuring access to and delivery of quality medical care

HB 1099 expands optometric scope of practice to permit some surgeries and injections. The optometrists argued the bill was necessary due to lack of patient access to services, and SDSMA joined with the South Dakota Academy of Ophthalmology to oppose the legislation as a matter of patient safety, but the bill passed both chambers by large margins after intense lobbying efforts from both sides.

SB 63 updates language related to the licensing process for ambulances and changes the definition of ambulance service "medical director" to permit nurse practitioners and physician assistants to serve in that role. After testifying in opposition to the bill during its committee hearing, the SDSMA worked with DOH to amend the bill to create an annual hardship exemption for ambulance services unable to find a physician medical director and allow for NPs and PAs to serve as program director in those cases. With the bill amended as such, the SDSMA dropped its opposition, and the bill was signed by the governor.

SB 64 was a companion bill to SB 63, in that it sought to permit NPs and PAs to serve as a supervisor to EMS personnel. The SDSMA testified in opposition to the bill in committee but worked with DOH to improve the bill. With the input of SDSMA, the bill was amended consistent with SB 63 and passed with broad support after SDSMA removed its opposition.

SB 147 creates a definition of palliative care in statute and was brought at the recommendation of the 2023 Study Committee on Sustainable Models for Long Term Care. Passage of the bill is the first step toward reimbursement for palliative care services. The SDSMA supported the bill and testified during committee hearings, and the bill passed overwhelmingly.

Advocating on other legislative priorities

SB 87 was introduced on behalf of DOH to revise provisions related to the State Board of Medical and Osteopathic Examiners and its advisory councils. The introduced bill expanded the Board to 17 members, with physician representatives outnumbered 8 to 9; it also required the Board to consult with the nonphysician councils prior to action and allowed the full 17-member Board to act on physician matters. SDSMA opposed the bill in its original form and provided opposition testimony based on concerns with these specific provisions. SDSMA consulted with DOH throughout the legislative process, and the bill was successfully amended to restore a 9-8 physician majority, to allow the Board to act without prior approval of the councils, and to limit matters of physician licensure to the physician representatives. With these amendments in place, the SDSMA dropped its opposition to the bill, which passed and was signed by the governor.

SB 136 expands access to the South Dakota Physician Well-Being Program to current students at the USD Sanford School of Medicine. The bill was filed at the request of the SDSMA, with the support of the USD Sanford School of Medicine and many other healthcare organizations, and the bill received wide, bi-partisan support in its passage. Information about the SD Physician Well-Being Program can be found at www.sdsma.org.

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