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South Dakota medicine

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Contents

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SPENDING THAT CAN WRECK RETIREMENT

MARCUS IWIG CFP®, CPA, MACC *Lead Advisor*

In more than a decade of working with clients, I've discovered that one thing tends to do more damage to financial plans than any other: Spending on a home. Spending on a home for personal use is often billed as a good investment. However in my experience, this is rarely the case. Three key mistakes in home spending often cause people to delay retirement or create unnecessary worry in retirement:

1. Not planning for home expenses in retirement
Every few years, you will have home upkeep expenses. You can expect to refresh or replace most of your home over the course of 25 years. Heading into retirement you want to plan for the spending needed to maintain your home. Without that in the plan, you may not save enough to cover all your needs, which could force you into making some tough choices in retirement.

2. Carrying a large mortgage into retirement
One of the financial keys to a successful retirement is spending flexibility. This allows you to reduce spending during tough market cycles and increase during good markets. In retirement, a significant mortgage is not an optional cost; it must be paid no matter what markets are doing. If you would like to buy a new home, come up with a plan to try and eliminate the mortgage before retirement.

3. Continual, unnecessary home projects
This is the most common and often the most damaging of the three key mistakes. As outlined above, every home will need to be maintained, but there's a difference between maintaining and enhancing. Don't get me wrong. Making your home more functional and enjoyable is great. The problem is when you find a new, unplanned project every couple of years that costs tens of thousands of dollars. The last decade of your working life often is when you can save the most. Replacing those savings with debt can push your spend rates well past a healthy point

The best way to avoid these mistakes is to come up with a plan by prioritizing the things you'd really like to change about your home and research what it will cost. Try to be realistic about how much value you and your family will get from the changes you are considering. Consider home spends that increase the enjoyment of your home the most, and stick to maintenance and necessary changes in other parts of your home.

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The Silent Disease (Sports-Related Concussions)

Lucio N. Margallo II, MD
President, South Dakota State Medical Association

In my role serving as team physician for athletic teams at Dakota Wesleyan University and the Mitchell School District, I'm responsible for the medical care and well-being of student athletes. It's exciting to have played a part in student athletes' ability to reach their full potential. I've had the opportunity to partake in athletes' greatest accomplishments, but I've also been there when things can quickly take a turn for the worse.

It is estimated that each year in the U.S., 38 million children and adolescents, and 170 million adults, participate in various physical activities including sports, which results in 1.7 million people with certain traumatic brain injuries, 1.4 million emergency department visits, and 275,000 hospitalizations. This equates to an estimated direct cost of $60 billion (Clinical Sports Medicine, June 2011). There is moreover an unofficial number of cases that do not seek medical consultation.

Symptoms of concussion include dizziness, headache, difficulty in concentrating, disturbances of vision or equilibrium, post-traumatic amnesia (loss of memory for events occurring after the injury) and loss of consciousness. The American Academy of Neurology defines concussion as a pathophysiologic disturbance characterized by clinical symptoms occurring with and without consciousness. Pathophysiology is due to glycolysis increasing lactic levels, elevated blood-brain permeability and hypermetabolic state leading to neuronal depression due to a decrease in blood flow, diminished magnesium, and hypoxemia.

All types of concussions are complex medical conditions because of sports injury and other etiologies manifested with a wide range of physical, cognitive, social, emotional, and behavioral symptoms leading to mild, moderate and severe traumatic brain injury (TBI), chronic encephalopathy and even death.

The long-term effects are advanced Parkinsonism, ataxia, pyramidal tract dysfunction and behavioral abnormality. Postmortem pathology has revealed cavum septum pellucidum formation in the cerebral fossa, segregation of the substantia nigra and accumulation of tau protein in the form of neurofibrillary tangle (dementia pugilistica noted in boxers like Muhammad Ali).

Here are specific sports-related statistics: 10 percent of contact sports athletes sustain concussions yearly; 63 percent of concussion cases are related to American football and 20 percent of football players will sustain concussions. Athletes who sustain a concussion are four to six times more likely to sustain a second concussion.

Forty U.S. states, including South Dakota, have enacted legislation that require athletes in school-sanctioned sports with concussion symptoms to be removed from competition and return to full-time sports participation only after being cleared by a physician. Current research does not support modifying treatment protocols based on gender. Females, however, have higher risk factors for injury and/or influence of injury severity.

Sideline assessment and diagnosis: A thorough and complete history and physical examination including neurological evaluation should be mandatory, as well as evaluation for balance, motor discoordination, confusion, disorientation and gait, together with facial and head injuries examination, appropriate neuroimaging (head CT, MRI), genetic testing for heterogeneous and homogenous APOE 3 and APOE4. (Note: elevated levels confer a 3-to-9-fold increase in developing various forms of dementia after TBI).

Recommended Treatment Protocols

1. Baseline imPACT test and post-concussion imPACT evaluation (UPMC — measuring brain function in a normal healthy state).
2. Follow safety precautions.
3. Follow the CDC Heads-up Program (education of coaches, administration, AT, athletes, and other medical personnel).
4. Immediate suspension of sports participation.
5. Use of proper equipment (helmets, mouth guards, etc.).
7. Clearance prior to return to full sports activities.
8. Supportive treatments and avoidance of certain medication.

Evaluating and managing patients with a sports concussion is important for team physicians like myself, in collaboration with athletic trainers, to be involved in. It is critical to appropriately diagnose, refer, and educate the patient's families/caregivers to achieve optimal recovery and reduce or avoid significant adverse health outcomes.

Aequitas Health Honor Society: Cultivating Leaders of Health Equity in Medicine

Sanyogita Chandra, MS IV

The white coat ceremony is a symbolic gesture. A sea of new medical students clad in crisp white coats, eyes glistening with excitement. An echo heard in the audience as the Hippocratic Oath is read and a new generation of future physicians swear to fulfill their duties as patient caretakers.

I think back to the day of my white coat ceremony in 2019. My classmates and I lined up for our class photo. Big smiles filled the room. Not even one of us could have predicted that eight months into our medical school careers, the COVID-19 pandemic would change the course of the world. As shutdowns began, my peers and I had not yet started clinical rotations and were confined to our homes with online lectures and exams. We watched in horror as the case numbers rose, hospitals became overpacked, and stories of medical professionals experiencing burnout at record rates flooded our social media feeds. As the pandemic continued to roar, evident health disparities were brought to the surface.

The CDC has summarized data from the COVID-19 pandemic, finding that people from racial and ethnic groups (American Indian or Alaska Native, Black or African American, and Hispanic or Latino) are more likely infected with the COVID-19 infection and more likely to be hospitalized, admitted to the ICU, and die from COVID-19 infection at younger ages as compared to their non-Hispanic white people.[1] In 2021, the Aequitas Health Honor Society was formed at the University of South Dakota (USD) Sanford School of Medicine with the purpose of recognizing medical students and physicians who are improving health equity in clinical practice and in society. Benson Hsu, MD, co-founder and president of Aequitas Health, states "Aequitas Health fills a gap in our recognition of medical students, especially those dedicated to the glaring issue of health inequities. Creating a home for medical students, the honor society not only inspires the future generation of physicians dedicated to addressing health inequities but also establishes a community of supportive physician leaders on this journey."

The honor society recognizes up to 10 percent of students in the graduating medical school class who are dedicated to fighting health inequities in underserved populations. There are physician members, as well. Each Aequitas Health Honor Society Fellow can publish online research, thought pieces, and commentaries through the online Aequitas Health Journal. Suzanne Reuter, MD, co-founder and vice president of Aequitas Health states, "Aequitas Health Honor Society is a fantastic organization because not only does it address health inequities in our community and state, it recognizes and rewards our medical students for all their efforts and work in these areas."

The Fellows from the class of 2023 are preparing a series of events tailored for medical students interested in advocacy. Physician advocacy is a vital aspect of medical professionalism. As licensed medical providers, physicians have the privileged position of being public advocates for their patients to policy makers. The advocacy series will provide an avenue to medical students to learn how they can be involved in advocacy now and as physicians.

New chapters of the Aequitas Health Honor Society are being formed at LCME-accredited medical schools throughout the U.S. and currently 20 percent of medical schools have adopted institutional chapters based on the founding chapter at USD Sanford School of Medicine.

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A Case of Neonatal Myeloid Sarcom

Halie Burdick, MD; Jordan Bormann, MD; KayeLyn Wagner, MD; and Amy Kerkvliet, MD

Abstract

Here we describe a cutaneous neonatal myeloid sarcoma (MS) case with a subsequent diagnosis of acute myeloid leukemia (AML) seven days later. Cytogenetic studies were unusual demonstrating a triple copy of KAT6A abnormality and complex 8;14;22 translocation involving the 8p11.2 region. MS may be the initial finding suggesting associated AML; therefore, the diagnosis of cutaneous MS may allow for expeditious evaluation/treatment of such leukemic disorders.

Introduction

Myeloid sarcoma (MS), otherwise termed chloroma, granulocytic sarcoma, or leukemia cutis, is a rare extramedullary tumor composed of myeloid blasts that arises most frequently in the skin, although a variety of anatomic sites have been reported.[1] Diagnoses in children are rarer than in adults, however, pediatric diagnoses have been reported in association with or preceding leukemic disorders.[2] Our case describes a pediatric patient who developed symptoms of MS 14 days after birth with subsequent diagnosis of AML exhibiting unusual cytogenetic studies.

Case Report

The male patient was born at 40 weeks 1-day gestation via uncomplicated spontaneous vaginal delivery, weighing 7 pounds 1.5 ounces and measuring 20.75 inches long at birth. The patient was conceived during a clomiphene citrate-induced ovulation cycle. The mother's medications included a prenatal vitamin and doxylamine and she did not use alcohol, tobacco, or other substances during the pregnancy. She did acknowledge a history of anemia. There is no family history of blood dyscrasias or childhood leukemia.

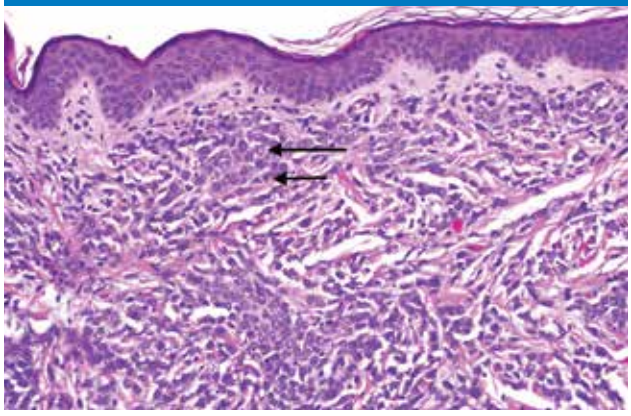
The patient presented at 15 days old with 1 day duration of nontender 8 mm tan/purple indurated papules on the abdomen, chest and right arm. The patient's past medical history is otherwise unremarkable. A punch biopsy from the abdomen demonstrated a dermal infiltrate composed of large cells with occasional prominent nucleoli, frequent mitosis and apoptosis e (Figure 1). The neoplastic cells were positive for CD68 and myeloperoxidase and were negative for CD99, synaptophysin, CD34, TdT, CD3, CD79a, tryptase, and C-kit (Figures 2 and 3). The pathological findings supported a diagnosis of myeloid sarcoma (MS). His complete blood count (CBC) at the time of diagnosis was within normal limits. The cutaneous lesions continued to spread on the patient's head, abdomen and legs and he was admitted to the hospital for further evaluation to determine the extent of disease at 21 days old. A CBC performed upon admission revealed an elevated white blood cell count of 76.3 K/uL and peripheral blood revealed 42 percent blasts diagnostic of acute myeloid leukemia (AML). A spinal tap was negative for blasts indicating no central nervous system involvement. Cytogenetic studies were unusual demonstrating a triple copy of KAT6A abnormality and complex 8;14;22 translocation involving the 8p11.2 region.

Chemotherapy induction consisting of ADE therapy resulted in skin lesion resolution within five days. The first phase of therapy was complicated by diaper dermatitis and Enterococcus bacteremia. Although the skin lesions had resolved, minimal residual disease (MRD) was positive at the end of induction. Four additional cycles of chemotherapy were given with epigenetic priming proceeding each cycle. The epigenetic priming consisted of daily intravenous decitabine for five days prior to therapy. The patient was MRD negative at the end of the second cycle of therapy and remained negative throughout the remainder of therapy. Negative MRD is defined as one or less leukemia cells per every 1,000 to 100,000 white blood cells and is an indicator for remaining in remission.[3] The central nervous system was negative at diagnosis and throughout treatment. The patient has been seen by pediatric oncology monthly with no evidence of disease recurrence.

Discussion

Myeloid sarcoma is a leukemic deposition in extramedullary sites.[1] Skin is one of the most common organs for MS to infiltrate; it typically presents as red to violaceous lesions of varying morphologies with no predilection for any certain location.[4] A diagnosis of MS is more common in adults, however, infants and children can develop MS without

Figure 1. The large arrow highlights a dermal infiltrate of large cells with round to oval nuclei and small but prominent nucleoli. A small arrow highlights an apoptotic cell (H&E, 200x).



related conditions, or, it can be associated with or precede leukemic disorders such as AML.[2] In AML, cutaneous MS can occur in 2-20 percent of cases.[5] Literature on isolated myeloid sarcoma at presentation is limited to case reports.[6-8]

MS pathology involves leukemic infiltrates surrounding appendages such as pilosebaceous units and sweat glands or vasculature. MS may also be visualized as coalescing layers of infiltrate in the subcutaneous tissue and dermis. The cells may line up in a single cell pattern, as sometimes seen in lobular carcinoma of the breast. This can lead to unusual spacing between collagen bundles. In patients with AML, it is common to see atypical mononuclear myelocytes and myeloblasts with little cytoplasm. Lysozyme and CD68 are most sensitive in regards to immunohistochemistry. Furthermore, positive staining for myeloperoxidase, Mac387, CD43, CD74, HLA-DR, and CD 45 are commonly seen in many cases.[9] Treatment often involves managing the underlying malignancy, if present. Chemotherapy and radiation are mainstays of therapy.[10]

MS can clinically be mistaken for inflammatory, neoplastic, and infectious etiologies. Further, the lesion described in this case fits the "blueberry muffin" rash description, which represents extramedullary hematopoiesis.[11] The classic "blueberry muffin" rash has many etiologies including infectious causes such as the TORCH group, hemolytic disease of the newborn, heredity spherocytosis, twin transfusion syndrome, malignancies such as neuroblastoma, AML, and Langerhans histiocytosis and congenital vascular lesions including hemangiomas, multifocal lymphangioendotheliomatosis, blue rubber nevus syndrome, and multiple glomangiomas.[12] Thorough work-up involving immunophenotyping, histology, complete blood count, and clinical correlation is necessary.

Figure 2. The arrows highlight CD68 positive myeloblasts (CD68, 200x).

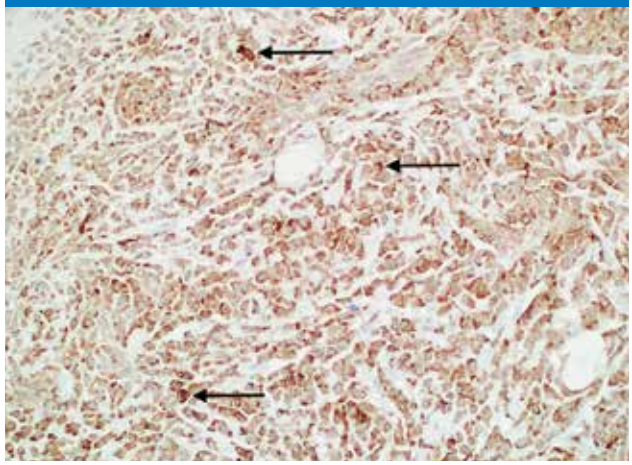
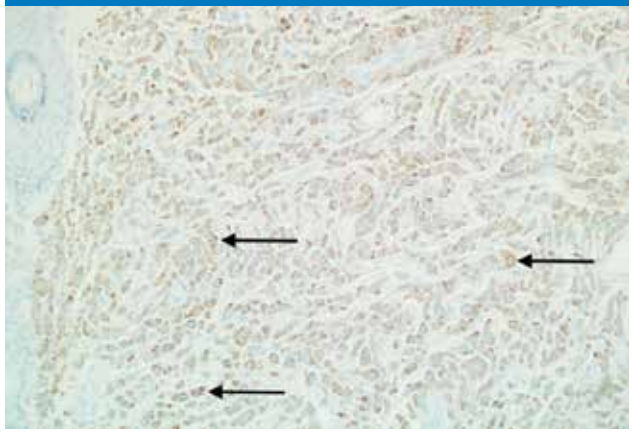


Figure 3. The arrows highlight MPO positive myeloblasts (MPO, 200x).



Our report demonstrates a case of MS in a neonate who developed a rare genetic variant of AML one week after diagnosis. Although rare, it is important to recognize MS as a potential cutaneous manifestation in the neonatal population. MS may be the initial finding suggesting associated AML; therefore, the diagnosis of cutaneous MS may allow for expeditious evaluation and treatment of such leukemic disorders.

Presented as a poster at the 57th Annual American Society of Dermatopathology Conference.

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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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Diffuse Ganglioneuromatosis of the Colon in a Patient with Neurofibromatosis 1

Kayla Hoerschgen, MD; and DesiRae Muirhead, MD

Abstract

Ganglioneuromas are rare, benign neurogenic tumors characterized by a proliferation of ganglion cells, nerve fibers, and support cells of the nervous system. They have been classified into three groups: solitary, polyposis, and diffuse. The diffuse type has several syndromic associations including multiple endocrine neoplasia syndrome type 2B and, less commonly, neurofibromatosis type 1. We report a case of diffuse ganglioneuromatosis in the colon of a 49-year-old male with a history of neurofibromatosis type 1. Gastrointestinal neoplasms associated with neurofibromatosis type 1 are reviewed.

Introduction

Ganglioneuromas are rare, benign neurogenic tumors characterized by a proliferation of Schwann cells, ganglion cells, and nerve fibers.[1] Ganglioneuromas have been classified into three groups: solitary, polyposis, and diffuse.[2] Diffuse ganglioneuromatosis is associated with multiple endocrine neoplasia syndrome type 2B (MEN 2B) and, less commonly, neurofibromatosis type 1 (NF1).[2] In this report, we describe a case of diffuse ganglioneuromatosis in a 49-year-old male with a history of NF1 who presented with vague abdominal complaints and abdominal distension. This case highlights a rare manifestation of NF1, reviews gastrointestinal neoplasms associated with NF1, and stresses the importance of recognizing neoplasms associated with genetic syndromes.

Case Presentation

A 49-year-old male was adopted as a newborn and within the past year had started to learn more about his biological family through an ancestry website. Through the website, he met a first cousin, which led to the discovery of his half-brother and several maternal cousins having a diagnosis of NF1. Curious to learn more, he was referred to neurology and a clinical geneticist. On physical exam he was noted to have axillary and inguinal freckling, seven neurofibromas, and 13 café au lait macules, meeting clinical diagnostic criteria for NF1. Additionally, a couple of months prior to his official diagnosis of NF1, he was admitted for small bowel obstruction and ileus that was managed non-operatively; however, since that time he continued to have abdominal distension, discomfort, and loose stools for which he presented to the emergency department. Physical exam revealed a distended and tympanic abdomen with mild tenderness. A CT scan of his abdomen revealed gaseous distension of the distal transverse colon and the splenic flexure with no abnormality identified at the transition points (Figure 1). These findings were identical to prior CT scans. He was subsequently admitted for further workup and management. To further evaluate, a water-soluble enema revealed no stricture or obstructing lesions at the transition points between the apparently normal colon and the dilated colon. He received supportive care with hydration and pain management. He then underwent a colonoscopy which revealed a dilated transverse colon with a suspected intermittent volvulus that was decompressed. A promotility agent was started, but he remained symptomatic and resection was recommended to prevent recurrence of the volvulus. The next day a hemicolectomy was performed.

The gross pathology revealed a segment of colon that was 83.2 cm in length with a maximum width of 13.5 cm. The transverse and descending colon had edematous and attenuated mucosa with prominent luminal distension. Within the wall of the dilated portion of the colon were focal indurated areas. No polyps or masses were identified. Microscopically, sections of the colon demonstrated architectural distortion of the crypts and a thickened bowel wall due to a diffuse proliferation of spindled cells with fibrillary, eosinophilic cytoplasm with scattered ganglion-type cells throughout the lamina propria admixed with eosinophils and lymphocytes (Figures 2 and 3). In addition to the diffuse proliferation, other areas demonstrated well-demarcated, nodular foci within the muscularis propria and

Figure 1. Axial CT of the abdomen showing the dilated transverse colon.

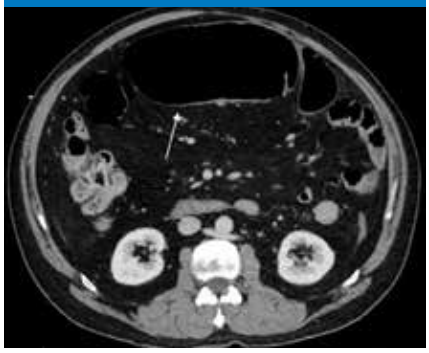


Figure 2. Colon with diffuse proliferation of spindled cells in the lamina propria. Hematoxylin and eosin stain (H&E), 4X magnification.

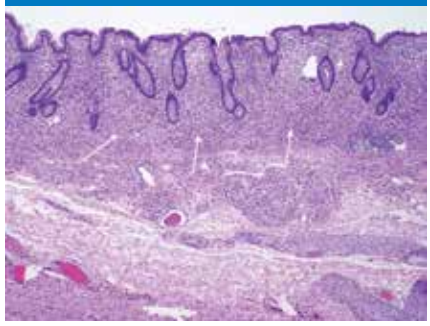


Figure 3. Haphazardly arranged spindled cells with eosinophilic cytoplasm and eosinophils. H&E 20X magnification.

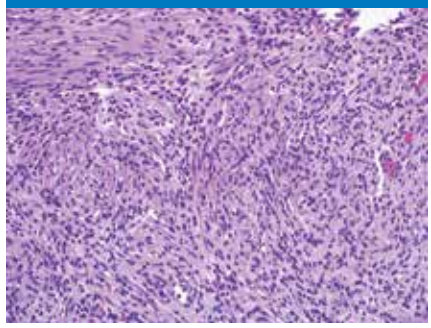


Figure 4. Spindled cells staining with S100 immunohistochemical stain. 4X magnification.

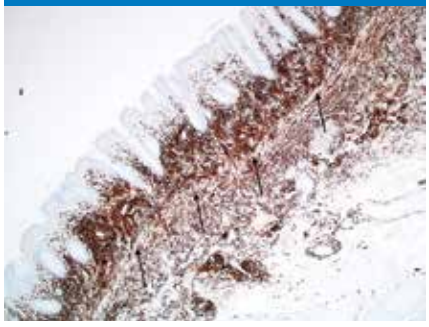


Figure 5. Clusters of ganglion cells within the lamina propria. H&E 20X magnification.

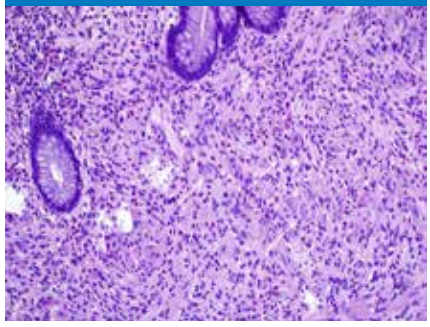
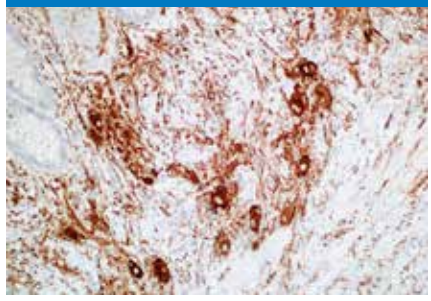


Figure 6. Clusters of ganglion cells within the lamina propria highlighted with synaptophysin immunohistochemical stain.



subserosal adipose tissue composed of similar appearing spindled cells. The spindled cells demonstrate positive S100 immunohistochemical staining (Figure 4). An increased amount of single, as well as clusters, of ganglion-type cells were identified in the lamina propria and submucosa of the affected areas and were highlighted with a synaptophysin immunohistochemical stain (Figures 5 and 6).

Discussion

Ganglioneuromas are considered rare, benign neurogenic tumors of the gastrointestinal tract. The exact etiology of their development is unknown. Different mechanisms have been proposed, but no specific gene or genes have been linked to their development.[2] Ganglioneuromas have been classified into three subgroups. The first is solitary polypoid ganglioneuromas. They present as asymptomatic pedunculated or sessile tumors that histologically resemble hyperplastic polyps, juvenile polyps, or adenomas with nerve ganglion found in nests in the mucosa or submucosa.[2] The second group is ganglioneuromatosis polyposis which is characterized by numerous sessile or pedunculated mucosal and/or submucosal lesions. These typically affect the terminal ileum and colon and histologically have variability in the ganglionic, neural, and supportive cell content.[2,3] The third category is diffuse ganglioneuromatosis, which develops as a result of proliferating nerve ganglion cells, nerve fibers, and supporting cells of the enteric nervous system.[4]

Diffuse ganglioneuromatosis primarily affects the colon; however, involvement of the terminal ileum, jejunum, and appendix have been reported.[4, 5] Symptoms can vary in severity and are thought to be the result of abnormal motility and include abdominal pain, constipation or diarrhea, megacolon, and abdominal distension. In most of the cases the mucosa appears unremarkable, with a rare report of ulceration identified.[4] All layers of the bowel wall can be affected, but may predominantly involve the myenteric plexus or submucosal plexus.[2, 3, 5] The bowel wall can appear diffusely thickened or have distinct submucosal nodularities or even stricture formation.[3] Diffuse ganglioneuromatosis histologically is composed of bland spindled cells with eosinophilic, fibrillary cytoplasm growing in an ill-defined and diffuse or nodular pattern. Amongst the spindle cells are ganglion cells occurring singly or in clusters.[5] The spindle cells are positive for S100 immunohistochemical stain.

The solitary and polyposis lesions have no known syndromic associations. However, the diffuse subtype has several syndromic associations including NF1, MEN-

2B, and Cowden syndrome.[3] Neurofibromatosis type 1 (NF1 or von Recklinghausen Disease) is an autosomal dominant syndrome that affects approximately 1 in 3000 individuals.[5,6] Most mutations are in the *NF1* gene, which codes a protein called neurofibromin that functions as a tumor suppressor.[6] Neurofibromatosis type 1 is characterized by café au lait spots, freckling, neurofibromas, optic nerve gliomas, pheochromocytomas, Lisch nodules, learning disabilities, and skeletal abnormalities.[1] Gastrointestinal neoplasms occur in an estimated 5-25 percent of patients.[6, 7] The neoplasms typically develop later in life and can be benign or malignant. The clinical manifestations of the neoplasms are variable and depend on the location and the extent of the disease. Neoplasms of the gastrointestinal tract in these patients can be grouped based on the cell of origin to include neurogenic neoplasms, interstitial cell of Cajal lesions, neuroendocrine neoplasms, and vascular lesions.[1] In general, neurogenic tumors are relatively uncommon in the gastrointestinal tract.[6] Tumors within this category include neurofibromas, which are the most common, ganglioneuromas, and malignant peripheral nerve sheath tumors.[6,7] Ganglioneuromas are a much rarer tumor in these patients with no studies concluding an estimated incidence. Lesions affecting the interstitial cells of Cajal can include hyperplasia, incidental gastrointestinal stromal tumor (GIST), or even multifocal GIST. While neurofibromas are the most common neurogenic tumor of the gastrointestinal tract in NF1, GIST is the most common gastrointestinal tract tumor overall in NF1 patients.[7] Neuroendocrine tumors associated with NF1 include pheochromocytomas and neuroendocrine neoplasms occurring in the periampullary region of the duodenum, typically somatostatinomas.[6, 7] Vascular lesions include narrowed or ectatic vessels, stenosis, aneurysm or arteriovenous malformations.[1]

In contrast to NF1, diffuse ganglioneuromatosis is more commonly reported with multiple endocrine neoplasia type 2B.[3] This is an autosomal dominant syndrome with a mutation in the *RET* gene. MEN-2B is associated with medullary thyroid carcinoma, pheochromocytoma, mucosal neuromas, and marfanoid habitus.[3] Gastrointestinal symptoms are very common in these patients with an incidence of approximately 60-90% and often these are the first symptoms that eventually lead to a diagnosis of MEN-2B.[8] Diffuse ganglioneuromatosis is observed in 40-90% of patients, making it one of the more common gastrointestinal manifestations of this syndrome.[8]

The third syndrome, Cowden Syndrome, is also associated with the diffuse type. Cowden Syndrome is an autosomal dominant disease with a germline mutation in the *PTEN* tumor suppressor gene. Approximately 1 in 200,000 people are affected with this syndrome and have an increased risk in breast, thyroid, and endometrial cancer, as well as numerous other lesions/neoplasms. Ganglionueromas have been reported in these patients, although it is quite rare.[3]

While the incidence of ganglioneuromatosis is low, it is an important entity to consider because often these patients fail conservative management and require surgical resection.[3] Diffuse ganglioneuromatosis, as well as, other gastrointestinal tract neoplasms associated with genetic syndromes are a challenging group of conditions to diagnose. The symptoms are non-specific and screening patients with NF1 is controversial with no screening guidelines in effect.[7] Our patient suffered from his symptoms for at least a year before his hemicolectomy and even at the time of surgery ganglioneuromatosis was not suspected. Knowledge about these neoplasms associated with genetic syndromes can aid in providing efficient and effective care. Additionally as previously mentioned, it is the gastrointestinal symptoms that may ultimately lead to a diagnosis of a genetic syndrome like MEN-2B. Overall this case discusses a rare manifestation of NF1 and reviews gastrointestinal neoplasms associated with NF1.

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Sanford Health currently offers autologous transplants. For an autologous transplant, a patient's healthy stem cells are harvested to be transplanted back after chemotherapy.

Allogenic transplants will be available in late 2022. CAR-T cellular therapy will be available in 2023. Allogenic transplants use healthy stem cells from a donor, and CAR-T cell therapy uses genetically modified T-cells to target cancer cells.

Seth Maliske, MD, is a hematologist and bone marrow transplant physician at the Sanford Roger Maris Cancer Center in Fargo. He witnessed the start of the new transplant program and has seen its effects firsthand.

"Having a stem cell transplant program here brings a lot of joy, energy and motivation to keep excelling, doing better and bringing more technology to the area," he said.

These programs make a difference for patients like Kathy Score, who was first diagnosed with cancer in 2018.

"When I was trying to decide where I should have my stem cell transplant, Dr. Maliske visited me in the hospital and explained everything. I felt very confident in him," Score said.

She chose Sanford Health for her transplant. By receiving care in Fargo, Score was able to stay close to her family and didn't have to travel far for her treatments.

She also benefited from integrated team care. Throughout her cancer journey, she worked with a variety of providers dedicated to keeping her comfortable, including a nutritionist, physical therapist and staff members providing massages and leading meditation.

"Those extra services make it not just a medical thing," she said. "They add all these services that people need to feel more human, more comfortable and more like they matter."

Patients experience the difference in care at the Sanford Roger Maris Cancer Center, and so do the providers.

"Being able to work in the cancer center and watching people become so overjoyed at what we're able to do for patients – it's a fun thing to be a part of," said Dr. Maliske.

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Advanced Stage Breast Cancer on Initial Presentation Following One Year Hiatus in Screening Mammography Due to COVID-19 Pandemic

Colton Powers, MD; Danielle Mack, MS IV; and Julie Raymond, MD, FACS

Abstract

Breast cancer is the second most common cancer and second leading cause of cancer death affecting women in the U.S., behind only skin and lung cancers, respectively. Modern screening mammography methods have contributed, in part, to a 40 percent decrease in breast cancer mortality since it was introduced in 1976. Therefore, regular breast cancer screening is vital to women's health. The COVID-19 Pandemic posed many challenges to healthcare systems worldwide. One challenge was the discontinuation of routine screening tests. We present a female patient who consistently participated in annual screening mammography and was confirmed negative for malignancy between 2014 and 2019. She did not get her mammogram in 2020 due to the COVID-19 pandemic and was subsequently diagnosed with stage IIIB breast cancer when she resumed her screening mammogram in 2021. This case illustrates one of the consequences of delayed breast cancer screening.

Introduction

Breast cancer is the second most common cancer affecting women in the U.S., behind only skin cancers. The average patient in this population has a 13 percent lifetime risk of developing breast cancer. Additionally, breast cancer is the second leading cause of cancer death in women.[1] Modern mammography methods were first developed in the late 1960s, which has become the primary method for screening for breast cancer since the American Cancer Society first recommended it in 1976.[2] Subsequently, the overall breast cancer death rate has declined 40 percent between 1975 and 2017.[3] This drastic decline in breast cancer mortality is attributed, in part, to improvements in screening with mammography, which has led to earlier diagnosis of breast cancer and thus more effective treatment.[4] Therefore, regular breast cancer screening is vital to women's health. The American Cancer Society currently recommends annual screening mammograms for patients with average risk starting at age 45. At age 55, patients have the option to continue annual screening mammograms or switch to at least every other year. Screening should continue in all women as long as they are in good health and have a life expectancy of 10 years.[5]

The coronavirus disease 2019 (COVID-19) pandemic posed unprecedented challenges to medicine across all specialties and hindered care for a majority of patients in one way or another. An American College of Emergency Physicians (ACEP) survey conducted in April 2020 reported that 80 percent of patients had fears of contracting COVID-19 during a hypothetical visit to an emergency department, and 73 percent were concerned about placing unnecessary burden on the health system.[6] Many patients, therefore, elected to forego seeking medical care. Others were turned away due to triage of resources. The COVID-19 Pandemic Breast Cancer Consortium published its "Recommendations for Prioritization, Treatment and Triage of Breast Cancer Patients During the COVID-19 Pandemic," in which all routine screening exams including mammography, ultrasound, and MRI were recommended to be suspended until the post-COVID-19 period.[7] The intention of various recommendations across healthcare systems in the U.S. was to mitigate risk during an unprecedented pandemic, but delays in care can unfortunately lead to adverse outcomes.

The purpose of this manuscript is to discuss the importance of yearly breast cancer screening and highlight one of the consequences of health system disruptions.

Case Presentation

History of Presenting Illness

The patient is a 76-year-old Caucasian woman who presented in May 2021 for asymptomatic, routine screening breast mammography. Her last bilateral screening mammogram

was in 2019. It was negative for evidence of malignancy at that time (Figure 1). She did not receive her 2020 screening mammogram due to the COVID-19 pandemic. Apart from 2020, she has consistently participated in annual screening mammography with negative findings, confirmed from the electronic medical record, since at least 2014.

Past Medical History

The patient took 1.25 mg of oral Premarin once per day as hormonal replacement therapy for 30 years following a hysterectomy in 1983. Her Premarin dose was subsequently tapered to 0.3 mg daily in 2015 and she has continued that dose since. Also of note, she has a history of breast biopsy for benign lesions in 1976 and 1978. She has a remote history of prior squamous cell skin cancer.

She currently drinks 3 standard drinks per week. She is a former smoker with an 18-pack-year smoking history. She has a history of hypertension and hyperlipidemia, but her medical history is not significant for other relevant illness. She has a family history significant for breast cancer in two second degree relatives and colon cancer in two other second degree relatives.

Diagnosis

The patient resumed regular screening mammography in May 2021, which identified an irregular mass measuring 33 mm with spiculated margins in the 1 o'clock position in the posterior region of the left breast (Figure 1). The right breast was negative for masses or calcification. Also included in the radiologist's report was a statement indicating that eight of the patient's past mammogram studies were retrospectively reviewed for quality assurance.

Ultrasound was performed for additional evaluation and revealed a 56 mm mass in the 1 o'clock position 3cm from the nipple with suspiciously enlarged axillary lymph nodes (Figure 2). Ultrasound guided breast biopsy was performed, taking multiple cores of the left breast massing using a 14 gauge automated biopsy needle. An ultrasound enhanced clip was left in the residual lesion and a post procedure 2 view mammogram was obtained. Histology of the biopsy revealed an invasive ductal carcinoma moderately to poorly differentiated (grade 2-3/3). The specimen was estrogen receptor (ER) positive, progesterone receptor (PR) negative, and human epidermal growth factor receptor 2 (HER2) positive. The lesion was further characterized with magnetic resonance imaging (MRI). The right breast was negative for masses or suspicious enhancement. The left breast findings revealed an irregular enhancing mass measuring 31x33x33

Figure 1. From left to right, benign 2019 screening mammogram of left breast; 2021 screening mammogram of left breast demonstrating irregular mass measuring 33mm (indicated with a red circle). A red circle was placed on the 2019 mammogram in the same area where the tumor subsequently developed, showing no evidence for concern.

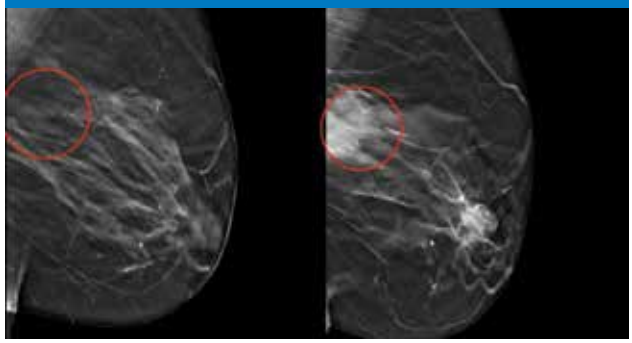


Figure 2. Limited ultrasound of left breast demonstrating a solid mass which is highly suggestive of malignancy. Two measurement markings identify the full extent of the mass in two dimensions.

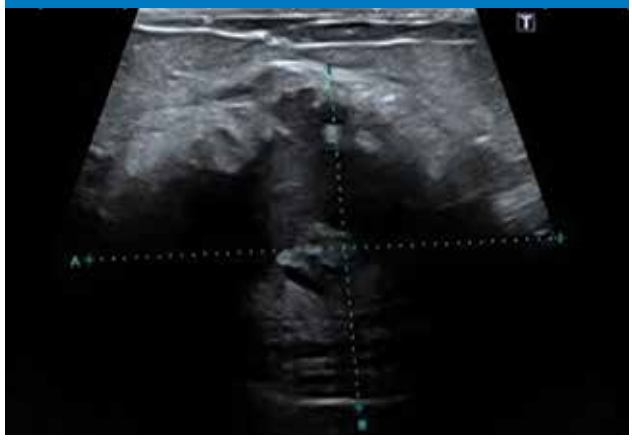


Figure 3. Bilateral breast MRI with contrast demonstrating a 31 x 33 x 33mm mass (indicated with a red circle) with evidence of invasion of the pectoralis muscle and left axillary lymphadenopathy which is concerning for metastasis.

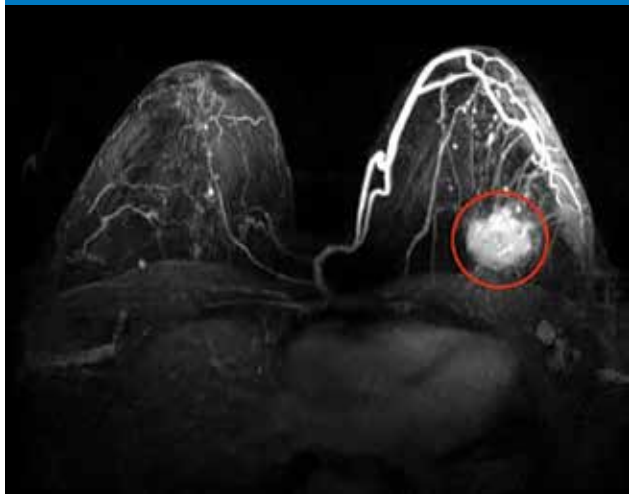
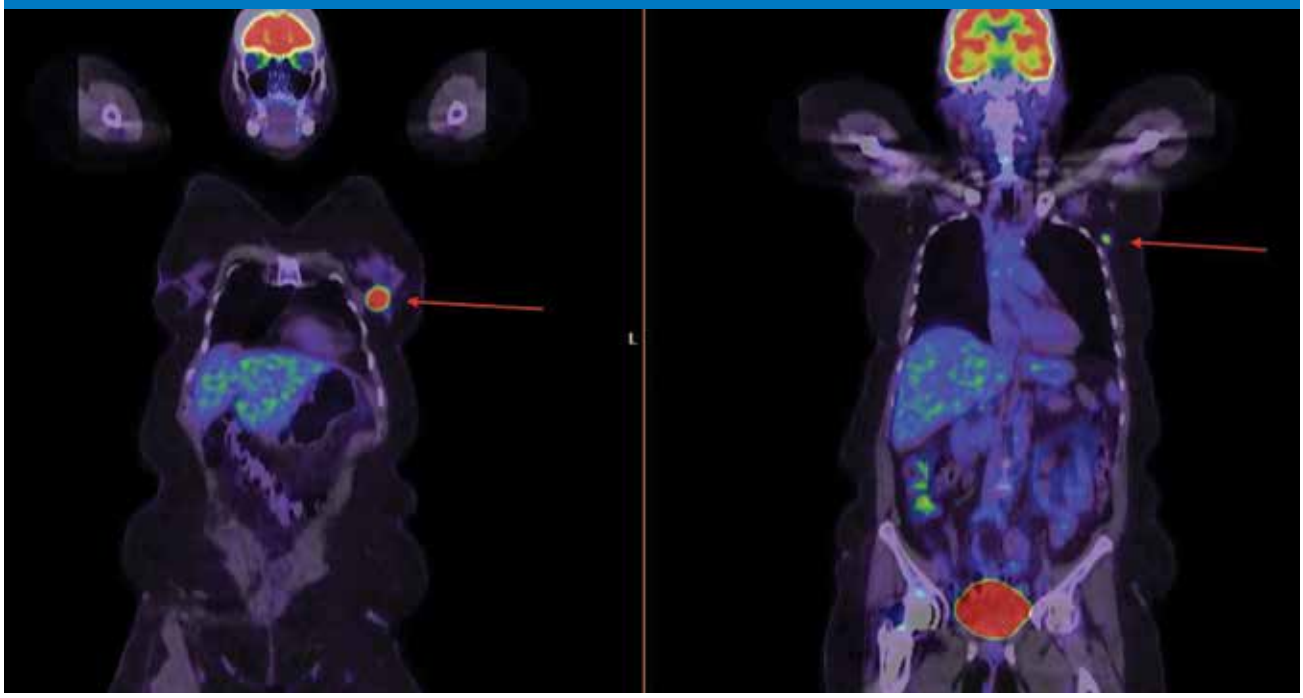


Figure 4. From left to right, PET/CT demonstrating FDG avid left breast cancer (indicated with red arrow) and an FDG avid left axillary metastatic lymph node (indicated with red arrow).



mm. Closest distance to the nipple was 89 mm and the closest distance to the lateral skin was 35 mm. There was a 9 mm satellite nodule anterior to the mass that may or may not be contiguous with the main mass. There was soft tissue thickening and enhancement of the lateral breast skin. There was abutment of the left pectoralis muscle with loss of the fat plane. A suspicious axillary node measured 13mm. There was no internal chain lymphadenopathy. No nipple retraction was apparent (Figure 3). FNA of the axillary node was obtained and was positive for malignancy.

A positron emission tomography-computed tomography (PET-CT) scan was completed and revealed a 3.9 cm mass in the left breast with a maximum standardized uptake value (SUV) of 16.31. Additionally, there was a hypermetabolic lymph node in the left axilla with a maximum SUV of 9.05 (Figure 4).

Differential Diagnosis

Stage IIIB moderately to poorly differentiated invasive ductal carcinoma of the breast.

Management

The patient was referred to a breast cancer surgeon, medical oncology, and radiation oncology. The initial planned treatment course will be neoadjuvant chemotherapy. Therapeutics chosen for neoadjuvant therapy are 6 cycles of Taxotere (docetaxel), carboplatin, Herceptin (trastuzumab), and Perjeta (Pertuzumab). Trastuzumab/Pertuzumab will follow for one year total. Mastectomy will then be performed as the option most favored by the patient. Adjuvant radiation therapy will be completed with a 4-field approach.

Discussion

This patient with a history of negative routine mammograms developed a stage IIIB ductal carcinoma after a single missed screening due to the COVID-19 pandemic. Although it is possible that this patient's cancer was missed on the 2019 screening mammogram due to a false negative result, modern digital mammography is very sensitive up to 97 percent.[8] Additionally, the radiologist indicated that they retrospectively reviewed two prior mammogram studies at that time to thoroughly assess the suspicion for malignancy.

Refer to Figure 1 to review the stark difference in appearance between the 2019 and 2021 screening mammograms, also note that these mammograms were performed at the same facility using the same technique. Because of the rather impressive appearance of the tumor at the 2021 screening mammogram, we argue that this is most likely not a case of mammogram occult or otherwise missed cancer in 2019, but rather an advanced cancer that may have been screening preventable, at least to some extent.

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Breast tumor growth rates are variable and are dependent on the individual tumor growth stage within the natural history of breast cancer progression, patient age group, and the heterogeneity of intratumor characteristics. Therefore, it is difficult to predict with certainty which individuals would be safe to extend their screening interval. Breast tumors typically take several months to years, on average, to develop to the point of being detectable on mammogram, but a subset of tumors called "interval breast cancers" exist.[9,10] The term interval breast cancer refers to a cancer that emerges within the regular screening interval—sometime after a negative screening mammogram and before the next one.

Factors that are associated with increased risk of interval breast cancer include high density breast tissue, current use of hormone replacement therapy, younger age, and family history of breast cancer. Patients who are diagnosed with interval breast cancers typically face a worse prognosis. A majority of studies identify interval breast cancers as representing up to 14.7 percent, 30 percent, and 38 percent of the cancers that occur in patients who participate in annual, biennial, and triennial screening programs, respectively.[11] This implies an increasing rate of otherwise screen-preventable disease is, in part, directly proportional to an increase in screening interval.

The major benefit of frequent and regular screening mammograms is that screening detected breast cancers are detected at smaller sizes and, subsequently, treated more effectively. However, this benefit is only found to occur in cancers which are detected within one year of the previous screening mammogram. This reinforces the importance of adhering to an annual screening program.[9]

The goal of regular screening mammography is not necessarily to prevent the development of cancer altogether, but to detect tumors at smaller sizes before significant progression occurs, when treatment options are more effective.

Any disruption in cancer screening and the subsequent delays in diagnosis are concerning for an increase in screening preventable advanced disease. Breast cancer is the second most common cancer in women worldwide and mammography is a vital and powerful screening tool for prevention of advanced disease. The morbidity and mortality of breast cancer have decreased in line with the adherence to regular screening due to identifying early disease.[12] The effects of delayed breast cancer screening are apparent in this patient and may be a harbinger of similar cases as patients return to their regular medical care. This patient as well as thousands like her may potentially experience increased morbidity and mortality related to delays in screening and treatment.

The World Health Organization (WHO) declared COVID-19 a pandemic on March 11, 2020. This patient, along with potentially thousands like her, cited the COVID-19 pandemic as the main factor for the delay in routine care. The fear and uncertainty that COVID-19 brings is felt across America and crosses socioeconomic and geographical boundaries.[13] Anxiety over illness, economic instability, and constantly evolving guidelines plagued patients throughout 2020. Public messaging by professional organizations regarding avoidance of viral exposure resulted in canceled and delayed appointments.[14] There was specific messaging for those susceptible to the virus such as the elderly and immunocompromised to stay home during the pandemic. The anxiety of this pandemic likely affected patient decisions about their care.[15]

In April 2020, the Centers for Disease Control and Prevention (CDC) and the Centers for Medicare and Medicaid Services (CMS) published guidelines recommending the suspension of non-urgent procedures, including preventative care screenings.[16] The overall approach to breast cancer was slowed during the COVID-19 pandemic. Due to concerns of safety and resource management, representatives from the American Society of Breast Surgeons (ASBrS), the National Accreditation Program for Breast Centers (NAPBC), the National Comprehensive Care Network (NCCN), the Commission on Cancer (CoC), and the American College of Radiology (ACR) met to provide guidance on the prioritization of breast cancer patients. This consortium categorized patients into three priority levels (A, B, and C). Group A patients had immediate life-threatening or symptomatically urgent conditions; Group B patients had conditions that were not immediately fatal but needed to be attended to during the pandemic. Group C patients had conditions that were deemed safe to defer until the pandemic was controlled. Group C included interventions such as screening mammography, ultrasound, and MRI.[7] This patient fit the classification of group C and therefore had screening delayed.

The volume of screening mammography was significantly affected during the pandemic. Other screenings similarly decreased during this period. In April of the pandemic, screening for breast, colon, prostate, and lung cancer were all significantly decreased compared to the same month in 2019.[17] In the months of March through April 2020,

numerous states in America saw their largest decrease in breast cancer screening. In one study, screening mammograms fell by 94 percent in March of 2020.[18] An additional study found a maximum decrease of 85.1 percent in the same month.[14] Another study observed that screening mammograms fell by 99 percent by mid-April.[16] The decreased screening subsequently manifested as a decrease in diagnosed breast cancer.[18]

The decline in screening mammography seemed to slow and rebound in the months of August to July 2020.[14,16,17] The prolonged delay in care consequently created a backlog of patients needing to schedule their mammography on top of the patients whose care was not interrupted by the pandemic. This backlog of care may slow the return to regularly scheduled screening, causing delays in care well beyond the delay of the initial lockdowns.[18]

The concern of a prolonged delay in regular screening mammography is an increase in the frequency of advanced stage cancer and thus reduced efficacy of medical intervention. Early in the pandemic, simulation technologies predicted that a delay in cancer screening for as little as 3 months would result in increased cancer incidence, advanced stage at diagnosis, and increased cancer deaths.[19] A diagnostic delay of a few months has the potential to affect breast cancer outcomes.[12] An Italian study found an increase in sentinel lymph node involvement in the post lockdown cohort.[20] Another study found a decrease in in-situ breast cancer diagnoses, an increase in node-positive disease, and an increase in stage III breast cancer.[21] A model proposed by The National Cancer Institute estimates an excess of 10,000 deaths (1 percent increase) from breast and colorectal cancer in the next 10 years because of the various COVID-19 pandemic related challenges discussed above.[22]

Conclusion

In conclusion, a patient with a negative breast screening history developed locally advanced breast cancer after a single missed mammogram due to the COVID-19 pandemic. Breast cancer screening was reduced nationwide for months before gradually returning to normal capacity. This case illustrates one of the consequences of delayed breast cancer screening in response to a public health threat and triage of medical resources. The cessation of routine screening for breast cancer during the COVID-19 pandemic was done to mitigate the risk imposed on the general public due to viral propagation, but the far-reaching effects of the decision to delay cancer screening have yet to be fully realized. Although the risk mitigation response was well-intended, a substantial increase in screening preventable mortality is inevitable and unfortunate. In the event of a future healthcare crisis, the risk of forgoing screening must be carefully considered. We hope that this manuscript will highlight the importance of regular cancer screening.

Many of the journal's readers are likely already aware of Dr. Julie Raymond's passing earlier this year. Dr. Raymond was a pillar of the oncologic community in western South Dakota, where she provided compassionate and comprehensive care for most of the area's breast cancer patients, and also mentored numerous medical students and physicians – including myself. I am incredibly grateful for the opportunity to have learned from Dr. Raymond. She was an exemplarily physician and mentor, and she is greatly missed by many.

– Colton Powers, MD

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A Case-Based Review of Cutaneous CD30-Positive Lymphoproliferative Disorders

Colby Felts, MD; and B. Joel Tjarks, MD

Abstract

CD30-positive lymphoproliferative disorders are a group of diseases which represent the second most common (30 percent) subgroup of cutaneous T-cell lymphomas. They present a challenging diagnosis given their similar findings histologically and clinically in comparison to other cutaneous pathologies. Use of immunohistochemical staining to identify CD30 positivity facilitates a more rapid development of the appropriate management plan. Here we present two cases of CD30-positive lymphoproliferative disorders (lymphomatoid papulosis and anaplastic large cell lymphoma), analyze the spectrum of CD30-positive lymphoproliferative disorders, and review potential mimics of these pathologies to ensure the proper workup, diagnosis, and management of such diseases.

Introduction

CD30-positive (CD30+) lymphoproliferative disorders (LPDs) are a group of diseases which represent the second most common (30 percent) subgroup of primary cutaneous T-cell lymphomas (CTCL) behind mycosis fungoides (MF) (55 percent).[1,2] They are defined by the expression of CD30 in atypical cells and comprise entities such as lymphomatoid papulosis (LyP), primary cutaneous and systemic anaplastic large cell lymphoma (PCALCL and SALCL), and large cell transformation of MF. These disorders present a challenging diagnosis given their similar findings histologically to other malignant cutaneous lymphomas and benign entities.[3] The diagnosis relies on a combination of patient history, clinical findings, and histopathologic interpretation, as clinical management is significantly different for each of these entities.[4]

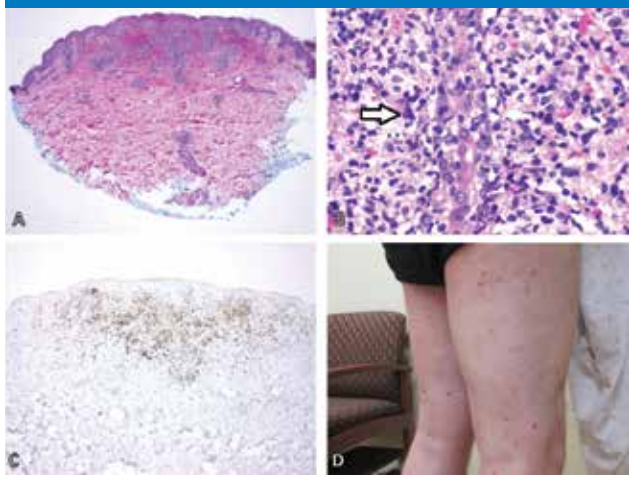
Here we present case reviews of LyP and PCALCL, discuss the CD30+ LPDs, and review potential mimics of these entities to ensure the proper workup, diagnosis, and management of such diseases.

Case 1

A 71-year-old male presented to his primary care provider for new asymptomatic skin lesions which started on his foot and progressed up to his back over the prior three weeks. Some lesions had self-resolved while others had presented in new areas. The patient had a history of diffuse large B cell lymphoma diagnosed nine years ago which was in remission following radiation and chemotherapy. Physical exam showed scattered erythematous papules and small nodules on his legs, lateral torso, and arms (Figure 1D). Several leg lesions had central hemorrhagic crusting. No lymphadenopathy was noted. The patient was initially given cephalexin for suspected folliculitis, but no improvement was seen. A punch biopsy was taken in addition to starting an oral Prednisone taper and topical corticosteroid.

A punch biopsy of a 0.4 x 0.3-centimeter lesion showed a vacuolar alteration of the basal layer keratinocytes with exocytosis of atypical cells into the epidermis. In the dermis, there was a wedge shape infiltrate within the

Figure 1. Wedge-shaped hemorrhagic inflammatory infiltrate (A hematoxylin and eosin, 40x) with epidermotropism composed of large atypical and pleomorphic lymphocytes (B, hematoxylin and eosin, 200x) which express CD30 (C, CD30 immunohistochemistry, 100x). (D) Clinical photograph showing crops of erythematous papules in various stages of healing.



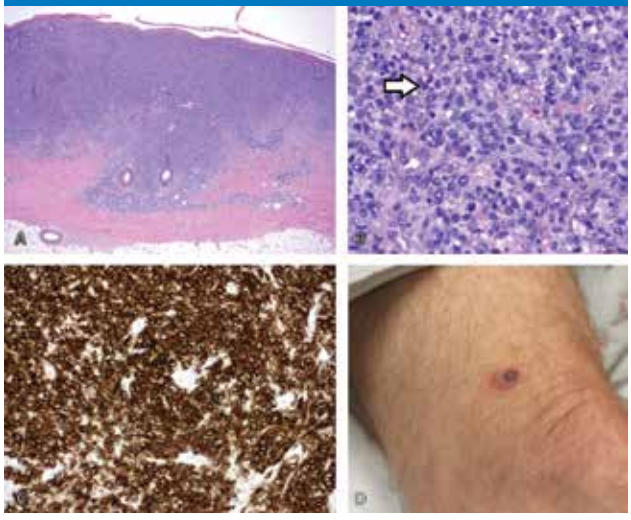
dermis composed of large atypical lymphoid cells with increased mitoses. Occasional eosinophils were noted. The large, atypical cells were strongly positive for CD30 and expressed CD3 without significant loss of CD7 or CD5. The CD4:8 ratio was within normal limits. CD20 labeled scattered background B lymphocytes. These microscopic findings were supportive of a CD30+ LPD, specifically LyP based on clinical correlation. The patient was referred to a dermatologist who recommended topical corticosteroids and observation for treatment while also scheduling a follow up with his oncologist given his history of diffuse large B cell lymphoma. There was no disease recurrence after 17 months of follow-up.

Case 2

An 85-year-old male presented to his dermatologist with a two-month history of an asymptomatic new skin lesion on his left distal anterior thigh. The patient denied systemic symptoms. His medical history included non-melanoma skin cancers but no history of other malignancies. Physical exam showed a 1.5 x 1.0-centimeter indurated, deep pink plaque without scale (Figure 2D).

Histologic sections of a punch biopsy showed compact orthokeratin overlying an attenuated epidermis and a compound atypical lymphoid infiltrate. Atypical lymphocytes were aligned along the dermal epidermal junction with prominent areas of epidermotropism. Within the dermis, there was a dense proliferation of large lymphoid cells with

Figure 2. Large, dense wedge-shaped inflammatory infiltrate (A, hematoxylin and eosin, 40x) composed of large atypical cells with pleomorphic nuclei and frequent mitoses (B, hematoxylin and eosin, 200x). The tumor cells show strong expression of CD30 (C, CD30 immunohistochemistry, 200x). (D) Clinical photograph showing a solitary erythematous and violaceous nodule.



finely granular cytoplasm, moderate nuclear pleomorphism, and scattered mitotic figures. The large cells expressed CD3, CD8, and CD30. CD4 highlighted scattered cells throughout the infiltrate to a lesser degree than CD8. CD20 highlighted rare B lymphocytes. CD56 labeled rare, scattered cells and PU.1 labeled many histiocytes throughout the infiltrate. An immunohistochemical stain for ALK was negative. These findings were compatible with a CD30+LPD. The histologic differential diagnosis included ALCL (primary or systemic), large cell transformation of MF, and LyP. The lesion was excised with clear 0.5 cm margins. Follow up with oncology to rule out systemic involvement revealed a negative full-body positron emission tomography (PET)-scan and laboratory evaluation. Therefore, clinicopathologic correlation supported a diagnosis of PCALCL. Follow up at 7 months revealed no disease recurrence or systemic spread.

Discussion

CD30, formerly known as Ki-1 antigen, is a transmembrane glycoprotein within the tumor necrosis factor (TNF) receptor superfamily.[5,6] This cytokine receptor on activated T and B cells interacts with CD30 ligand (CD30L) and co-factors (CD28 or Il-4), which are also present on activated T and B cells.[5,7] Once triggered, the CD30 receptor cascade activates nuclear factor (NF)-kB to either begin apoptosis or low levels of proliferation.[3]

CD30+ LPDs are defined by the expression of CD30 in atypical lymphoid cells, although CD30 expression can be seen in other common neoplastic and nonneoplastic disorders (e.g., cutaneous Hodgkin's lymphoma, CD30+ large B-cell lymphoma).[3] In addition to CD30 expression, CD30+ LPDs may share similar histomorphology, creating a diagnostic challenge.[3] The clinical history is essential (such as timing, size, and number of lesions) to differentiate these entities as prognosis and management is widely variable, depending on the diagnosis.[4]

Lymphomatoid Papulosis

LyP is the most common CD30+ LPD. It has classically been described as "clinically benign, but histologically malignant" due to the presence of large, atypical CD30-positive lymphocytes, but benign clinical course.[8] This condition occurs primarily in adults but has been described in some children[9] with the most common presentation around 35 to 45 years old and in a 1.4:1.0 male to female ratio.[9] Estimates have placed the prevalence in the U.S. around 1.2 to 1.9 cases per million people.[11] LyP clinically presents with variable numbers of erythematous papular to nodular

lesions (Figure 1D), typically on the trunk or extremities. The hallmark feature is spontaneous regression of the lesions, typically over four to six weeks.[1] Patients often present with lesions in various stages of healing, including superficial scars and hypo/hyperpigmented macules.[1,3] In comparison to PCALCL, lesions of LyP are usually smaller with a diameter around 0.3 to 1.0 cm and rarely larger than 2.0 cm.[3] Nearly 50 percent of patients have symptomatic lesions with pain, pruritus or other superficial changes.[12] More importantly, patients with LyP have nearly zero systemic symptoms or metastatic activity.[3]

Histologically, LyP shows features mimicking cutaneous lymphomas with large, atypical CD30-positive cells. Five histologic subtypes (A-E) have been described; however, despite the histologic presentation, subtypes are not significant prognostic or therapeutic predictors.[13] The most common form type A (80 percent) shows atypical lymphocytes in a wedge-shaped heterogenous infiltrate with neutrophils, eosinophils, and histiocytes (Figures 1A and 1B).[12,13] LyP type A has a mixed infiltrate which histologically mimics Hodgkin lymphoma while subtypes B and C mimic MF and ALCL respectively.[3] Types D and E are more recently described and are most likely to be misinterpreted as aggressive lymphomas.[14] Type D shows marked epidermotropism with CD8 expression, mimicking aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma. Type E is angioinvasive.[13] Other subtypes including type F (folliculotropic) and type G (granulomatous/gamma delta positive) have been proposed.[10] Given most patients have multiple lesions, various histologic types can synchronously be seen in the same patient.[15] The diagnosis is clinically and histologically challenging, evidenced by reports that definitive diagnosis is often delayed one to three years[16] from initial presentation.

Management is based on the size of involved area, symptomatology, and cosmetic concerns.[1,16] If lesions are asymptomatic, of limited distribution, and avoid cosmetically sensitive areas, reassurance and clinical follow-up is acceptable.[16] The 5-year survival rate excluding secondary malignancies is 100 percent[1] and most lesions self-resolve over the course of weeks to months.[17] If lesions are large, symptomatic (itching, painful, etc.), or involve cosmetically sensitive areas, low dose methotrexate is the treatment of choice.[1] Secondary treatment options include high potency topical corticosteroids (group 1) or ultraviolet (UV) phototherapy which includes either psoralene + long wave UV (PUVA) or short wave UV (narrow band UVB).[1,3] Refractory lesions may be amenable to anti-CD30 monoclonal antibody therapy, but this should be reserved for severe cases.[18] Recurrence appears in over 40 percent of patients once medical treatment is stopped.[19] While treatment can reduce healing time, there is no evidence it alters the nature course of the disease.[1] If LyP is suspected, recommended workup includes a skin biopsy for histological and immunohistochemistry analysis.[3] A complete blood count (CBC) with differential, blood chemistry, and lactate dehydrogenase (LDH) are also recommended to rule out systemic manifestations.[19] Perhaps most importantly, patients diagnosed with LyP should receive life-long follow-up to monitor for development of secondary hematologic malignancies. While the exact risk is unclear, and specific risk factors have not been established, secondary malignancies have been reported in 5-60 percent of LyP patients.[3] MF and ALCL are the most common secondary malignancies, but systemic B-cell lymphomas may occur. Treating LyP does not reduce the risk of cutaneous or systemic lymphoma.[1,12]

Primary Cutaneous Anaplastic Large Cell Lymphoma

Cutaneous involvement by ALCL may be primary (PCALCL) or a secondary (SCALCL) manifestation of systemic (SALCL) with skin involvement.[20] This difference is critical for patient management and outcomes. PCALCL represents 1.7 percent of peripheral T-cell non-Hodgkin lymphomas (NHLs) and 9 percent of CTCLs.[12,21] Compared to LyP, PCALCL patients are frequently older (median age 60 years old) and more likely to be male (3:1 male-to-female).[17] This malignancy is more common in immunosuppressed individuals such as those with human immunodeficiency virus (HIV) or organ transplants.[4] Clinically, PCALCL predominately presents as a single erythematous to violaceous nodule or tumor greater than 2.0 cm in diameter (Figure 2D) with no predilection for a particular body region.[22] These clinical findings are in contrast to the smaller and recurrent crops of LyP. Not all cases are singular with around 20 percent being multi-focal.[1] PCACL has increased risk of metastatic activity to both lymph nodes and other extracutaneous areas, although this only occurs in approximately 13 percent of cases.[24]

Most cases of PCALCL are histologically described as sheets of large CD30+ tumor cells (>75 percent of cells by definition[25]) with nuclear pleomorphism, frequent mitoses, and prominent, eosinophilic nucleoli. (Figures 2A and 2B).[1,3,25] "Hallmark cells" with horseshoe-shaped nuclei may be present, but are not required for the diagnosis. LyP type C shows identical histological features to PCALACL and the distinction requires clinical correlation.[3] In a smaller percentage of cases (20-25 percent), PCALCL lacks the

anaplastic appearance and is described as a wedge-shaped heterogenous infiltrate with neutrophils, eosinophils, and histiocytes, similar to LyP type A.[1,3,17] Anaplastic lymphoma kinase (ALK) is almost always negative in PCALACL, yet nearly 50 percent of SCALCL are ALK positive.[24] Additionally, PCALCL is usually cutaneous lymphocyte antigen (CLA) positive and epithelial membrane antigen (EMA) negative whereas SCALCL shows opposite staining.[17,24]

Initial management of PCALCL consists of ruling out SCALCL[12], which tends to present with B symptoms (fever, chills, fatigue, night sweats, weight loss) and requires a more complex workup. Thorough evaluation with a CBC with differential, blood chemistry, LDH, contrasted tomography (CT) with PET of the chest, abdomen, and pelvis assists in ruling out systemic disease.[19] The presence of lymphadenopathy (>1.5 cm) also warrants a lymph node biopsy.[3] Clinical presentation drives the treatment strategy and first line treatment consists of radiotherapy or surgical excision for solitary or few lesions.[1] Radiotherapy is preferred due to the difficulty of margin assessment of an inflammatory process and lack of consensus recommendations for surgical margins.[3] Low dose methotrexate provides another option if the patient is not a candidate for radiotherapy.[1] Extensive lesions typically warrant multi-agent chemotherapy, although high rates of recurrence (40-70 percent) exist following treatment.[19,23] Brentuximab, a chimeric anti-CD30 antibody, is FDA approved for the treatment of SALCL and has been used off label for PCALCL.[26]

Despite potential metastatic activity, overall outlook for PCALCL remains quite positive. Skin-limited disease has a 5-year survival rate over 95 percent.[22] If more than one lymph nodes is involved, the 5-year survival rates drop to 76-95 percent.[17] Surprisingly, regression is seen without treatment in 28 percent of cases which may suggest a relationship between CD30+ LPDs and LyP.[23] In fact, research has shown the more the lesion looks like LyP histologically, the more likely it is to spontaneously regress.[17]

Systemic Anaplastic Large Cell Lymphoma

SALCL represents 3 percent of adult NHLs[26] and 10-20 percent of childhood lymphomas.[28] This malignancy is differentiated from PCALCL in a multitude of ways but maintains CD30 expression and similar histology. Depending on ALK expression, SALCL shows a bimodal age distribution with the median age of ALK(+) cases at 34 years old and ALK(-) cases at 58 years-old.[29] Clinically, only 20 percent of SALCL cases have skin lesions, but cutaneous involvement is more often multifocal than PCALCL and represents a poor prognostic indicator.[3,29] Although both SALCL and PCALCL are typically asymptomatic, the presence of systemic symptoms significantly increases the likelihood of SALCL.[30] While ALK positivity is a common differentiating factor from PCALCL, SALCL lesions can also show *DUSP22-IRF4* and *TP63* gene rearrangements[31] as well association with the nucleophosmin (NPM)-ALKt(2;5) translocation.[32] Fluorescence in situ hybridization (FISH) can be helpful in diagnostically challenging cases. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) is the first line treatment for SALCL[33] with Brentuximab showing a 86 percent response rate in those that failed initial therapy.[34] ALK(+) SALCL has a 5-year survival rate of 70 percent with the rate dropping to 49 percent for ALK(-) SALCL.[29]

Large Cell Transformation of Mycosis Fungiodes

Although CD30+ LPDs are classically thought of as LyP and PCALC, the large cell transformation of MF complicates this schema. MF represents 55 percent of primary CTCL.[2] Large cell transformation is estimated to occur in 8-55 percent of advanced-stage MF.[36] The evolution is defined by the change from small atypical cerebriform lymphocytes (Figure 3) to clonally identical large cells with nuclei which are four or more times larger than a typical lymphocyte nucleus.[35,36] The large cells should represent greater than 25 percent of the infiltrate.[37,38] As the transformation occurs, the density of atypical lymphocytes and percentage of large cells increases (Figure 4).[35] Uncommonly, MF may also show large cell morphology upon initial presentation.[35]

Transformed MF may express CD30, providing a confusing clinicopathologic picture when the differential includes other CD30+ LPDs. Clinical course is the most effective measure to

Figure 3. Erythematous plaques with scale consistent with plaque stage MF.

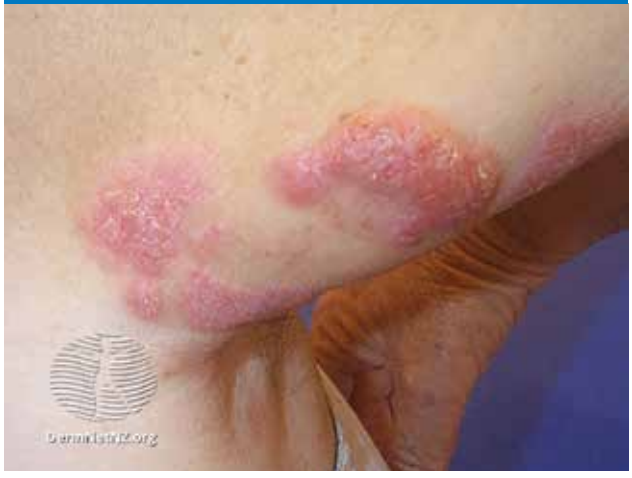
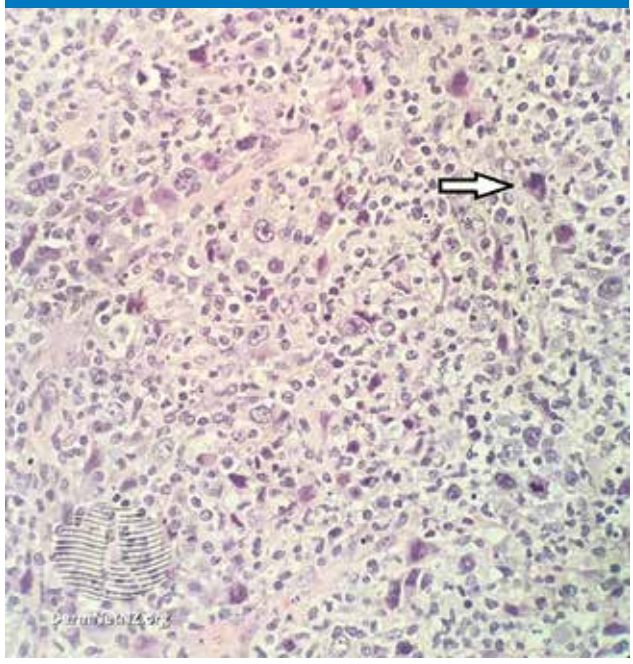


Image courtesy of DermNet

Figure 4. Hematoxylin and eosin stained section showing large atypical cells with pleomorphic nuclei consistent with the large cell transformation of MF.



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determine whether the CD30+ proliferation is transformed MF or other CD30+ LPD.[39] Therefore when making a diagnosis of PCALCL, MF must be ruled out. Prognosis of large cell transformation of MF is relatively poor with a mean five-year survival of <20 percent[37] and median survival of 19-36 months.[40,41] Outcomes can be estimated using a combination of stage at transformation, degree of skin involvement, folliculotropism, and percentage of cells with CD30 positivity.[35] Interestingly, increased CD30 expression may be associated with better outcomes.[36]

Mimics

Adding to the difficulty in diagnosing CD30+ LPDs are clinical mimics of these cutaneous lesions. This paper will highlight four inflammatory or infectious lesions which should be considered in the differential. These include pityriasis lichenoides (PL), arthropod reactions, lymphomatoid medication reaction, and viral exanthems.

Pityriasis Lichenoides

PL is an inflammatory reaction which exists as a spectrum from pityriasis lichenoides et varioliformis acuta (PLEVA) to pityriasis lichenoides chronica (PLC).[42] The etiology of the disease is uncertain and both PLC and PLEVA can simultaneously be present.[43,44] While the exact prevalence is unclear, one study found the average age at diagnosis was 29 years old[45] with another study showing almost 80 percent of lesions occur in individuals under 60 years of age.[45,46] PL is also more common in children (20 percent of cases) than CD30+ LPDs.[47] Clinically, PLC presents with small erythematous and slightly scaly papules with a relapsing-remitting course (Figure 5). The median length to clearance of the lesions in adults is 16.4 months.[42,44,48] Systemic symptoms are rare in PLC.[42] PLEVA is often more severe than PLC and may present with systemic symptoms such as fever and lymphadenopathy.[43] Patients present with an acute eruption of crops of 2-3 mm erythematous macules which evolve into papules or vesicles. Hemorrhagic necrosis may be present.[42,43] The distribution is frequently symmetric on the trunk, buttocks, or proximal extremities.[43] As both PLC and PLEVA lesions mature, they resolve with hypo/hyperpigmented macules similar to LyP.[44]

Figure 5. Small, erythematous papules with light scale consistent with PL.

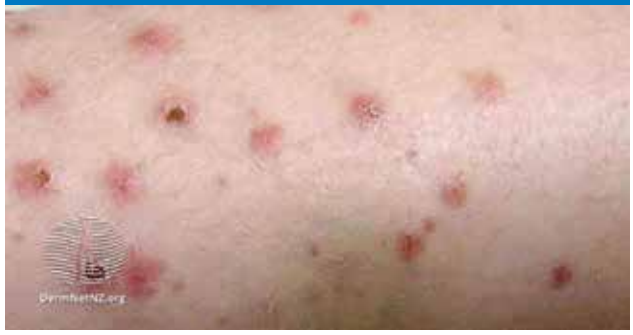


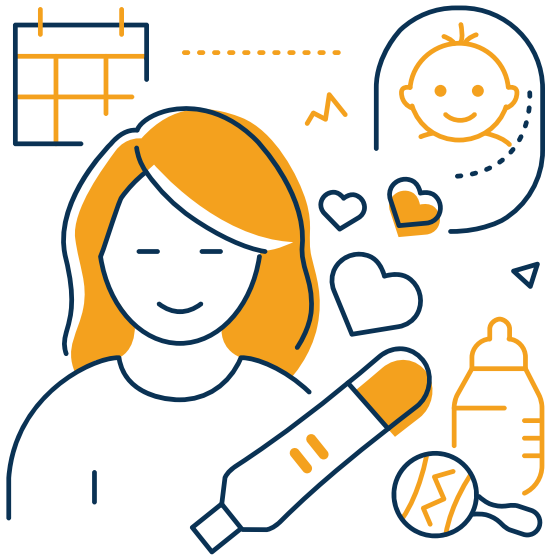
Image courtesy of DermNet

Histologic findings in PLEVA show an interface lymphocytic infiltrate with lymphocyte and erythrocyte exocytosis. Neutrophilic inflammation and ulceration may be present. In the dermis, the infiltrate involves the superficial vascular plexus in a wedge-shaped distribution.[49] PLC appears similar to PLEVA histologically, albeit much less destructive.[49] Rare cases of CD30+ PLC/PLEVA have been described in the literature creating histologic overlap with other CD30+ LPDs, specifically LyP type D.[50,51] A clear standard of treatment is lacking as proposed therapies may be confused with auto-resolution of the lesions.[42] Management is directed toward symptomatic treatment and preventing cosmetic disturbances.[42] Narrow band UVB therapy is most commonly used as first-line therapy with subsequent treatment including oral erythromycin, topical corticosteroids, and low-dose methotrexate.[42]

Arthropod Reactions

Arthropod reactions can also have clinical and histologic presentations similar to CD30+ LPDs. The most common

MEDICAID INCENTIVE *for initiating* PRENATAL CARE



The South Dakota Department of Health and Department of Social Services are WORKING TOGETHER to provide services for pregnant women.

In an effort to identify women early in their pregnancy who are already on Medicaid when they become pregnant, the SD Medicaid program is offering a **$10 incentive**:

- **Bill CPT code 0500F** when initiating prenatal care
- Reimbursable once per pregnancy

This CPT coding identifies moms who are eligible for education and case management services through the Department of Health's Office of Child and Family Services.

Please share this information with your billing professionals and colleagues who provide maternal services.

South Dakota Department of Social Services
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Figure 6. Erythematous papules with central hemorrhagic necrosis consistent with arthropod bites.

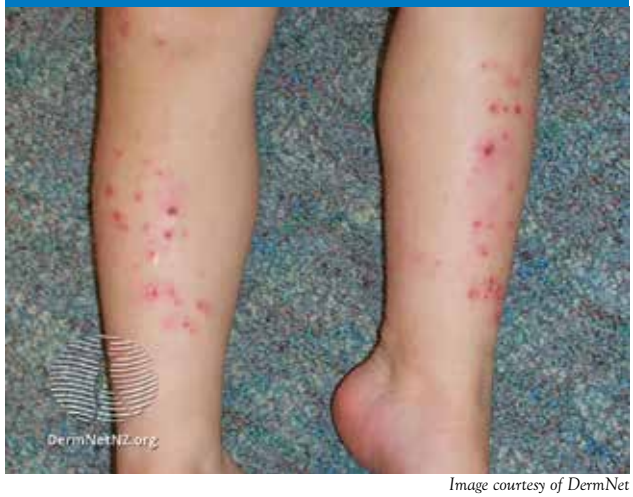

Image courtesy of DermNet

arthropod reactions in humans result from bites and stings from insects, spiders, scorpions, ticks, and mites.[52] Clinical findings are dependent on the etiology but generally involve erythematous papules, nodules, or vesicles with potential ulcerations or bite marks (Figure 6).[49] Histologic findings show dermal edema with widespread superficial and deep lymphocytic inflammation in a perivascular and wedge-shaped distribution.[49,53] Numerous eosinophils are often present; though are not required for the diagnosis.[49,52] Occasional studies have reported CD30 positivity in histologic analysis of arthropod bites, emphasizing the importance of clinicopathologic correlation when also considering CD30+ LPDs.[54,55] Most treatment options are for symptomatic control and eliminating future complications which include removing the stinger, cooling the area, topical anesthetics, antihistamines, and topical steroids.[56]

Lymphomatoid Medication Reaction

Lymphomatoid medication reactions represent a type of cutaneous pseudolymphoma.[57] These lesions are not felt to represent allergic hypersensitivity reactions to a particular medication, but instead are more likely a result of immune dysregulation from alterations of lymphocyte function.[58] The most common medications associated with lymphomatoid medication reactions are ACE inhibitors, anticonvulsants, antidepressants, antihistamines, antipsychotics, beta blockers, calcium channel blockers, and statins.[57] Clinically, these lesions can encompass a wide range of presentations but tend to appear similar to MF with asymptomatic erythematous nodules, patches, or plaques (Figure 7).[1,2,57] Microscopically, these lesions may resemble MF, LyP, or ALCL.[59] Often, there is a superficial band of infiltrative lymphocytes and histiocytes in the dermis, although the lymphocytes are typically polyclonal and non-atypical.[1,57] Similar to the other CD30+ LPD mimics, studies have reported CD30 positivity in lymphomatoid medication reactions, which emphasizes the necessity of strong clinicopathologic correlation in establishing the diagnosis.[60,61] Lymphomatoid medication reactions can last for months following removal of the offending agent, which is significantly longer than the few days needed to clear many other classic dermatologic medication reactions.[58]

Viral Exanthems

Viral exanthems represent that final mimic of CD30+ LPDs to be discussed. Vaccinations like measles, rubella, and varicella have made classical viral exanthems less common than drug exanthems.[62] Cutaneous involvement is often seen in viral illnesses such as parvovirus B19, human herpesvirus family, coxsackie, and acute HIV.[63] Interestingly, some latent viruses like Human Herpesvirus-6 (HHV-6),

Figure 7. Large, erythematous patches following drug administration consistent with a lymphomatoid medication reaction.

Image courtesy of DermIs

Figure 8. Widespread, erythematous macules and papules consistent with a viral exanthem.

Image courtesy of DermNet

cytomegalovirus (CMV), or EBV are hypothesized to be the root cause of specific drug exanthems.[62] Although the clinical presentation differs based on the etiology, the classic viral lesion is a widespread maculopapular exanthem (MPE) lacking scale (Figure 8) and is commonly associated with systemic symptoms such as fever, malaise, and headache.[49,62,63] Histopathologic findings in viral exanthems are relatively nonspecific and include focal spongiosis, papillary dermal edema, and mild lymphohistiocytic inflammation with red blood cell extravasation.[49] Although uncommon, viral exanthems with CD30 positivity have been reported.[64] Treatment is primarily symptomatic with specific therapies aimed at the underlying viral etiology.

Conclusion

In conclusion, we presented case reviews of both LyP and PCALCL, discussed the CD30+ LPDs, and reviewed potential mimics of these pathologies to ensure the proper workup, diagnosis, and management of such diseases. Given the overall favorable outcomes of these pathologies, it is important to separate these disorders from other high-grade malignant cutaneous diseases. Reviewing these disorders and their potential mimics will assist in a more rapid and correct diagnosis of these lesions.

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Abortion and The Hippocratic Oath: Historical Aspects

Amrita Bhagia, MS II; Andrew Nerland, MS II; Mitchell van Kalsbeek, MS III; and Henry Travers, MD, FACP

Of many controversial aspects in the practice of medicine from Hippocrates to the present, perhaps none have engaged the minds, hearts and pens of physicians, scholars, philosophers, politicians, theologians and the public in general more than the deliberate termination of fetal life through induced abortion. While the Hippocratic Oath presumably was not the first document to mention abortion,[1] those specific Orphic writings are lost. Nardi extensively documented abortion in antiquity,[2] including references to Plato, Aristotle, the Stoics and the Septuagint version of Exodus 21:22-23. Platonic and especially Aristotelian references included the concept of formed vs. unformed fetuses, a concept also found in Exodus.

A document of substantial provenance, the Oath is believed to precede the Christian era, although the earliest references to it come only after the birth of Christ.

In the 2,000 years since the Oath's first mention, political, theological, medical and ethical writings related to abortion have grown exponentially, many of them, beginning in antiquity, invoking the Oath's prohibition as a normative Hippocratic ethic. Today, as Veatch and Mason[3] speculated in 1987, "It may well turn out that the physician steeped in secular liberal political philosophy with its respect for the individual and its commitment to the liberal theory of justice would have as much trouble being Hippocratic as the physician in the Judeo-Christian tradition would." Here, we examine the Oath to gain an historical perspective of its relevance within the modern abortion controversy. There are three features of the Hippocratic Oath that make it important to understand historically: it is a document broadly recognized throughout our culture; it is often taken as a reflection of ancient views of medical ethics; and it has a central place within the Hippocratic tradition.

Though some believe a passage in Pliny the Elder's description of a 200-year-old speech by Cato in his 1st century CE *Natural History* referenced the Oath, Pliny's work is, at best, a mention of a *common* oath, not a specific one.[4] The first unequivocal reference ascribing the Oath to Hippocrates came in the first century CE. Scribonius Largus, in the preface to his 44-48 CE *Compositiones Medicamentorum*, originally composed in Latin, wrote:

> "Hippocrates, the founder of our calling, transmitted the beginnings of this discipline in the form of our sworn oath, which ordains that no physician should give, or even show, an abortifacient drug to a pregnant woman."[5]

One might think that Scribonius had seen a version of the Oath, but he did not reference a precise source. The lexicographer Erotian (1st century CE) listed the Oath in a bibliography of Hippocratic works,[6] although no ancient manuscript has yet been found. The earliest existing *document* containing any part of the Oath is among the Oxyrhynchus papyri* dated in the 3rd century CE.[7] The papyrus (fragment 2547), written in Greek, was identified four decades after publication of W.H.S. Jones's scholarly review of all then-extant manuscripts of the Oath.[8]

Jones used Greek manuscripts from the 11th, 12th and 14th centuries CE to construct a translation of the Oath he called the "Pagan Oath" and noted three remarkable versions: one in the Vatican Library (Urbinas 64 fol. 116, 10th or 11th century CE) containing a modification "so that a Christian may take it;" one designated Ambros. B 113 sup. from the 14th century CE (the Christian form) and one from the Scorialensis collection (∑ II 5 fol. 28^{v}, 3rd century CE) which mixes both the pagan and Christian versions.[8]

Barns,[9] writing after the discovery of the text in the Oxyrhynchus papyrus, described differences between the incomplete fragment and that of the Ambros. B referred to above. The section referring to abortion was not part of the papyrus. Noting multiple word substitutions in various versions of the Oath, Jones, Barns and others[10] concluded that a given version came from accidents of translation, from variations in textural opinion and from cultural and religious influences.

Examples of these variations illustrate the different understandings developed within the English translations.

Pagan

Similarly I will not give a pessary to a woman to cause abortion.[8] This is Jones's consensus translation where he uses the word πεσσόν (pessary). In the Ambros B. manuscript which gives both a pagan and a Christian version, πεσσόν is modified by the adjective φθόριον, the root word of which means the action or agency of causing death.

Christian

Similarly I will not give treatment to women to cause abortion, treatment neither from above nor from below.[8] The

underlined text does not appear in the pagan version. The word φάρμακον (remedy or treatment) is substituted for πεσσόν (pessary).

Scribonius

No physician should give, or even show, an abortifacient drug to a pregnant woman.[11] Prioreschi's translation of this reads *Hippocrates...began his teaching with an oath in which it was decreed that no abortifacient be given or revealed to a pregnant woman by any physician.*[12] Scribonius's extension of the prohibition to "even show" or reveal abortifacient drugs is not found in any other version of the Oath.

These textural differences lead to several questions. Is the Oath consistent with other Hippocratic teaching? Why do the texts differ concerning the specific methods of causing abortion? Is there any significance to be attached to the *first* characterization of the Oath coming *after* the beginning of the Christian era? Insofar as many interpretations of the Oath concluded it created a moral status for the fetus such that its life could not be terminated, exploration of these questions might influence the *degree* of moral authority regarding abortion that we assign to the Oath.

Is the Oath Consistent with Other Hippocratic Teaching?

In the entirety of the Hippocratic Corpus, except for the Oath, there are only rare allusions (pharmacological) and one direct reference to abortion. Nowhere except the Oath is the physician enjoined from advising or performing abortions. In *Nature of the Child*, the author described a mechanical method of abortion ("I told her to spring up and down so as to kick her heels against her buttocks") without any associated ethical reference.[13] In *Nature of Women*, there are instructions for the preparation of drugs to expel the fetus, prepare pessaries and compound contraceptives.[14] Galen's commentaries on Hippocratic works offer no references to the practice,[15,16] and he avoids the topic altogether.[17]

Pseudo-Galenic texts, compiled by Kuhn in the early 19th century, occupy some 20 volumes and were likely written in the third and early 4th centuries CE.[18] Among them is *Whether the Fetus Is a Living Creature* in which the author attributed to Hippocrates the notion that the fetus acquired the status of a living creature at conception. In another, *Gaurum*, the author declared the fetus lacked the ability to act in its own self-interest until birth, but that conclusion was not credited to Hippocrates.[19] The authorship of *Gaurum* (also titled *To Gaurus* or *Pro Gauros*) has been attributed to Porphyry (234-305 CE).[20]

There is, thus, no evidence of the proscription of abortion in the Hippocratic Corpus or commentaries upon it other than in the Oath, except for pseudoepigraphic examples written after the 1st century CE. Those, as well as Hellenistic works, often proclaimed an Hippocratic provenance only to add legitimacy to the writing.

Why Do Texts Differ Concerning Specific Methods of Causing Abortion?

The answers to this question require knowing the origin of the Oath. As two centuries of scholarship have shown, we continue to swim in a sea of speculation. The dating of the Oath to the late fifth or early fourth century BCE through previous scholarly consensus has been challenged recently. von Staden's careful linguistic study of the Oath[21] produced no firm conclusion about its origin, suggesting only that "... re-examination of the date of the *Oath* might be called for." von Staden gave numerous examples of "words, expressions, forms, constructions, and semantic usages found in the Oath [that] recur in no other Hippocratic texts."[21] The word πεσσός (pessary) appears in the singular *only* in the Oath, for example. The word translated as "the Art" (τέχνη) appearing in the Oath is different from a similar term (ἐπιστατειν) translated as "knowledge" or "understanding" found in *Precepts*, a late addition to the Hippocratic Corpus.

Tolsa suggested that the Oath had multiple authors.[4] He produced a chart comparing a 2nd or 1st century BCE inscription from a cult in Philadelphia with the Oath showing the words φθὸρτον (abortifacient) and πεσσόν (pessary) were each tied to a different tradition. Jan Bremmer, in his examination of the terms *pure* (ἁγνός) and *holy* (ὅσιος) in both the Oath and in an inscription at the Epidaurian Asclepeion, indicated that "it is now likely that in the course of the Hellenistic period some doctors had adapted their Oath to the growing stress on mental purity."[22] In suggesting a date no earlier than the 1st century BCE for the Epidaurian inscription, Bremmer noted these terms and a synonymous word in the Oxyrhynchus papyrus (εὐσεβής) were not used in classical times.

While, as Tolsa concluded, "the textural transmission of the Hippocratic writings before the first century A.D. remains a black box," he offered the "plausible hypothesis" that the abortion text in the Oath came from conditions arising between the mid-2nd century BCE and the 1st century CE and came from Greek physicians in Rome.[4] If this hypothesis is correct, then the different word choices came from the preferences and specific beliefs of writers who transmitted the Oath, an example of which is evident in the version Abros B from the 14th century described by Jones.

Related to the specific words used in prohibiting abortion in

the Oath is the remarkable sentence that closes the section. The statement "In purity and holiness I will guard my life and my art" was, as von Staden, in agreement with Bremmer, pointed out, "unparalleled in the Corpus."[21] Edelstein referred to this phrase (ἁγνῶς και ὁσίως - purity and holiness) as "indicative of standards of a different, a more elevated character."[23]

Is there any significance to be attached to the *first* characterization of the Oath coming *after* the beginning of the Christian era?

Exploring this question puts us squarely in the middle of Tolsa's black box. To begin with, given the scope of Hellenistic medical writing, the absence of clear references to the Oath is remarkable. This extends, particularly, to its absence in Galenic writings. Further, as noted above, the Oath's language is distinctive not only within the Hippocratic Corpus, but also within the context of Greek oaths generally.[21] Moreover, Edelstein in 1943 drew the parallel between the Oath's abortion prohibition and the Pythagorean view of life beginning at conception, noting that Platonic and Stoic ideas otherwise dominated the Corpus.† Finally, we have the earliest manuscript of the Oath dating from the 3rd century CE.

Edelstein's support for a fourth century BCE date for the Oath came directly from his ideas of its Pythagorean origin, and he dismissed the neo-Pythagorean revival in the 1st century BCE as embracing values different from its earlier incarnation. Against this view is evidence of a Pythagorean influence on the development of Christian values,[24] an influence that would not be inconsistent with a later dating of the Oath.

Tolsa[4] suggested that 2nd century CE editions of the Corpus "already had the Oath at the beginning," but he qualified that conclusion with the word "probably." Similarly, Nutton called this conclusion "...likely, although far from certain."[25] What is certain is that the Oath does not appear, certain highly speculative indirect allusions aside, prior to the first half of the first century CE and then only as a reference from a Roman author (Scribonius).

If the Oath were written after the beginning of the Christian era based on Christian values, one would have to assume the existence of an organized set of such values which did not exist at the time of Scribonius's writing. We think it is more likely that the Oath was composed prior to the birth of Christ and that its textural versions underwent numerous revisions by numerous authors both before that supposedly seen by Scribonius and afterward.

Discussion

This review of its historic provenance suggests that the Oath as we know it from existing documents is not "Hippocratic" in the sense of a sacred tradition passed down from the Father of Medicine. It is, rather, a document that was either composed in the first century prior to Christ's birth or was modified from an earlier version to its current texts beginning at that time. Its genesis came from religious traditions that were also, at least partly, incorporated into Christianity, although the path by which this happened is shrouded in mystery. The dating of extant manuscripts, the absence of manuscripts or references prior to the 1st century CE, the linguistic uniqueness of the Oath when compared to the Hippocratic Corpus, the variations in specific text words and the religious foundations of the Oath argue against the traditional Hippocratic authority so long attributed to the Oath.

The Oath today has found considerable utility in discussions of varied viewpoints about abortion. About its publicly accepted status as normative Nutton wrote:

> Above all, the later normative status of the *Oath* has given it a preeminence in discussions of ancient medical ethics that it did not have until centuries after it was composed, and which has tended to distort, at least in the public mind, perceptions of medical ethics, or deontology, of Antiquity.[26]

Nutton showed how the Oath was adapted to fit Christian, Muslim and Jewish "environments" and considered such adaption indicative of "its validity [resting] in its ideas rather than its words."[26] Indeed, a 2nd century CE inscription on an Athens temple‡ followed some of the essence of its ideas in a list of duties of the physician to "cure with moral courage" and "be like God savior equally of...all."[27] This 2nd century view, like those of today, reflects something other than an Hippocratic tradition.

* These papyri were discovered in Egypt and *collectively* date from the 3rd century BCE to the 7th century CE.

† Edelstein's view of a Pythagorean origin for the Oath has not received much support from modern scholars. Nonetheless, if one takes his observations to indicate a Pythagorean *influence* on the Oath's development, that conclusion is harder to refute.

‡ Oliver says the Hippocratic Oath is mentioned in this inscription, but the Greek text uses only the word ὁρκος or oath without any qualifiers.

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DR. SUNDEEP ALAPATI JOINS SANFORD HEALTH

After practicing medicine in other parts of the country, Sundeep Alapati, DO, has joined Sanford Health as a head and neck surgical oncologist at Sanford Ear, Nose and Throat Clinic in Sioux Falls. He is optimistic about Sanford Health and all it has to offer.

"I'm really looking forward to being at a health system that does the little things," Dr. Alapati said. *"I think it makes it easier to practice medicine and a lot easier to care for patients."*

Before Dr. Alapati moved to South Dakota, Sanford Health was the only thing he knew about the state.

"The reputation is fantastic," Dr. Alapati said. "*My father was a travel ER physician and worked at various Sanford hospitals. He said it was the best hospital system he worked for in his 40-year career."*

Vast experiences
Dr. Alapati brings a wealth of experience and wisdom to his role as a head and neck surgeon, including a fellowship in head and neck surgical oncology at Memorial Sloan Kettering Cancer Center in New York City.

After his fellowship, Dr. Alapati served as the director of head and neck surgery at the Jacobi Medical Center in the Bronx, New York. During that time, he also served as an assistant professor of otorhinolaryngology and head and neck surgery at the Albert Einstein College of Medicine.

"I got to see a lot of interesting things from people from all over the world with New York being as diverse as it is," Dr. Alapati said. *"I got to participate in great research projects, as well, and my mentors were world-renowned."*

After New York, Dr. Alapati moved to his hometown of Huntsville, Alabama, and started a head and neck surgery program.

"I started six months before COVID-19, which presented many challenges. However, I was extremely busy, and that helped me grow," he said.

Many hats
Dr. Alapati's expertise as a head and neck surgeon is not limited to oncology.

Besides treating patients with head and neck cancer, Dr. Alapati has developed a strong interest in thyroid disease.

"It's almost always curable," he said. *"You really get to think about the quality of life. We're focused on avoiding overtreatment, including procedures that could be debilitating."*

Dr. Alapati also helps patients who struggle with sleep apnea.

"I started building that as part of my practice and found I enjoyed it," stated Dr. Alapati. *"I found it to be very rewarding because you can help people quickly."*

A philosophy of individualized care
Whatever the diagnosis, Dr. Alapati takes a scientific approach that focuses on an individual's needs and circumstances, helping him tailor their treatment plans.

"As a physician, you're happiest when your patients are happy and doing well," Dr. Alapati said. *"I just want them to have the best possible outcomes."*

To refer a patient to Dr. Alapati, call the Sanford Ear, Nose and Throat Clinic at (605) 328-8200.

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Nonalcoholic Fatty Liver Disease in Women with Polycystic Ovarian Syndrome: A Narrative Review

Katerina N. DeHaan, MD; Jena Preszler, MD; and Keith Hansen, MD

Abstract

Polycystic ovarian syndrome (PCOS) has been estimated to affect 10-15 percent of women in the U.S. Emerging research has found higher rates of nonalcoholic fatty liver disease (NAFLD) among PCOS individuals. While the mechanism continues to be poorly understood the aim of this review is to convey the most recent knowledge regarding the pathogenesis, diagnosis, and treatments for NAFLD in PCOS patients. Elements of insulin resistance, hyperandrogenism, obesity, and chronic inflammation are culprits in the pathogenesis of NAFLD in these patients therefore early liver screening and diagnosis is essential. Although liver biopsy remains the gold standard, advances in imaging modalities show accurate diagnosis and some can even assess the risk of progression to cirrhotic states. Apart from lifestyle modifications resulting in weight loss, other treatments with bariatric surgery, thiazolidinediones, angiotensin-converting enzyme inhibitors (ACE-I)/angiotensin-receptor blockers (ARBs), and vitamin E show promising results.

Introduction

Polycystic ovarian syndrome (PCOS) has been estimated to affect 10-15 percent of women in the U.S.[1] Based on the Rotterdam criteria, PCOS is characterized by enlarged cystic ovaries, hyperandrogenism, and anovulation and is often a clinical diagnosis after exclusion of other endocrinopathies. Common associated abnormalities include insulin resistance, obesity, dyslipidemia, cardiovascular disease, dyslipidemia, metabolic syndrome, sleep disturbances, and psychological effects.[2] PCOS can remain undetected for years and many women seek treatment when faced with fertility issues due to chronic anovulation. Emerging research has found higher rates of nonalcoholic fatty liver disease (NAFLD) among PCOS individuals. While the correlation and mechanism contributing to liver disease in these patients continues to be poorly understood, recent studies have found a two-fold increase of NAFLD in women with polycystic ovarian syndrome.[3] As lipids accumulate in the liver, it leads to chronic inflammation and liver injury. Over time, NAFLD may evolve to fibrosis, cirrhosis, and possibly hepatocellular carcinoma.[4]

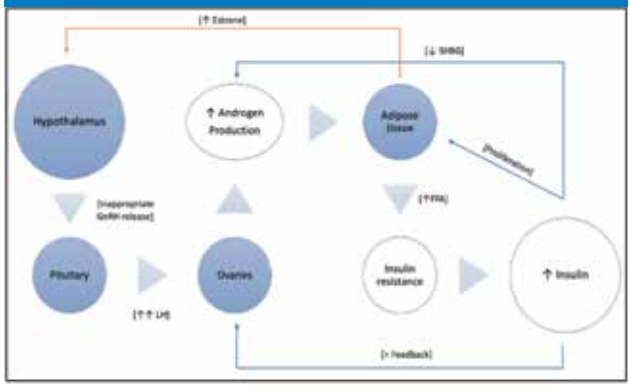
Recent data depicts an increasing rate of NAFLD in women with PCOS of all reproductive ages regardless of BMI.[5,6] The question being addressed is whether these two pathologies act independently or synergistically. Because NAFLD has a silent and insidious progression it is imperative to explore early diagnosis and treatment by understanding the biological mechanisms by which it occurs. Therefore our aim for this review is to convey the most recent knowledge regarding the pathogenesis, diagnosis, and treatments for NAFLD in PCOS patients.

Pathophysiology of NAFLD in PCOS

Although the exact pathogenesis of NAFLD in the setting of PCOS is multifactorial, there are a few key hallmarks of PCOS which are thought to propagate NAFLD. Generally, in PCOS there is a central dysregulation of gonadotropin-releasing hormone (GnRH) by the hypothalamus. Over time this deviation from normal physiology imbalances the biochemical pathways resulting in hyperandrogenism (HA), insulin resistance (IR), obesity, and inflammatory cytokines.[7] These features are proposed to be the major factors driving towards NAFLD.

Insulin resistance (IR) is a common overlapping comorbidity seen in PCOS and NAFLD independently. Although obesity can significantly promote IR, this resistance can be seen in both lean or obese PCOS women.[8] As seen in Figure 1, the overproduction of androgens trigger free fatty acid (FFA) release and lead to insulin production. In return, insulin positively acts on the ovaries driving further hyperandrogenemia by upregulating enzymes key in androgen production by the ovary and adrenals. An abundance of FFAs produced by this uninterrupted cycle are taken up and

Figure 1. Pathophysiologic biochemical pathways leading to hyperandrogenism, insulin resistance, obesity, and inflammation in PCOS.



stored by the liver. In the liver, insulin encourages collagen formation as well as decreases the production of sex hormone binding globulin (SHBG), resulting in increased circulating free androgens.[9] A large retrospective cohort study in the United Kingdom demonstrated increased testosterone and decreased SHBG among NAFLD and PCOS groups than those with PCOS alone.[9]

Chronically elevated levels of androgens manifest as hirsutism, acne, and alopecia. A meta-analysis of 17 studies found a 2 times higher prevalence of NAFLD in women with PCOS, independent of BMI or geography.[11] While further stratification showed no increase in NAFLD prevalence among non-HA PCOS women.[11] Androgens are known to act directly on liver LDL receptor transcription factors perpetuating lipid accumulation in the liver and dyslipidemias.[12] Moreover, a study performed on female rats suggests IR and HA have synergistic effects on NAFLD. Independently, rats with IR or HA showed evidence of hepatic lipid accumulation while those rats with HA and IR showed significant inflammatory response and hepatic cell damage.[13] Other similar studies confirm the combination of IR and HA trigger liver steatosis.[14] Finally, androgens contribute an overall increase in visceral adiposity.[15]

In obese women, adipokines and inflammatory mediators released by adipose tissue create a chronic state of inflammation and propagate NAFLD.[16] In fact, PCOS rats treated with anti-inflammatory agents resulted in weight loss, reduced androgen levels, and positively altered lipid metabolism.[17]

Diagnosis

In order to screen for NAFLD in PCOS patients it is crucial to appropriately diagnose the triggering disease. This requires a history, physical exam, pelvic ultrasound, and laboratory testing fulfilling at least two out of three Rotterdam criteria. For patients lacking obvious signs of hyperandrogenism consider measuring total testosterone, free testosterone, and DHEA-S levels. Ovulatory dysfunction or anovulation can be characterized by a history of irregular menses or amenorrhea. Workup if amenorrheic would include total and free testosterone, sex hormone-binding globulin, TSH, prolactin, 17-OHP, and FSH. Finally, pelvic ultrasound depicting an ovary volume of >10 ml or >12 follicles measuring 2-9 mm in at least one ovary fulfills the polycystic criteria.[18]

As previously described, it is imperative for PCOS patients with evidence of insulin resistance, hyperandrogenism, and/or obesity to be monitored for NAFLD. The diagnosis of NAFLD requires (1) evidence of hepatic steatosis by imaging or histology, (2) lack of alcohol consumption, (3) no alternative cause for hepatic steatosis, and (4) no other cause of chronic liver disease. Common alternative causes of hepatic steatosis are alcohol use, hepatitis C, parenteral nutrition, Wilson's disease, severe malnutrition. Additionally, causes for chronic liver disease, such as hemochromatosis, autoimmune liver disease, chronic viral hepatitis, alpha-1 antitrypsin deficiency, and drug-induced liver injury should be ruled out.[19]

The importance of a proper diagnosis in this condition is to distinguish between simple steatosis (NAFL) and nonalcoholic steatosis (NASH), as the latter can lead to fibrosis and cirrhosis. Initial laboratory tests such as a lipid panel, hepatitis antibodies, serum AST/ALT, and ferritin are useful when working through the differential. Evidence of hepatic steatosis can be confirmed by imaging or histology. The gold standard for diagnosis is percutaneous liver biopsy.[20] Liver biopsy is also useful for distinguishing NAFL from NASH, grading the severity of injury, and staging the degree of progression to cirrhosis.[20] Guidelines for when to obtain a biopsy are not clear and may not be the best first line study, especially for screening purposes. In general, liver biopsy should be considered if the diagnosis is unclear after obtaining standard laboratory tests, imaging, if there is evidence of cirrhosis or if the patient is at increased risk for advanced disease and would benefit from the additional information provided by biopsy.[21]

While liver biopsy may be the gold standard, an initial workup for NAFLD includes noninvasive imaging studies. Options for imaging consist of ultrasound, CT, and MRI. In a patient who has never had imaging done before, ultrasound is the best place to start. The main advantages of ultrasound are availability and low cost, however, it may not detect hepatic fat content in obese patients or if the hepatic fat content is

Table 1. Comparison of diagnostic tools. Clinical decision tools such as the NAFLD fibrosis score (NFS) or fibrosis-4 index (FIB-4) can help identify patients who are in the low-risk or high-risk category for developing advanced fibrosis and ultimately cirrhosis.

NFS variables	FIB-4 index variables
Age, AST/ALT, platelet count, **BMI, serum glucose, albumin**	Age, AST/ALT, platelet count
Score < -1.455 = low risk Score -1.455 – 0.675 = indeterminate Score > 0.675 = high risk	Score < 1.3 = low risk Score 1.3 - 2.67 = indeterminate Score > 2.67 = high risk

less than 20 percent.[21] MRI with proton density fat fraction or spectroscopy is the gold standard to assess the amount of liver fat if as low as 5-10 percent, but it is costly and has limited availability. Another imaging study to consider when quantifying liver fat content is the ultrasonography-based transient elastography (TE). This tool can measure liver stiffness as well as potentially evaluating the severity of NAFLD at the same time.[20,21] Another noninvasive method, the ultrasonographic fatty liver indicator (US-FLI) has been shown to correlate with the histological evaluation of NAFLD and can help to identify patients with increased risk of steatohepatitis needing liver biopsy.[22] In addition to imaging studies, clinical decision tools such as the NAFLD fibrosis score (NFS) or fibrosis-4 index (FIB-4) can help identify patients who are in the low-risk or high-risk category for developing advanced fibrosis and ultimately cirrhosis. These diagnostic tools are compared in Table 1.[23]

In patients with PCOS, it is important to detect NAFLD early as appropriate intervention at the stage of simple steatosis can help prevent disease progression. It would be reasonable for patients with PCOS to have an evaluation consisting of aminotransferase levels, assessment of hepatic steatosis by ultrasound, especially if they have metabolic syndrome.[22] However, in the practice guidance from the American Association for the Study of Liver Diseases, routine screening in high-risk groups attending primary care, diabetes, or obesity clinics is not advised at this time due to uncertainty in the diagnostic tests and treatment options.[19] Due to conflicting recommendations from sources, we will outline an option for diagnosis of NAFLD for primary care providers as suggested in a recent review article from Budd & Cusi, 2020.

1. Recognize patients with abnormal transaminases, history of fatty liver, or incidental finding of fatty liver on imaging
2. Exclude other causes of hepatic disease and steatosis
3. Confirm NAFLD using imaging studies (ultrasound)
4. Explore the patient's risk assessment for fibrosis
    1. Look for contributing conditions such as T2DM or metabolic syndrome
    2. Perform diagnostic studies such as FIB-4 or NFS
    3. Consider TE or US-FLI
5. If low risk → periodically reevaluate the patient for progression
6. If high risk → consider referral to hepatology to perform liver biopsy[23]_

Treatment

There are some recent developments in pharmacotherapy and novel agents for treatment of NAFLD, with the initial recommended step of weight reduction. Methods for weight loss include dietary changes, physical activity, and behavioral modifications.[24] A randomized controlled trial by Promrat et al. concluded that weight reduction of at least 7 percent after lifestyle modifications resulted in a significant improvement in the liver histological findings.[25] Although successful, this method may not be the most sustainable as many patients have difficulty with weight loss. Weight loss medications or bariatric surgery can be considered.

Patients who fail lifestyle interventions or have advanced disease may benefit from pharmacotherapy. There is limited trial evidence for many of these treatments, but a few have potential benefits. The most studied pharmacotherapy is thiazolidinediones, such as pioglitazone, which help improve insulin resistance and promote peripheral fatty acid uptake, diverting them away from the liver. This treatment was shown to improve insulin sensitivity, aminotransferase levels, steatosis of the liver, and inflammation. Although thiazolidinediones are one of the first-line treatments for NAFLD, review on the drug was concerned for cardiovascular morbidity when used in patients with PCOS.[26] However, more recent studies show that this may be a promising treatment, providing both metabolic and reproductive effects[27]. Another therapy that has shown potential benefit is vitamin E. Vitamin E helps to prevent the nonenzymatic oxidation of cells, which has been thought to play a role in the pathogenesis of NASH.[24] Other agents such as metformin, statins, ursodeoxycholic acid, and polyunsaturated fatty acids have been investigated but have shown no clear benefit, therefore are not recommended to treat NAFLD specifically.[24]

Cardiovascular disease is the leading cause of death in patients with NAFLD, thus management of blood glucose, lipids, and blood pressure is essential. Pioglitazone, GLP-1a agonists, and SGLT2 inhibitors can be useful for treating diabetes

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as well as reducing cardiovascular disease risk. Control of lipids can be achieved with a statin. Blood pressure control with angiotensin-converting enzyme inhibitors (ACE-I) and angiotensin-receptor blockers (ARBs) have also been shown to decrease liver fibrosis in patients with NAFLD.[23]

For PCOS specifically, a combination of lifestyle modifications, weight loss, and metformin is recommended. Metformin improves the sensitivity of peripheral tissue to insulin and decreases circulating insulin levels in the patient. It also has a beneficial effect on androgen excess by increasing steroid hormone binding globulin and decreasing androgen levels. The drug has been used for decades to treat the metabolic and menstrual dysfunction in PCOS.[22] While metformin is not specifically indicated for treatment of NAFLD, the improvement in PCOS should ultimately help decrease the risk and progression of NAFLD in these patients.

Conclusion

Growing evidence has linked NAFLD as an unfortunate complication of PCOS. Key features such as insulin resistance, hyperandrogenism, obesity, and chronic inflammation are culprits in the development and progression of NAFLD. It is imperative to properly screen and diagnose fatty liver changes in PCOS patients with imaging modalities and laboratory testing. Lifestyle modifications resulting in weight loss is the most important treatment in the management of both conditions.

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A Concise Review of Neonatal Dermatology

Halie N. Burdick, MD; Allen A. Wellman, MS IV; and Kathryn M. Anderson, MD

Abstract

Skin findings in neonates carry a wide differential diagnosis, ranging from self-limiting rashes to something more sinister, as cutaneous changes can be an indicator of a serious underlying infectious process. Even benign rashes can cause great concern for families and providers. Pathologic rashes pose a potential risk to the neonate's health. Therefore, it is important to diagnose skin findings and provide any necessary treatment swiftly and accurately. This article provides a concise review of neonatal dermatology with the goal to aid providers in diagnosing and managing neonatal skin conditions.

Introduction

Skin is a complex organ. Its functions include providing protection from outside insults, decreasing water loss, and allowing for cooling through perspiration. Neonatal skin is largely matured in utero by 34 weeks, but still has several differences when compared to adult skin.[1] Neonatal skin, in general, is more fragile and permeable. Therefore, neonates are more susceptible to infection, at higher risk for heat loss, and more sensitive to chemical or thermal damage.[2] As such, pediatric providers must be familiar with the wide differential diagnosis of neonatal rashes and other skin findings. It is of the utmost importance that providers be familiar with cutaneous findings in neonates to ensure a timely diagnosis and, if needed, treatment.

A thorough skin exam is an important part of the neonatal assessment after delivery and at each interaction between the neonate and health care provider. When a provider first identifies a rash, lesion, mass, or other cutaneous change, they should perform a thorough inspection of all skin surfaces, including the scalp. Additionally, it is crucial to consider the gestational age, past medical history to date (with close attention to maternal history), and overall clinical status of the neonate. Many neonatal skin findings do not require additional work up and can be managed conservatively. Providers who are familiar with neonatal dermatology can be confident in their diagnosis based on history and physical exam. In situations of a term, well appearing neonate with a clear diagnosis, providers can follow the neonate clinically to ensures cutaneous finding progresses along the expected course and guarantee the neonate remains well appearing.

Importantly, whenever a neonate with a skin finding is clinically unstable or there is concern for evolving systemic infection, providers should have a low threshold for transfer to a facility with a higher level of care if their facility is not able to meet the neonate's needs. Special caution should be taken with preterm infants who can decompensate quickly from underlying infectious causes of neonatal rashes. Providers should not hesitate to obtain consultation from neonatologists, pediatric dermatologists, pediatric infectious disease physicians, or other subspecialists as deemed necessary if the diagnosis is uncertain. This consultation may involve transfer to another facility pending access to subspecialists and temedicine. Telemedicine and/or transmitting images via secure electronic health systems can allow for remote consultation. These remote options can help define the diagnosis, guide initiation of treatment, and assist in triaging for transfer to another facility. When the diagnosis is unclear after appropriate consultation and non-invasive work-up (if possible), skin biopsy performed by a dermatologist may be necessary to aid in diagnosis and management.

Benign Skin Findings Present at Birth

Vernix Caseosa

Vernix caseosa, also known as vernix, is a normal neonatal skin finding. It appears as a thick, white film that covers neonates at birth and is partially formed by the neonatal sebaceous glands during the final trimester.[3] The vernix helps the neonate with the transition from intrauterine to extrauterine life. Functions of the vernix include waterproofing the neonatal stratum corneum, lubrication of the birth canal, and providing antimicrobial defense.[4] Vernix also has antioxidant, moisturizing, and wound healing properties.[4]

Congenital Dermal Melanocytosis

Congenital dermal melanocytosis appears as a blue-gray patch most often found on the lumbar and sacral-gluteal region (Figure 1). This benign skin finding is most often seen in dark skinned neonates.[5] The pathophysiology behind congenital dermal melanocytosis is abnormal melanocyte migration. Rather than migrating to the stratum basale layer of the epidermis, melanocytes remain in the dermis producing the darker colored skin.[5] If tenderness or multiple patches in different stages of healing are observed, non-accidental trauma should be considered and ruled out. Congenital dermal melanocytosis is a benign condition that requires no further work up or treatment and typically regresses by 1 year of age.[5]

Sucking Blisters

Sucking blisters occur due to vigorous sucking on the affected region while in utero, most commonly occurring on the forearms, hands, or fingers.[6,7] The incidence has been reported at one in 250 live births.[6] Sucking blisters appear as single or multiple sterile fluid-filled vesicles that form erosions. The focal presentation, rapid resolution, and lack of additional vesicle formation points toward a diagnosis of sucking blisters as opposed to herpes simplex virus, varicella infection, or bullous impetigo.[6,7] The blisters resolve once the infant stops sucking on the lesions and do not require any further treatment.[6]

Transient Vascular Phenomena

Cutis Marmorata and Harlequin Color Change

Cutis marmorata (CM) and harlequin color change are types of transient vascular phenomena. These transient vascular phenomena are a normal neonatal physiologic occurrence. CM is a vascular response to cold that gives the skin a reticular appearance (Figure 2). This normal manifestation usually self-resolves by the age of two and requires no treatment.[8] Although CM usually disappears with warming, there is a congenital form called cutis marmorata telangiectasia congenita (CMTC) which is persistent.[8] CMTC can be associated with musculoskeletal anomalies, vascular abnormalities, cardiac defects, neurological defects, or ocular abnormalities and warrants further work-up.[9]

Harlequin color change involves erythema on the dependent portion of a neonate's body with simultaneous pallor on the opposite nondependent portion of the body. This finding is normally observed in the second through fifth days of life.[10] Harlequin color change occurs without provocation or physiologic changes in the neonate and usually lasts between 30 seconds to 20 minutes.[10] This transient, benign entity is self-resolving and requires no treatment or further management.

Benign Neonatal Eruptions, Bumps, and Plaques

Erythema Toxicum Neonatorium

While erythema toxicum neonatorium (ETN) is a rash of unknown etiology, it is thought to be a result of microbes colonizing the skin at birth.[11] This rash typically appears within the first few days after birth, but can appear any time within the first two weeks of life.[12] The appearance is described as erythematous macules, papules, and pustules (Figure 3). Histology shows eosinophils and

Figure 1. Congenital dermal melanocytosis.

Figure 2. Cutis marmorata.

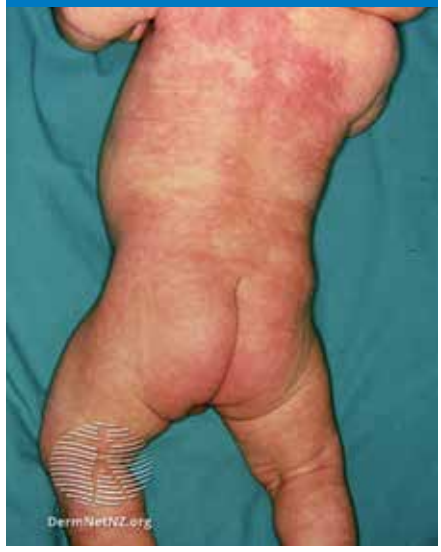

Figure 3. Erythema toxicum neonatorum.

Figure 4. Transient neonatal pustular melanosis.

Figure 5. Neonatal cephalic pustulosis.

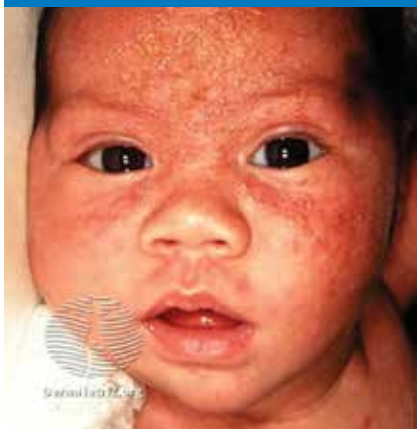

Figure 6. Milia.

Figure 7. Miliaria.

neutrophils in the dermis and perifollicular papules and pustules with eosinophils.[12] No laboratory work up is needed. This rash is benign and resolves within a week or two without any sequelae, but parental reassurance is paramount as rashes can be a source of great concern.[13]

Transient Neonatal Pustular Melanosis

Transient neonatal pustular melanosis is a rash that starts in utero. The rash occurs in three stages: pustules, followed by ruptured vesico-pustules with a halo-type rim of scaling, and finally hyperpigmented macules (Figure 4).[14] The etiology of this rash is unknown, but it is more commonly seen in infants with darker skin. A Wright's stain of the pustules will show neutrophils, which can be used to differentiate this rash from erythema toxicum where eosinophils predominate. No treatment is necessary as transient neonatal pustular melanosis is benign and typically resolves in weeks to months.[15]

Sebaceous Hyperplasia

Sebaceous hyperplasia appears as yellow-white papules located commonly around the nose or upper lip with a reported incidence as high as 89 percent of newborns.[16,17] The rash is driven by androgens the neonate is exposed to in utero that come from either the mother or the neonate.[17] Treatment is not usually needed as this skin finding resolves as maternal hormone levels decrease during the first few weeks of life. [17]

Neonatal Cephalic Pustulosis

Neonatal cephalic pustulosis is a benign rash that is a variation of acne and appears in the neonatal period. It is thought to be due to inflammation caused by neonatal skin colonization with Malassezia species.[18] This rash presents in the first three weeks of life and can involve the cheeks, eyelids, chin, neck, and upper chest.[19] It is characterized by numerous pustules in the locations previously mentioned and is differentiated from neonatal acne by the absence of comedomes (Figure 5). Although this lesion is benign and typically self resolves, topical ketoconazole can be used for persistent cases.[19]

Milia

Milia is found in approximately half of neonates at birth and appears as tiny papules (Figure 6).[20] These are superficial cysts filled with keratin originating from the pilosebaceous unit that are typically located on the face.[20] This is a clinical diagnosis and there is not treatment needed as milia normally self resolves.[20]

Miliaria

Miliaria commonly known as "heat rash", "prickly heat", or "sweat rash" has several subtypes including miliaria crystallina, miliaria rubra, and miliaria profunda. Miliaria crystallina has an incidence around four to nine percent and is usually seen within the first two weeks of life.[21] Miliaria rubra is the most common subtype of miliaria and typically appears within one to three weeks of age.[21] Miliaria is caused by blockage of eccrine sweat glands either by cutaneous debris or bacteria and there is an increased risk with sweating.[21] The different subtypes of miliaria involve different layers of skin and therefore appear slightly different, but generally appear as shown in Figure 7. Miliaria crystallina involves the superficial layer of the epidermis with superficial vesicles.[21] Miliaria rubra is deeper with an inflammatory response that creates erythematous vesicles and papules.[21] This can be differentiated from folliculitis by minimal follicular involvement. Miliaria profunda is located at the dermal-epidermal junction with large, tense flesh-colored papules.[21] No treatment is needed but entering a cooler and drier environment to decrease sweating can hasten improvement.[21]

Seborrheic Dermatitis

Seborrheic dermatitis has a reported incidence of 72 percent

Figure 8. Seborrheic dermatitis.

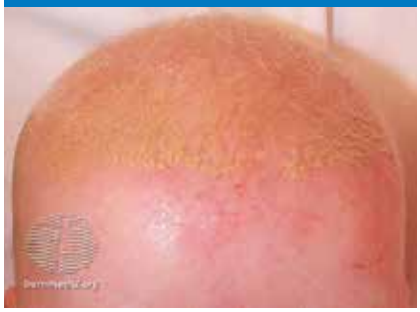

Figure 9. Infantile hemangioma.

Figure 10. Blueberry muffin rash.

in the first three months of life.[22] The etiology is not certain, however, there are several plausible explanations including maternal hormones, microorganism metabolism including *Malassezia species*, and the presence of increased fatty acids.[22] The rash appears as red patches of greasy, yellow or white scale (Figure 8) and can commonly be found on the scalp, central face, and chest.[23] The combination of seborrheic dermatitis, diarrhea, and failure to thrive should prompt evaluation of underlying immunodeficiency.[23] By itself seborrheic dermatitis is a benign, self-resolving rash, but common treatments include topical emollients or steroids, shampoos, or antifungals.[22]

Hemangiomas

The appearance of hemangiomas includes a bright red to violaceous macule or papule most often present on the head and neck (Figure 9). Hemangiomas in infants can be separated into two distinct categories of either infantile hemangiomas or congenital hemangiomas. Infantile hemangiomas have an incidence of approximately 5 percent with risk factors including maternal vaginal bleeding in the first trimester, progesterone use, preeclampsia, placenta previa, premature birth, low birth weight, and advanced maternal age.[24,25] Congenital hemangiomas have lower incidence and are rare. While congenital hemangiomas are fully grown at the time of birth, infantile hemangiomas will typically present prior to four weeks of age and go through a growth phase until the fifth month.[24] Some of the potential complications of infantile hemangiomas include ulceration, bleeding, and congestive heart failure in large lesions due to arteriovenous shunting.[24] Although most involute with time, treatment options for complicated or refractory hemangiomas can include beta-blockers or laser treatment.

Neonatal Skin Findings Requiring Further Work Up

TORCH Infections

TORCH stands for toxoplasmosis, other (syphilis, parvovirus B19, listeria), rubella, cytomegalovirus, and herpes. These infections occur by maternal-fetal transmission and can carry serious consequences, including severe disability or death.[26] A common cutaneous finding in many TORCH infections is the characteristic blueberry muffin rash. This rash consists of round or oval one-to-seven-millimeter non-blanching, violaceous papules, nodules, and purpuric macules representing manifestations of extramedullary hematopoiesis (Figure 9).[27,28]

Table 1 provides a concise review of the risk factors, skin manifestations, associated findings, and management for each TORCH infection.

Impetigo

Impetigo is a superficial infection caused by *Staphylococcus aureus* (which causes bullous or non-bullous impetigo) and occasionally group A *Streptococcus pyogenes* (which causes non-bullous impetigo).[35,43] Impetigo neonatorum presents within the first few days to weeks of life as pustules, vesicles, or bullae containing clear or purulent fluid.[35,44] The vesicles and bullae denude easily and can develop a characteristic honey-colored crust, although crusting is often absent. The raw, inflamed erythematous bases beneath the lesions may be painful or pruritic and develop a scaling border. Bullous impetigo is the most common cause of ulcerative lesions on the buttocks and intertriginous region of infants, although it also commonly occurs in the axillae, neck, trunk and groin.[35,43] Conversely, the non-bullous form has a predilection for the face and extremities.[44] Although this condition may resolve in two or three weeks, treatment for impetigo not complicated by systemic infection includes antibiotics. Decisions on drug and route (oral versus topical) are informed by culture results and local sensitivities.[32,43]

Staphylococcal Scalded Skin Syndrome

Staphylococcal Scalded Skin Syndrome (SSSS) is a severe bullous condition caused by exfoliative toxins A and B producing strains of *S. aureus*.[45] The toxins proteolytically cleave desmoglein-1 leading to acantholysis, blistering and

Table 1. TORCH stands for toxoplasmosis, other (syphilis, parvovirus B19, listeria), rubella, cytomegalovirus, and herpes. This table provides a concise summary of risk factors, skin manifestations, associated findings, and management for TORCH infections in neonates.

Infection	Risk factors	Skin manifestations	Associated findings	Management
Toxoplasmosis[29]	Owning cats, cleaning litter boxes, exposure to soil or contaminated water, eating undercooked meat, poor hygiene[30]	Petechia and purpura, maculopapular lesions[31]	Chorioretinitis, intracranial calcification, microcephaly, blindness, hydrocephalus, seizures, thrombocytopenia, anemia, jaundice	Postnatal treatment with sulfadiazine, pyrimethamine, and folinic acid
Syphilis [32]	Maternal syphilis infection, especially early and untreated	Desquamating vesiculobullous or maculopapular lesions classically on palms and soles, jaundice [32-34]	Hepatosplenomegaly, hemolytic anemia, rhinitis as a neonate	Benzathine penicillin G
Parvovirus B19[35]	Parvovirus B19 infection during pregnancy, especially before 20 weeks gestation	Subcutaneous edema, petechiae, blueberry muffin rash[28]	Fetal anemia, hydrops fetalis, polyhydramnios, high-output heart failure, pericardial effusion, pleural effusion, in-utero fetal demise	In-utero blood transfusion, IVIG [36]
Listeria[37]	Consuming deli-style or smoked meats, unpasteurized soft cheeses, unpasteurized milk, raw or frozen produce, or melons during pregnancy	Early-onset: maculopapular or papulovesicular rash Granulomatosis infantiseptica: widespread micro-abscesses and granulomas	Early-onset: bacteremia, meningitis, pneumonia, jaundice, lethargy Granulomatosis infantiseptica: hepatic and splenic granulomas	Penicillin G, ampicillin
Rubella	Maternal infection prior to 20 weeks gestation (most defects occur from exposure prior to week 10)[38]	Blueberry muffin rash, reticular erythema, hyperpigmentation, jaundice[35,39]	Cataracts, pigmentary retinopathy, micro-ophthalmia thrombocytopenia, patent ductus arteriosus and other cardiac defects, sensorineural deafness, hepatosplenomegaly microcephaly [35,37,38]	Supportive management, regular examination of affected organ systems[40]
Cytomegalovirus (CMV)[35]	CMV is the most common intrauterine infection in the United States. Transplacental infection, due to primary maternal infection (most common) or recurrent infection can transmit to the fetus	Petechiae, purpuric macules, blueberry muffin rash, jaundice, maculopapular eruption, rarely vesicles[31]	Chorioretinitis, periventricular calcifications, ventriculomegaly, microcephaly, hepatosplenomegaly, anemia, sensorineural deafness, seizures, mental retardation [27,35]	Intravenous ganciclovir, oral valganciclovir; for symptomatic infants six months of treatment improves audiologic and neurodevelopmental outcomes[27,35]
Herpes simplex virus (HSV)	Maternal infection with HSV, especially primary infection occurring during gestation [41]	Vesicles on an erythematous base, petechiae, purpura, bullous lesions, ulcerations, pustules, scarring[31,35,41,42]	Central nervous system abnormalities (calcifications, microcephaly, microphthalmia, chorioretinitis), hepatomegaly, limb abnormalities [34,39]	High dose acyclovir: will not reverse organ damage sustained in-utero but may prevent progression;[35,41,42] isolation precautions should be followed [35,41,42]

epidermal necrolysis.[46] Bullae are flaccid and Nikolsky sign positive, easily rupturing to reveal moist crusting skin which heal without scarring.[46] SSSS most commonly presents between days three and seven of life. It begins as a bright erythema of the face, neck and flexures before blistering and denuding. Intense perioral and periocular crusting is typically observed, though the oral mucosa is spared.[47] Culture swabs from intact bullae will be negative as the fluid within is sterile. Treatment includes hospitalization with administration of parenteral antibiotics and supportive care with intravenous fluids and electrolytes.[46,47]

Candida

Neonatal candidiasis typically presents as a localized diaper dermatitis or as oral thrush.[48] Candida diaper dermatitis findings can range from erythema, edema, and confluent vesicopustular lesions to moist scaly plaques with characteristic satellite pustules.[47,49] A rare congenital cutaneous form of candidiasis can occur as desquamating erosive erythematous macules, papules, and pustules which are widespread, including palms and soles.[45,47,48] Mucocutaneous candidiasis occurs in the form of oral thrush, with discrete friable white plaques on an erythematous base present on the tongue, gingivae, buccal mucosa, or oropharynx.[48] In otherwise healthy term neonates, candidiasis usually resolves in one to two weeks, however topical or systemic antifungals may be used depending on severity and extent of infection.[47-50]

Conclusion

This concise review highlights many cutaneous conditions that can be found in neonates. Skin findings presented in this paper range from benign to potentially dangerous etiologies, such as those occurring in the setting of TORCH infections. The pediatric provider must be familiar with neonatal skin to differentiate between rashes that can be followed conservatively and lesions with the potential for serious sequelae that require additional work up. Timely diagnosis and appropriate management of neonatal rashes is important to maintain neonatal health.

Photos courtesy of DermNet NZ.

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Staying Up to Date on Immunization Recommendations

Deidra Van Gilder, PharmD; and Alexia Stumpf

It is no secret that scheduled immunizations play a large role in keeping patients safe and healthy. The healthcare team is a critical part of recommending the appropriate vaccinations for patients. Unfortunately, compliance with vaccine schedules, especially multiple-dose vaccine series, is subpar.[1] Furthermore, over two-thirds of patients trust healthcare providers as the most reliable source of vaccine information.[2] Immunization recommendations are one of the most impactful interventions that can be made to better the health of the patient and the community. Due to the importance, it is critical that providers are up to date on current vaccination recommendations. This presents a challenge because of ever-changing vaccine schedules. This article will provide practical ways to stay up to date with immunization schedules to ensure all patients are properly vaccinated in addition to highlighting some of the most recent changes into specific vaccines.

Immunization schedules are revised and updated and new guidelines published at least once a year, making it critical for providers to be continually informed on any updated recommendations. With such frequent changes it can be challenging to know which vaccines patients are due to receive. Fortunately, there are numerous resources to help healthcare providers stay up to date on current immunization schedules. These resources include authoritative sources, websites, printable schedules, and even digital apps. With all these resources readily accessible, making up-to-date immunization recommendations has never been easier.

The Centers for Disease Control and Prevention (CDC), the U.S. Food and Drug Administration (FDA), and the Advisory Committee on Immunization Practices (ACIP) are just a few of the authoritative sources that can be utilized to find accurate immunization information. The CDC website has easy-to-follow visual schedules specifically designed to help healthcare providers follow which immunizations a patient should receive based on their age.[3] The CDC website also has recommendations on which vaccines to administer to specific patient populations. Meanwhile, the FDA website includes information on which disease states each vaccine covers, along with its scheduled administration age, dosages, and potential side effects.[4] The FDA bases recommendations solely on approved indications tested through clinical studies and other data submitted by the vaccine manufacturer. At the same time, the ACIP holds meetings to address making changes in vaccine schedule recommendations.[5] Their guidelines consider a wide variety of aspects in addition to the FDA indications such as additional clinical studies, disease burden, gaps in data, health impact, and cost effectiveness of vaccine schedules. These additional considered factors result in ACIP recommendations occasionally differing from FDA indications.

Another website, www.immunize.org, formerly known as the Immunization Action Coalition, is a one-stop-shop for all vaccine-related information.[6] This website provides resources for the healthcare team such as administration instructions, vaccine specific information, vaccine schedules for all ages, and even laws, package inserts, and reporting instructions, among many other helpful documents and printouts.

For a more readily accessible reference source, the Shots Immunization App for mobile devices is a great option.[7] This app allows providers to build a customized vaccine schedule based on age of the patient, child catch-up schedules, patient specific conditions, and special circumstances. The Shots Immunization App also has information about each vaccine and recommendations separated by various conditions to find the most accurate information for patients.

While these resources are each great tools to stay up to date with future changes in vaccination schedules, there have been a few recent changes that are important to note as well. For example, previously the pneumococcal conjugate vaccine (PCV) had two different commonly utilized variations: 13-valent PCV (PCV13) and 23-valent pneumococcal polysaccharide vaccine (PPSV23).[8] Two new recently approved pneumococcal vaccines include a 15-valent PCV (PCV15) and a 20-valent vaccine (PCV20) for adult patients who are eligible to be vaccinated for pneumococcal pneumonia. Adults 65 and older and ages 19-64 with certain medical conditions or risk factors (i.e. alcoholism, chronic heart/liver/lung disease, cigarette smoking, diabetes mellitus, chronic renal failure, nephrotic syndrome, immunodeficiency,

iatrogenic immunosuppression, generalized malignancy, human immunodeficiency virus, Hodgkin disease, leukemia, lymphoma, multiple myeloma, solid organ transplants, congenital or acquired asplenia, sickle cell disease or other hemoglobinopathies, CSF leak, or cochlear implant) who have not previously received PCV should receive one dose of PCV (either PCV15 or PCV20). When PCV15 is used, it should be followed by a dose of PPSV23 one year later. A minimum interval of eight weeks can be considered for adults with an immunocompromising condition, cochlear implant, or cerebrospinal fluid leak. Adults who have only received a PPSV23 may receive a PCV (either PCV20 or PCV15) ≥1 year after their last PPSV23 dose.

Another recent update focuses on the use of the recombinant zoster vaccine (RZV) for high risk patients.[9] This vaccine has traditionally been used in patients over 50 years of age to prevent the herpes zoster infection. Unfortunately, there is a considerable patient population under the age of 50 who are at high risk for herpes zoster infections due to certain medical conditions or risk factors. This vaccine was recently approved for use in patients 19 years or older who have these conditions that would predispose them to a herpes zoster infection. The second dose of the RSV series is typically given two to six months after administration of the initial dose. If the patient has an immunocompromised condition, this timeline can be accelerated to receiving the second dose one to two months after the first.

Immunization recommendations are one of the easiest interventions that can be made by the healthcare team. Immunizations can prevent patient harm as well as improve the overall health of the community. The more vaccines patients have completed, the better protected they are. While it is always important to remain up to date with vaccine schedules, recent advancements in technology allow providers to stay more up to date than ever with current immunization recommendations.

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- No medical record
- No information disclosed to employers or licensing board.

SDSMA health leadership courses begin in October – enroll today!

The SDSMA Health Leadership Institute (HLI) is now accepting participants for its 2022-23 cohort! The HLI helps physicians balance life and work, sharpen their skills in practice management, and train for future leadership positions.

The program offers current and future leaders the opportunity to gain an in-depth knowledge of the role leadership plays in medicine. It prepares participants for roles within their practice location or health system, and provides professional development, community engagement and leadership skills training. Learn more about the SDSMA HLI at sdsma.org.

Six monthly sessions will be held with courses beginning in October, from 5:30 p.m. to 9:30 p.m. CT on Fridays and 8 a.m. to 12 noon on Saturdays.

- October 14-15, 2022
- November 18-19, 2022
- December 16-17, 2022
- January 20-21, 2023
- February 24-25, 2023
- March 24-25, 2023

SDSMA CENTER FOR PHYSICIAN RESOURCES
Health Leadership Institute

How to enroll – Those interested in participating may contact:

- Barb Smith – bsmith@sdsma.org
- Justin Ohleen – johleen@sdsma.org

Telehealth extension passes U.S. House

The U.S. House of Representatives earlier this month voted for a bipartison bill that extends Medicare telehealth payment and regulatory flexibilities through the end of 2024. The SDSMA applauds Rep. Dusty Johnson for voting for this bill.

The SDSDMA will meet with South Dakota's congressional delegation during August Recess and will urge Sen. John Thune and Sen. Mike Rounds to vote yes on this legislation in the Senate.

The number of patients seen via telehealth has increased 50-175x compared with pre-pandemic numbers. Practices have built successful telehealth processes that are making care more accessible and convenient for patients. The benefits of expanded telemedicine are clear; therefore, it's important to build on these gains and permanently fix the restrictions on telehealth coverage, removing barriers so all patients can access services with telehealth technology.

Legal Brief Highlight: Medical Records Privacy – Disclosures Without Patient Consent

Patient health information is protected from disclosure under both state and federal law and privacy rules mandated by the Health Insurance Portability and Accountability Act of 1996 (HIPAA). However, law provides for circumstances where a patient's health information may be disclosed without his or her consent.

The federal privacy rules provide for the disclosure of protected health information without the patient's consent in certain circumstances as described below:

- Administrative or judicial proceedings pursuant to an order of the court of administrative agency, or pursuant to a subpoena;
- Law enforcement and criminal investigations and related court orders, warrants, subpoenas, or summons issued by a judge or grand jury;
- Protection of the health or safety of others;
- Treatment, payment and other health care providers for the purposes of a referral or coordination of treatment;
- Investigative or oversight agencies for regulatory activities such as audits, investigations, inspections, licensure or disciplinary actions;
- Reporting suspected abuse or neglect of children, disabled adults and the elderly;
- Public health activities for the reporting of statistical data;
- Parents or guardians of a minor or adult subject to a guardianship; and
- Workers' compensation claims or proceedings.

More information is available in the SDSMA legal brief *Medical Records Privacy – Disclosure Without Patient Consent* at sdsma.org. The SDSMA provides legal briefs for member physicians on a variety of rules and regulations that apply to the medical profession.

Bill advances that would streamline prior authorization in Medicare Advantage

The U.S. House Ways and Means Committee has passed legislation that would streamline prior authorization in Medicare Advantage plans. The proposed legislation aims to cut unnecessary delays in care. The "Improving Seniors' Timely Access to Care Act of 2022" would:

- Require Medicare Advantage plans to implement electronic prior-authorization programs that adhere to newly developed federal standards, as well as establish real-time decision-making processes for items and services that are identified as "routinely approved."
- Mandate that Medicare Advantage plans issue accelerated prior authorization decisions for all other services in Medicare Part C.
- Enhance transparency by requiring Medicare Advantage plans report to the Centers for Medicare & Medicaid Services on the extent of their use of prior authorization and the rate of approvals and denials.
- Hold plans accountable for making timely prior authorization determinations and providing rationales for denials.

Too often, prior authorization has resulted in delayed, denied or abandoned care. American Medical Association data shows that more than one-third of physicians report that prior authorization led to a serious adverse event, such as hospitalization, disability or even death, for a patient in their care. The three members of South Dakota's congressional delegation — Sens. Rounds and Thune, and Rep. Johnson, are co-sponsors of legislation aiming to fix prior authorization. During August Recess visits the SDSMA will discuss the importance of fixing prior authorization with our congressional delegation.

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In Memoriam

Richard "Rip" Porter, MD

SDSMA President 1991-92

Richard Porter, MD, affectionately known as "Rip," "Doc" or "No Slack Quack" — was born Sept. 12, 1936, in Mitchell. He graduated from Dakota Wesleyan University in 1959 and Washington University School of Medicine, Saint Louis, Missouri, in 1963, and was accepted into an internal medicine residency at Sacred Heart Hospital in Yankton.

Dr. Porter served as president of the South Dakota Medical Association 1991-1992. He volunteered and participated in SDSMA activities in numerous capacities throughout his decades of association membership, along with his wife Marlys. Dr. Porter was appointed to the South Dakota Board of Medical Examiners in 1986. His medical career in the state included practicing family/internal medicine at the Yankton Clinic and Sacred Heart Hospital, Fort Meade Veterans Medical Center, VA Primary Care Clinic in Rapid City, and the Military Entrance Processing Station in Sioux Falls.

Michael Pekas, MD, who was SDSMA president two years prior to Dr. Porter, described Dr. Porter as "a very personable person, very easy to work with, with a positive can-do attitude. He was helpful to all, and even with his very impressive military record, he was humble and unassuming. He was fun to hang around with and had a great sense of humor. He will be greatly missed."

Dr. Porter entered the Army in May 1966, and after basic training at Fort Sam Houston, was assigned to the 101st Abn. Div., Fort Campbell, Kentucky, as a battalion surgeon for the 2nd Bn. 506th Inf. 3rd Bde. and graduated from the basic airborne course to be offered at Fort Campbell that September.

He was reassigned to the "No Slack" 2nd Bn. 327th Abn. Inf. Duc Pho, RVN arriving in country May 1, 1967 and returned April 13, 1968 dragging an old duffel bag covered with numerous decals from places like Du Pho, Qui Nhon, Quang Ngai, Chu Lai, Phuoc Binh, Song Be, Tan Son Nhut, Nha Be, Phu Bai, and the A Shau Valley with side trips to Bien Hoa, Long Binh, Phan Rang, Nha Trang, BanMe Thuot, and Da Nang.

He was discharged from the Active Army April 14, 1968, and returned to private practice in Yankton. In March 1972 he joined the South Dakota Army National Guard assigned to the 730th Medical Clearing Co., Vermillion. In 1986 he was reassigned to STARC as the state surgeon for the South Dakota National Guard. In November 1990, he returned to the 730th Medical Clearing Co. commanding the unit during mobilization to Fort McCoy, Wisconsin, Nov. 25, 1990, followed on by deployment from Volk Field on Jan. 19, 1991, to King Fahd Air Base, Saudi Arabia. The 730th provided mobile tactical medical support to the 2nd ACR and forward elements of the 1st Cav. during the ground war. The unit remained in Iraq for six weeks following the cease-fire on a humanitarian mission caring for sick and wounded Iraqi civilians. The old duffel bag was dragged out of Saudi Arabia May 3, 1991, with a few new decals on it from places like Dhahran, Hafar al-Batin, Tapline Road, KKMC; An Nasiriya, Basra, Ur, and Kuwait City. Dr. Porter retired from the Army National Guard on November 1, 1999.

Richard married Marlys Herman June 12, 1962, in Yankton. Together they raised two daughters Valerie and Jodi and resided in St. Louis, Missouri; Graceville, Minnesota; Fort Campbell, Kentucky; Yankton; Ft. Meade; Rapid City; and Sioux Falls.

Health Promotion and Personal Safety

Debra Johnston, MD

The annual wellness exam is one of my favorite things to do as a doctor. It's a chance to talk about one of my passions: health promotion.

As most patients expect, our health promotion discussion includes smoking cessation, diet, and exercise. Perhaps more surprising is our conversation regarding personal safety. We talk about sunscreen, seatbelts, helmets, distracted driving or driving under the influence. And I ask if their guns are locked up.

I grew up in Iowa and I live in South Dakota. Both are states where hunting and guns are such a part of the culture, we don't think twice about people having guns in their homes. The same can be said about many states in our region.

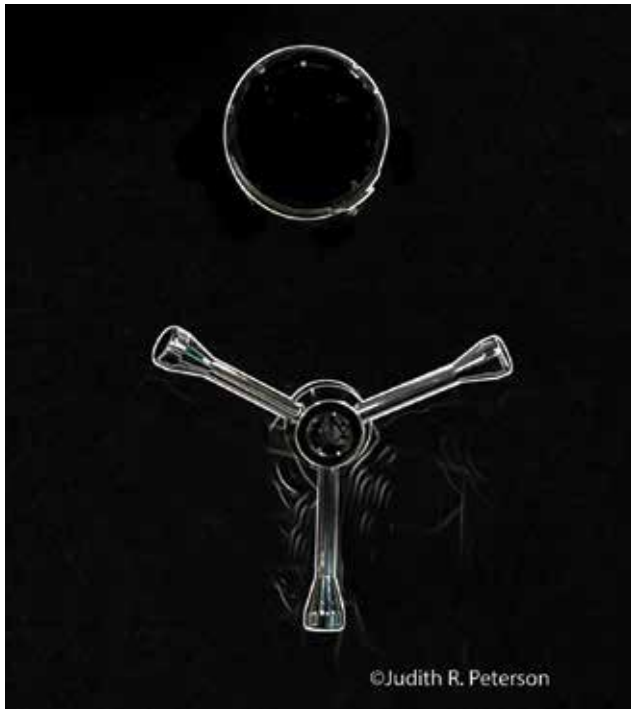
So why do I ask if guns are locked up?

Guns are a popular target of thieves. Anyone can have a break in, and you don't want to make it easy for the thieves to profit from the act, or worse still, hurt someone. More importantly, however, is the safety of people in the home.

Sometimes parents tell me confidently their guns are well hidden from their children. They usually reconsider when I ask, "Did you know where your parents hid the Christmas presents when you were young?"

Sometimes parents tell me their children have been taught not to touch guns. However, those same children, when asked at their well child visits, often tell me they would pick up an unattended gun to bring it to an adult. Research bears this out.

Protecting children in the home from unintentional injury is only part of the story. I also hope to prevent intentional injury. Although guns are used in only about five percent



of suicide attempts, they are involved in more than half of suicide deaths. In fact, nationwide, over 50 percent of gun deaths are suicides.

The underlying causes for suicide are complex and many, but once a person decides to do it, there is often a very brief period before acting on that decision. For many individuals, if they are unable to carry out their plan in those first few minutes, or if that plan involves a less lethal means, the moment of crisis passes. People are far more likely to survive a suicide attempt that does not involve a gun, while more than 80 percent of people who attempt suicide using a gun die.

Keeping guns unloaded and locked up, keeping ammunition somewhere separate, removing the guns from the home if someone is struggling: these are actions that can save the life of someone you love. It could even be your life. This topic is indeed integral to health promotion.

Debra Johnston, MD, is part of The Prairie Doc® team of physicians and currently practices family medicine in Brookings, South Dakota.
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