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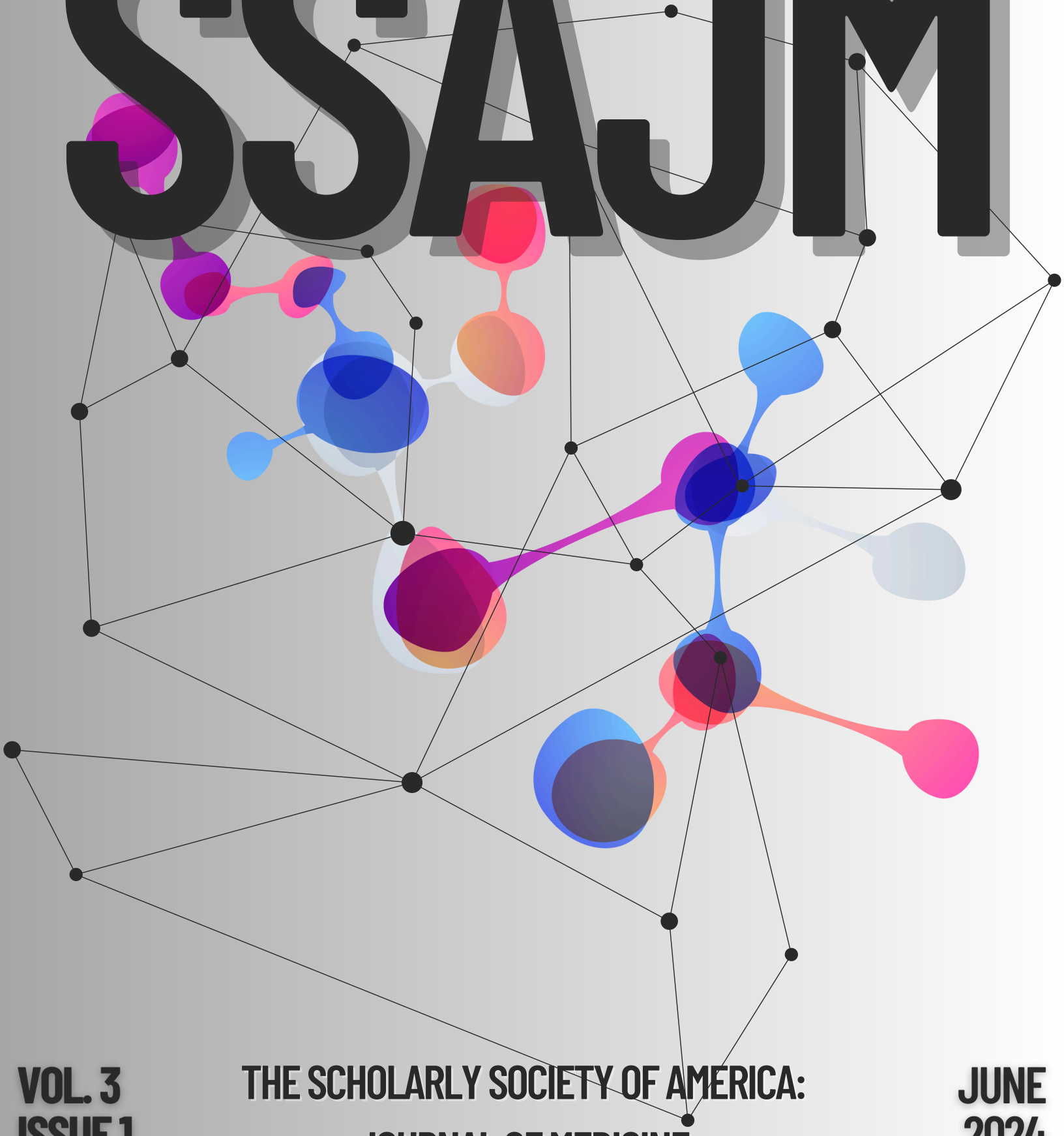

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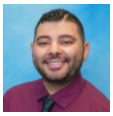

Peter Iskander, MD:
Born and raised in Toronto, Ontario, Dr. Iskander completed his medical degree at AUA before joining The Wright Center for GME for his Internal Medicine residency. As the current Chief of Scholarly Activity of his program, he helped establish the SSAJM with his team to promote research and publications for all residents. He currently serves as our Chief Editor and Co-founder. In his free time, he loves to cook/bake and rarely passes up the opportunity for a game of volleyball!

Edwin Mogaka, MD, PhD:
Dr. Mogaka is the current Resident Leader for Scholarly Activity for Family Medicine at The Wright Center for GME. Dr. Mogaka has a Ph.D. in Psychology with a concentration in Educational Psychology from the Harold Abel degree from the Medical University of the Americas in the West Indies. He is a founding member of the Editorial Board at SSAJM.

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Dr. Simin Nasr is a board-certified Family Medicine physician and a board-certified Geriatrician at The Wright Center for GME & CH in Scranton. Born and raised in Iran, she is a graduate of the Belarusian State Medical University in Minsk, Belarus. She completed an obstetrics and gynecology residency at Gilan University of Medical Sciences in Iran, then stayed in her native country for several years while providing OB-GYN services in both community-based and hospital settings. After immigrating to the United States, Nasr joined the Medical College of Wisconsin's Family Medicine – All Saints Residency Program and developed a keen appreciation for working with older adult patients. She subsequently completed a Geriatric Medicine Fellowship at UPMC in Pittsburgh. She is a founding member of the Editorial Board at SSAJM and a faculty mentor for the board.

Anand Maligireddy, MD:
Dr. Anand Maligireddy is an Internal Medicine resident physician at The Wright Center for GME. He serves as their Resident Leader for Scholarly Activity. With a rich background in research, including his previous role as a Research Fellow at Mayo Clinic and his current position as a Research Collaborator at the same institution, Anand brings a wealth of knowledge and dedication to advancing medical understanding. He is unwavering in his commitment to patient care and his passion for academic excellence. He is a founding member of the Editorial Board at SSAJM.

Tony Abdelmaseeh, MD:
Dr. Tony Abdelmaseeh is a board-certified pediatrician and a Family Medicine resident physician at The Wright Center for GME. Dr. Abdelmaseeh completed his Pediatrics training at Lincoln Hospital in the Bronx, New York. Interested in practicing full-scope family medicine, he is a founding member of the Editorial Board at SSAJM.

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Dr. Amninder Singh is an Internal Medicine resident at The Wright Center for GME. He brings with him a wealth of experience, having served in the Indian military and acting as a reviewer for various medical journals. Dr. Singh is passionate about clinical research, particularly in Cardiology, and actively encourages fellow residents to get involved. He is a founding member of the Editorial Board at
SSAJM.

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Dr. Pancholy completed his Internal Medicine residency at SUNY Stony Brook and his general and interventional cardiology fellowship at Presbyterian Medical Center in Philadelphia. He is a certified specialist in advanced heart failure and transplant cardiology. He currently serves as the Program Director for the Cardiology Fellowship at The Wright Center for Graduate Medical Education. He is also a faculty member at Geisinger School of Medicine and the director of Cardiac Catheterization at Wilkes-Barre VA Hospital. Over his distinguished career, he has 70+ US patents, led in multiple RCTs, and is one of a select few honored as a Masters of SCAI for innovation and advancement in Interventional Cardiology.

Dr. Tapan Buch, MD:

Dr. Buch completed his residency and Cardiology training at The Wright Center for Graduate Medical Education. He is an Adult Non-invasive cardiologist in the Northwell Health system where he focuses on prevention and lifestyle modifications, cardiac imaging, vascular/venous disease, and education. He has a particular interest in advancing the integration of emerging cardiac technology.

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Dr. Edward J. Dzielak is a dual board-certified in Internal and Geriatric Medicine. He currently serves as the Program Director for the Geriatrics fellowship at The Wright Center for Graduate Medical Education. He earned his medical degree from the Philadelphia College of Osteopathic Medicine medical school and is also a graduate of the Scranton Temple Residency Program (now The Wright Center).

Dr. Tanureet Kochar, MD:

Born and raised in India, Dr. Tanureet Kochar moved to the United States where she completed her Internal Medicine residency at the Charleston area Medical Center in Charleston, West Virginia. She went on to pursue further training in Geriatrics and Sleep Medicine at the Detroit Medical Center in Michigan! She is a current faculty member with The Wright Center for Graduate Medical Education. Her interests include dementia care, elder abuse, home care for the elderly, and improving the quality of life in older adults. Aside from working, she enjoys dancing, cooking, and all aspects of being a mom.

Dr. Nirali Patel, MD:

Dr. Nirali Patel is a board-certified Internal Medicine and board-eligible geriatric physician. She earned her medical degree from the Medical University of Lublin, Poland, and completed her Internal Medicine residency and Geriatrics Fellowship training at The Wright Center for Graduate Medical Education. She is a current Associate Program Director of the Geriatrics Fellowship Program and core faculty of the Internal Medicine Residency Program.

INFECTIOUS DISEASE:

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Dr. Gary Decker is a board-certified Infectious Disease specialist who completed his Fellowship training at Georgetown University in Washington, DC. With over 30 years of wealth of knowledge and experience, he helps in the management and treatment of various diseases in the Scranton region of Pennsylvania.

Dr. Mary Louise Decker, MD:
Dr. Mary Louise Decker is a board-certified physician currently serving as an Infectious Disease Medical Director for The Wright Center for Community Health. Her duties include managing The Wright Center's Ryan White HIV and Infectious Disease/Hepatitis-C Clinic. She completed her residency in internal medicine and her fellowship at Georgetown University School of Medicine, Washington, D.C.

Dr. Pragya Dhaubhadel, MD:
Dr. Dhaubhadel is a board-certified and fellowship-trained specialist in Infectious Diseases. Her clinical and research interests include antimicrobial stewardship, Hepatitis-C virus infection, and HIV. She earned her medical degree from Lady Hardinge Medical College in India and then moved to the United States, where she completed her residency and a fellowship in infectious diseases at Harlem Hospital Center.

INTERNAL MEDICINE:

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Dr. Babic is a board-certified Internal Medicine physician practicing primary care and hospitalist medicine in Scranton, PA. After completing his medical degree from the University of Belgrade Medical School in Serbia, he traveled to NYC to undergo residency training at the Icahn School of Medicine at Mount Sinai, where he served as Chief Resident.

Dr. Douglas Klamp, MD:
Dr. Douglas Klamp is a board-certified Internal Medicine physician and a current program director of the Internal Medicine Residency Program at The Wright Center for Graduate Medical Education. Dr. Klamp earned his bachelor's degree in biology from Pennsylvania State University and graduated from Johns Hopkins School of Medicine. He completed his residency in primary care Internal Medicine at Alameda County General Hospital in Oakland, California.

Dr. Erin McFadden, MD:
Dr. McFadden is a board-certified Internal Medicine physician in Scranton, PA. She completed her medical degree at Temple University School of Medicine. She currently serves as a medical director at The Wright Center for Community Health.

Dr. Roop Parlapalli, MD:
After obtaining his medical degree from Sri Venkateswara Medical College, Dr. Parlapalli went on to complete his residency at The Wright Center for Graduate Medical Education in Internal Medicine. He currently works as an academic hospitalist at the Geisinger Community Medical Center in Scranton, PA where he is involved in teaching medical students and residents. He is also an active member of multiple medical societies including, but not limited to, ACP, SHM, and SGIM. His fields of interest entail clinical reasoning, medical education, and hospital medicine.

LIFESTYLE MEDICINE / NUTRITION:

Walter Wanas, RDN:

Walter is a registered and licensed dietitian in Scranton, PA. He currently serves as the Director of Lifestyle Modification and Preventive Medicine for The Wright Center for Community Health. He is a graduate of Pennsylvania State University and Marywood University's dietetic certification program. Walter works closely with fellow Wright Center care teams to help address and improve long-term care and reverse chronic medical conditions.

NEUROSURGERY / NEURO-ONCOLOGY:

Dr. Michael Karsy, MD, PhD, MSc:

Dr. Karsy is a neurosurgeon who has a special interest in cranial skull base and spine neurosurgeries. He obtained his medical degree from the New York Medical College and completed a Neurosurgery residency at The University of Utah. He went on to further his education to pursue a Fellowship in Minimally Invasive and open skull base surgery at Jefferson Medical Center. He also serves as an assistant professor of neurosurgery at Drexel University College of Medicine in Philadelphia, PA.

NEPHROLOGY:

Dr. John Prior, DO:

After completing his residency at the Philadelphia College of Osteopathic Medicine, Dr. Prior went on to obtain a Fellowship in Nephrology from Hahnemann University Hospital. He currently provides quality care in the greater Scranton area of Pennsylvania.

PULMONARY / CRITICAL CARE:

Dr. Nikul Patel, MD

Dr. Patel is a graduate of Albert Einstein Medical Center in Philadelphia where he completed his residency and went further to pursue a Fellowship in Critical Care and Pulmonary Medicine. He currently helps serve in the Scranton region.

RHEUMATOLOGY:

Dr. Nevena Barjaktarovic, MD

Dr. Barjaktarovic is a dual board-certified physician in Internal Medicine and Rheumatology providing diagnosis and treatment for a wide range of rheumatic and inflammatory conditions. She obtained her medical degree at Belgrade University, Serbia, and completed her residency in Internal Medicine at Icahn School of Medicine. She went further to pursue her Fellowship in Rheumatology at Albert Einstein College of Medicine-Montefiore Medical Center in the Bronx.

Dr. Amninder Singh

Meet an Editor

- Where did you complete your education?
  - My journey began at the prestigious Armed Forces Medical College (AFMC) in Pune, India. The rigorous academic environment, combined with military training, provided a strong foundation for my medical career. The skilled and disciplined medical professionals helped it instill in me a sense of duty and a commitment to excellence.

- Career in the Indian Army
  - Upon graduating, I served as a Medical Officer in the Indian Army. I was stationed in different parts of India, often in remote and challenging environments. The diverse medical conditions honed my clinical skills and decision-making abilities. I retired from the army as a Major, reflecting my years of dedicated service and leadership roles.

- Current Pursuits and Future Aspirations
  - I am currently PGY-2 Internal Medicine resident and have just accepted a Chief role in Scholarly Activity; a position that will allow me to lead and mentor other residents in their research endeavors. I aspire to pursue a Fellowship in Cardiology in the future. Cardiology has always fascinated me due to its complexity and critical role in overall health. The heart is a remarkable organ, and understanding its functions and diseases is crucial for saving lives.

- What Got You Into Research?
  - My passion for research was ignited during my undergraduate days. The college's emphasis on scientific inquiry and evidence-based practice laid the groundwork for my research interests. I have always been inquisitive on the 'why' and 'how' behind medical phenomena. One of my key motivators has been the rapid advancements in AI technology and its potential to revolutionize healthcare.

- Favorite Hobbies
  - I have a deep love for hiking and photography, Traversing diverse terrains offers a perfect escape from the rigors of the medical practice, providing me with a sense of peace and connection with nature. This is complimented with photography; allowing me to capture the beauty of the landscapes I explore. It enhances my observational skills and provides a balanced perspective on life, reminding me of the importance of slowing down and appreciating the world around us.

- Any Career Advice for Our Readers?
  - My foremost advice is to be humble and always willing to learn. Don't be afraid to step out of your comfort zone and explore new areas of interest. Make sure to find a balance between professional and personal life. Lastly, never underestimate the power of mentorship. Seek mentors who inspire you, guide you, and challenge you to grow; similarly be that for others.

Intersections of Medicine and Spirituality: A Journey in the ICU

By: Dr. Natasha Khalid, MD

Navigating a busy day in the ICU amidst sudden code blues and intubations, one can easily overlook one's own dietary needs and mental wellness while steadfastly attending to a patient's critical vitals. Such was the scenario on a particularly tough Wednesday, filled with challenges yet marked by productivity. I had been tending to Jill for a while now, her fierce battle after a lung transplant and a myriad of complications not going unnoticed.

Despite our best efforts, we foresaw a grim prognosis. Consequently, palliative care became necessary, and the family faced the arduous decision to withdraw treatment. While this step was deemed best for the patient, its weight pressed heavily on the family's shoulders. In such trying times, our hospital ensures that a chaplain visits the family, offering spiritual solace as we focus on the medical aspect of the ailment.

Having dedicated a decade to the practice of medicine, I remain steadfast in my commitment to the scientific understanding of the disease process and the application of evidence-based practices. Nevertheless, my experience also revealed the profound influence of prayers and spiritual support in guiding patients' families through challenging decisions and difficult transitions. It is a source of reassurance to have a chaplain who collaborates with us in our clinical decision-making process, enhancing the holistic care we provide alongside palliative measures.

In essence, while the scientific aspect of medicine remains fundamental, it's imperative to recognize and embrace the profound impact of spirituality on health and healing. By integrating spiritual care into our medical practice, we not only enhance the quality of care but also affirm the inherent dignity and worth of every individual we serve.

As I made my way to the elevator, intent on grabbing a much-needed coffee to recharge for the remaining hours of my shift, I was joined by the chaplain, freshly done with his duties in the ICU.

"How have you been?" he asked.

"It’s been a long day, and I’m in dire need of coffee," I replied.

"If you have a moment, may I ask you a few questions about your religion to better understand how to approach Muslim families?" he inquired.

I consented, and we sat in the cafeteria for a few minutes, delving into discussions on how Muslims navigate grief and how their faith guides them through death, including what to recite and translations to ease the heart. The chaplain shared his observations of various religions' responses to grief and how different practices aid individuals during tough times. In turn, I shed light on my religion and beliefs, offering insights on how to approach Muslims during moments of distress. This exchange deepened his understanding of grief management in my community and allowed me to appreciate the breadth of his role in the hospital.

With my curiosity piqued, I asked about a practice I noticed in the chapel during Ramadan when I visited to perform my obligatory prayers.

"I noticed people leaving names in a bowl at the chapel. What does that signify?" I queried.

"When people seek prayers for their loved one's health, we encourage them to leave their names on a paper at the desk, ensuring they're included in our daily prayers," he explained.

This brought to mind a similar practice back home, ensuring prayers during pilgrimage and Friday prayers in mosques for those grappling with various ailments, be it financial, health-related, or grief-stricken.

As the day gradually waned, I found myself captivated by the striking similarities among various religions and their approaches to prayer. Despite the intricate variations in religious customs, funeral rites, and ceremonial rituals, the universal theme of seeking comfort in a divine presence and the belief in an afterlife remained steadfast. This realization underscored the profound unity that transcends cultural boundaries and religious affiliations.

The bond between the chaplain and myself enhanced as we engaged in a genuine exchange of insights into our respective spiritual practices. This mutual sharing enriched our understanding of diverse cultures and belief systems, fostering a sense of empathy and connection. Armed with this newfound understanding, I felt better equipped to empathize with and relate to my patients on a deeper level.

Whether it was delivering distressing news or elucidating complex medical concepts, this enhanced awareness enabled me to approach patient care with greater sensitivity and cultural competence. By acknowledging and respecting the diverse spiritual beliefs of those under my care, I could establish a more meaningful rapport and provide support that resonated with their individual needs and values. In essence, this shared journey of cultural exchange and mutual understanding strengthened my ability to provide compassionate and holistic care to my patients.

Natasha

When Uncommon Turns Severe: Massive Gastrointestinal Bleeding in Gastric Hyperplastic Polyps

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1. University of Maryland Medical Center Midtown Campus, Baltimore, MD
2. University of Maryland Medical Center, University of Maryland School of Medicine, Baltimore, MD

Clinical Course:

A 58-year-old woman with a medical history of alcohol use disorder presented with hematemesis. She was admitted to the intensive care unit (ICU) after she was found to have a hemoglobin level of 3 gm/dl and an INR of 1.7. She required a transfusion of 5 units of Packed Red Blood Cells (PRBCs) and 1 unit of Fresh Frozen Plasma (FFP. Urgent esophagogastroduodenoscopy (EGD) showed two 25-35 mm multi-lobulated polyps with stigmata of recent bleeding at the gastroesophageal junction. Histopathology was consistent with hyperplastic polyps (Figure 1-2). Polyp resection was deferred to be done by the advanced endoscopy team. She was treated for alcoholic hepatitis and acute kidney injury on the medical floor and several days later, she had sudden-onset bouts of hematemesis resulting in hemorrhagic shock requiring transfer back to the ICU. Repeat EGD showed two 25-35 mm pedunculated bleeding polyps at the gastroesophageal junction. Bleeding was controlled by epinephrine, and hemostatic clips were placed along each polyp's stalk. She had ongoing bleeding after EGD, thus left gastric artery embolization was performed by interventional radiology. After the procedure, she remained hypotensive with worsening acute kidney injury. As a result, she required continuous renal replacement therapy, vasopressor support, and prolonged ICU. Unfortunately, she passed away within the next few days due to multiorgan failure.

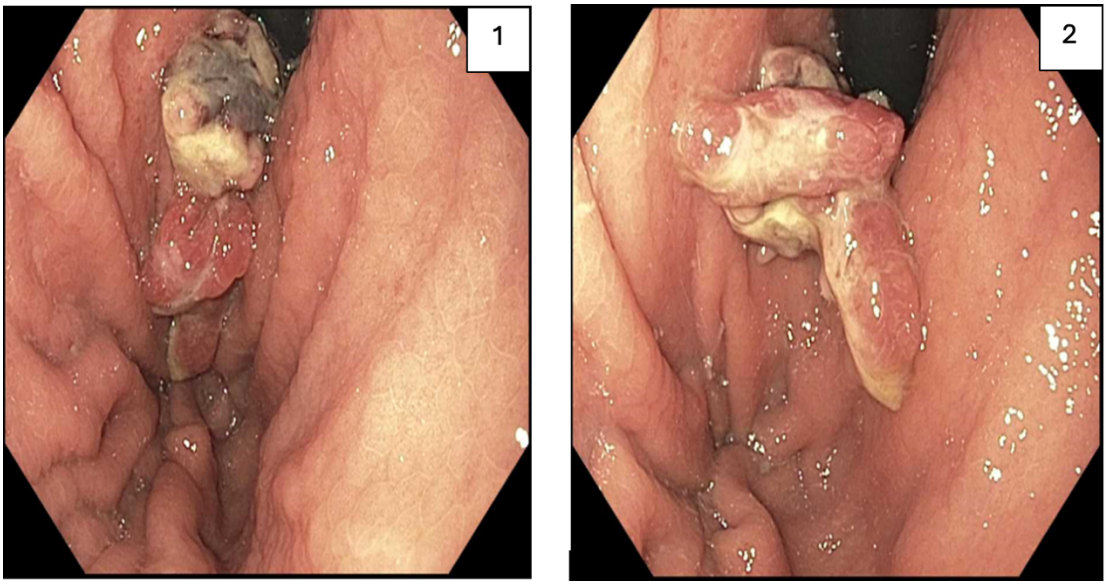

Figure 1-2: Two multilobulated hyperplastic polyps at the gastroesophageal junction (GEJ) with stigmata of recent bleeding in Figure 1.

Take away:

Gastric hyperplastic polyps are among the most common gastric polyps[1-3]. They are more common in older individuals and are usually asymptomatic. Other times, they present with anemia due to chronic blood loss. This article highlights the uncommon occurrence of massive GI bleeding in these polyps. The management of our patient was further complicated by alcoholic hepatitis resulting in encephalopathy, coagulopathy, and hepatorenal syndrome. Interestingly, our patient did not have esophageal varices, the presumed source of massive GI bleeding in similar patients.

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Treatment-Resistant Depression: A Growing Concern Among the Elderly

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Abstract:

Depression is a common concern in the elderly population which can further exacerbate other chronic medical conditions. We present a case of a geriatric patient who experienced persistent depressive symptoms despite multiple trials of first-line treatments. The patient's depression significantly impacted their quality of life and posed challenges for their caregivers. Given the treatment-resistant nature of the condition and limited therapeutic options, electroconvulsive therapy (ECT) was initiated. The patient underwent a series of ECT sessions, resulting in marked improvements in depressive symptoms and overall functioning.

Introduction:

Depression is one of the most prevalent mental disorders in the aging population. Up to 10% of older adults seen in primary care and 30-50% of those in institutional/long-term care facilities suffer from clinically significant depression [1-3]. When it is not successfully treated, depression becomes a persistent problem in as many as 40% of older adults [4-5]. Rates of chronic depression are particularly high in individuals with chronic medical illnesses. Treatment options become limited once individuals exhaust most of the recommended therapies. As primary care providers, we often face the complexity of managing depression in the elderly and how devastating it could be to the patient and their caregivers.

Case Presentation:

An 85-year-old male presented to a geriatric clinic with a past medical history of congestive heart failure (CHF), irritable bowel syndrome (IBS), osteopenia, refractory depression with passive suicidal ideation, new onset drug-induced parkinsonism, and ambulatory dysfunction post COVID. The patient was hospitalized a year prior due to similar suicidal ideation. He was initially doing well on duloxetine and aripiprazole, which was discontinued due to parkinsonian-like symptoms. His history showed that he had been on several classes of antidepressants (i.e. SSRI, SNRI, atypical antidepressants, and antipsychotics), however, nothing alleviated the symptoms. He was also undergoing counseling, but there was no improvement in his signs and symptoms of depression. Genesight psychotropic test was performed which showed resistance to all classes of drugs that he had been previously taking. He was further managed as treatment-resistant depression and was offered ECT. Our team opted to pursue ECT vs ketamine therapy due to the patient's age. The patient was initially on a three-times-per-week schedule and soon tapered to weekly treatments. His antidepressants were also slowly weaned down. The patient and his caregiver noted significant improvement just after the first week of ECT; he had become more independent in his activities of daily living (ADLs) and no longer expressed any active suicidal ideation.

Discussion:

ECT remains the gold standard of treatment for resistant depression, despite the stigma associated with its adverse effects. It has been used with various patients and is crucial in managing depression in older individuals and those who do not respond to pharmacotherapy, who express suicidal ideation, and with comorbid psychosis, bipolar depression, or severe catatonia. In geriatric patients, ECT achieves a faster and more complete remission rate [6,7]. It has also been shown to play a role in treating superimposed mood disorders [8]. In conditions such as mild cognitive impairment (MCI), dementia, Parkinson's disease (PD), and stroke, ECT has been proven to enhance clinical results, reducing the percentage of life years spent with untreated depression from 50.2% to 32.9% over a four-year period. Patients who have previously undergone two to three different treatment regimens find ECT to be cost-effective as well [7]. Recent studies indicate that ECT does not worsen memory impairment in geriatric patients. ECT utilizes electrodes placed on the patient's head to administer an electrical stimulus, which depolarizes neurons in the brain and induces a seizure in an anesthetized patient [9]. This results in positive physiological changes in the brain. When considering ECT for a patient, it is essential to provide educational materials such as tutorials, brochures, family discussions, and videos to the patient before initiating treatment [8]. Prerequisites for geriatric patients undergoing ECT include standardized medical assessments, cardiology, neurology, pulmonology, and anesthesia reviews to prevent potential complications. Patients over the age of 50 should have their electrolytes, complete blood count, and EKG evaluated, along with assessing the status of any other pre-existing comorbid conditions. ECT is safe for patients with pacemakers, atrial fibrillation, a history of abdominal aortic aneurysms, and intracranial aneurysms. A typical acute ECT treatment involves three sessions per week for 6-12 weeks. Clinical response is usually observed after this regimen, and it is advisable to discontinue treatment if a clinical response is observed or if the patient has plateaued [9]. Maintenance ECT, along with pharmacotherapy, has been proven to be effective in the treatment of resistant depression, resulting in lower readmission rates and shorter hospitalization stays [8]. It is recommended for severely ill patients with a psychotic spectrum illness [9]. Studies demonstrate that depressive symptoms can be successfully treated regardless of pre-existing cognitive impairment and that ECT only causes brief and temporary cognitive abnormalities in patients without dementia [6]. The most common side effects of ECT include headache, muscle pain, and nausea, with a risk of serious complications such as prolonged seizures and death. The risk of mortality secondary to ECT, however, is approximately 1 in 10,000 patients [9]. In the geriatric population, ECT is becoming an important therapy method for relapse prevention [6].

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A Rare Case of Liver Granulomatous Disease Secondary to Argyria

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1. The Wright Center for GME, Scranton, PA
2. Dow Medical College, Karachi, Pakistan
3. Memorial Hermann The Woodlands, Houston, TX

Abstract:

This case report discusses a rare occurrence of liver granulomatous disease secondary to Argyria, a skin disorder resulting from silver exposure. A 61-year-old male presented with fatigue, weakness, and bluish skin discoloration. A diagnostic workup revealed liver granulomas and silver deposits on pathology. History was significant for prolonged ingestion of silver tablets which prompted treatment cessation, antibiotic therapy, and a tapering course of Prednisone. Argyria's association with liver granulomatous disease emphasizes the need for awareness and comprehensive diagnostic evaluation in such cases.

Introduction:

Argyria is a rare skin disorder that can be acquired through ingestion or overexposure to silver. The excess can deposit on the skin and stain the mucous membranes, causing them to turn a bluish-slate gray color [1–3]. It can be classified into three subtypes. Generalized argyria occurs due to extensive exposure to silver, leading to its absorption by the dermis and resulting in a grayish-blue or metallic appearance of the skin. Localized argyria, alternatively, occurs when silver is deposited in specific areas of the skin, typically through incisions or absorption via sweat gland pores lastly, argyrosis refers to the accumulation of silver in the eye [1].

Argyria can also lead to the development of liver granulomas, a disorder that can also be commonly manifested in sarcoid disease. The granulomatous disease is characterized by the growth of tiny collections of inflammatory cells in any part of the body. It can also affect various other organs such as the lungs, lymph nodes, eyes, skin, and heart [4,5]. Although the exact cause of this disorder is unknown, some theories suggest an autoimmune association secondary to an abnormal immune response to bacteria, viruses, dust, or chemicals. In response to these associated factors, the body triggers an immune response, which leads to a collection of inflammatory cells called a granuloma [6,7]. Awareness should be noted of Argyria’s rare association with granulomatous disease.

Clinical Course:

A 61-year-old Caucasian male with a past medical history of type 2 diabetes mellitus, depression, and reflux disease presented to the emergency room exhibiting fatigue, weakness, and bluish discoloration of the upper extremities and face. Laboratory results revealed elevated creatinine levels at 5.39 mg/dL (baseline 1.04 mg/dL), sodium levels of 128 mmol/L, and calcium levels of 16.3 mg/dL (corrected calcium 12.3 mg/dL). Parathyroid hormone was low at 3.6 pg/mL, while PTH-related peptide was < 2.0 ng/mL. The ferritin and iron panel were within normal limits. However, calcitriol levels were high at 140 ng/ml, alongside an elevated alkaline phosphatase

level of 711 U/L and a normal ACE level of 80 mcg/L. The remainder of liver enzymes were within normal limits. Abdominal ultrasound indicated right renal cortical thinning, while a chest x-ray showed patchy nodular infiltrates in both lungs. CT scans of the abdomen/pelvis revealed a possible non-obstructing right renal stone and significant heterogeneous attenuation of liver parenchyma with multiple abdominal and retroperitoneal lymph nodes. A positron emission tomography/computed tomography scan demonstrated patchy areas of increased metabolic activity throughout the liver and a reticulonodular pattern in the lungs. A non-targeted liver biopsy revealed granulomatous inflammation, portal fibrosis with focal areas suggestive of micronodule formation, and significant silver deposits with moderate fibrosis stage on trichrome stain. Pulmonology consultation was sought for possible sarcoidosis, but no bronchoscopy or lung biopsy was recommended. Blood cultures, Streptococcus pneumonia, Legionella, and COVID-19 tests yielded unremarkable results. Further infectious workup for hepatic granuloma, including tests for Histoplasmosis, Coccidioidomycosis, Toxoplasmosis, Candidiasis, Coxiella burnetii, Brucellosis, Mycobacterium tuberculosis, HIV, Hepatitis B and C, Epstein Barr virus, Cytomegalovirus, Schistosomiasis, Enterobius vermicularis, and Strongyloides, were all negative. Malignancy workup, including tests for CA 19-9, carcinoembryonic antigen (CEA), and alpha-fetoprotein (AFP), also yielded negative results. Autoimmune causes were explored, with negative findings for antimitochondrial antibodies and primary biliary cirrhosis. Liver biopsy excluded PBC diagnosis. IgE, IgG, and IgA levels were all unremarkable. The patient later on reported a history of oral silver tablets ingestion, consuming 32 oz daily for over 20. Following treatment with IV Ceftriaxone and Doxycycline for pneumonia, the patient was recommended to discontinue the silver tablet supplementation and was initiated on a long-term tapering dose of Prednisone: 20mg for 21 days, 15mg for 21 days, and 10mg for 21 days. His condition improved, and he was discharged with a follow-up scheduled in Hepatology for further evaluation.

Discussion:

Argyria is a Greek word derived from “Argyros” for silver. Silver exposure can be via inhalation, transdermal, or even oral into our respiratory and gastrointestinal tracts [3]. Silver is used in various medicines, such as antimicrobials, astringents, and caustic agents, resulting in systemic deposits in different body parts. The risk of exposure to silver exists in different occupations such as silver mining, metalwork, jewelry crafting, and the photographic field. Argyria may be present either in specific areas or across the entire body, depending upon the method and quantity of silver absorption [7,8].

Upon exposure, silver salt is catalyzed by light and goes through a reduction process leading to diverse pigments such as sulfides and chlorides. These pigments, characterized by their chemical stability and low solubility, gradually store in various body tissues. They notably affect skin melanocytes, increasing their activity and resulting in irreversible skin discoloration, particularly in regions exposed to sunlight. The body naturally keeps a small amount of silver, causing its cumulative presence to rise with age. This accumulated silver, bound to proteins, is spread throughout tissues. As silver levels increase, photoactivation and metal reduction contribute to the formation of a bluish-gray discoloration in areas exposed to light [8].

Argyria may slowly look like a gray or bluish tint on the skin, spreading gradually throughout the body. However, it is generally considered harmless and not associated with malignancies. The silver deposits can occur both locally and throughout the body. In the case of our patient, the cause was the ingestion of silver over a period exceeding 20 years which resulted in skin discoloration and liver granulomas [3,8].

The clinical evaluation to differentiate argyria from other conditions presenting with skin discoloration involves considering various possible causes. Generalized argyria can resemble metabolic pigmentation disorders, although these are rare. A comprehensive clinical evaluation is vital for accurately recognizing the underlying cause [7].

Despite argyria primarily impacting the skin and superficial tissues, there have been rare cases where silver deposition in the body has been linked to the development of liver granulomatous disease, causing challenges for diagnosis as it can mimic other prevalent conditions. Although silver deposition in the liver is not characteristically associated with liver damage, it has been noted in some cases to exacerbate existing liver conditions [7].

The skin signs in argyria may be similar to those of other conditions such as cardiac cyanosis, metastatic melanoma with melanuria, hemochromatosis, and methemoglobinemia. This similarity in presentation can carry challenges for healthcare providers, making the diagnosis of argyria a consideration in rare cases [3].

Skin biopsy was done to evaluate for silver deposition; under microscopic examination, the skin showed small granular black pigment deposits located within the basement membranes of the epidermis and sweat ducts. The pigment displayed bleaching when treated with a solution containing 1% potassium ferricyanide in 20% sodium thiosulfate, confirming the presence of silver ions within it [9].

Cessation exposure to silver and protecting the skin from sunlight with sunscreen can prevent further worsening of pigmentation. However, treatments like chelation therapy, hydroquinone application, and dermabrasion are ineffective in treating the condition [7].

Conclusion:

Argyria is a rare skin disorder from ingesting or exposure to silver which can cause liver granulomatous disease like sarcoidosis. Diagnosis can be challenging to ascertain in the presence of non-specific symptoms and treatment protocol includes discontinuation of silver ingestion and symptomatic treatment.

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A Rare Case of Isolated Primary Endometrial Carcinoma of the Abdominal Wall

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Abstract:

Endometriosis is a common disease in women of reproductive age that is characterized by the occurrence of endometrial tissues outside of the uterus. In some rare cases, sites of endometriosis can also potentially develop into carcinoma. We present a case of a patient found to have a rare form of primary endometrial carcinoma of endometrial cells in the abdominal wall that were suspected to be seeded from a prior abdominal surgery (cesarean section) performed nearly 25 years ago. There is not much known in terms of favorable treatment plans and the prognosis is overall generally poor.

Introduction:

In most developed countries, carcinoma of the uterus is the most frequently diagnosed gynecological malignancy, with a peak incidence between 65-74 years of age, usually in postmenopausal women [1]. In the US, it affects 1-2% of women, with roughly 20-30 new cases per 100,000 women per year. Furthermore, it is the fourth most common cancer in women (after breast, lung, and colorectal cancer). Endometrial cancers can generally be divided into two histological types, the majority of which are those of endometrial origin (Type I) that tend to affect women who are approaching menopause. On the other hand, Type II endometrial cancers (which make up roughly 10-20%) are cancers that originate mostly from other cell types, such as serous, clear cell, mucinous, and even undifferentiated cells.

Several risk factors are associated with the development of endometrial carcinoma, the most important factor being long-term exposure to increased estrogen levels. This would include things such as nulliparity, early menarche and late menopause, PCOS, obesity, and unopposed estrogen replacement therapy to name a few. Additionally, some genetic mutations, such as in the PTEN tumor suppressor gene, are also associated with Type I endometrial cancers. Conversely, protective factors would include low estrogen states or high progestin/progesterone levels; this would include things such as multiparity, combination OCPs, and even regular physical exercise. Type II cancers are usually estrogen-independent and are more associated with endometrial atrophy, and therefore post-menopausal women.

Diagnosis is commonly achieved via endometrial sampling, commonly performed as a part of pelvic exams. Alternatively, a biopsy can be obtained via hysteroscopy or dilation & curettage. Pathologically, positive results would reveal endometrial hyperplasia either with or without atypia. Furthermore, results could also reveal a pronounced proliferation of disorganized glandular tissue, which is characteristic of endometrial adenocarcinoma. Additionally, imaging (i.e. transvaginal/abdominal ultrasonography, CT, MRI, etc.) can also play a role in identifying abnormalities in structures and assessing for any metastatic spread commonly found in the lungs and pelvis. There are no routine screening tests for endometrial cancer as there are for cervical and breast.

Endometriosis is a common and chronic disease in women of reproductive age that is characterized by the occurrence of endometrial tissues outside of the uterus [2]. In some extremely rare cases, sites of endometriosis can also potentially develop into sites of carcinoma, which is what this case study hopes to explore.

Clinical Course:

A 45-year-old female, with no significant past medical history, presented to the emergency department with complaints of an abdominal lump in her left lower quadrant that she had noticed two days prior. The patient also noted some drainage of red-tinged fluid as well. She was alert, and comfortable and did not present with any acute distress. At that time, the patient denied any abdominal pain, nausea, vomiting, fevers, chills, changes in bowel habits, or any other gastrointestinal symptoms. She also denied any gynecological symptoms and noted that she was still menstruating. She did admit to having a previous cesarean section nearly 25 years ago. The patient also mentioned an intentional 80 lb weight loss in the previous few months while on a Weight Watchers diet. Vital signs were unremarkable except for tachycardia of 120 beats per minute (BPM). A complete review of systems was wholly negative. Physical examination revealed a soft, non-distended, and non-tender abdomen with cystic fluid collection in the left lower quadrant that was inferior to the lateral edge of a prior C-section scar. A slightly mobile 3 cm mass in the subcutaneous space could be felt in the left lower quadrant below the incision site. Additionally, deep to the incision site was an additional 4-5 cm mass that seemed adherent to the surrounding tissue with an overlying large fluid collection; no obvious cellulitis or inflammatory changes on the skin surface could be appreciated. Compression of the area expressed a large amount of thin hemorrhagic fluid with air bubbles. General surgery was consulted; the wound was incised, drained, and repacked with ribbon gauze. The remainder of the abdomen, as well as the physical exam, was unremarkable. Lab work was significant for low Hgb levels of 9.9 g/dL and an elevated alkaline phosphatase level of 146 units/L. Blood cultures were negative. The patient was started on clindamycin.

Initial CT imaging revealed a large complex soft tissue mass with fluid and multiple pockets of air in the left ventral abdominal wall of the lower abdomen involving the rectus abdominis muscle measuring 10x11x12cm. Mass was concerning for abscess and possible malignancy. Additional CT findings included enlarged left inguinal and left iliac chain lymph nodes. Follow-up transvaginal ultrasound imaging of the abdomen revealed a normal appearance of the uterus and right ovary, with non-visualization of the left ovary; there was redemonstration of a cystic mass, similar to what was found on abdominal CT. Repeat CT abdomen imaging revealed an unchanged solid cystic mass and lobulated lesions of the left hemipelvis.

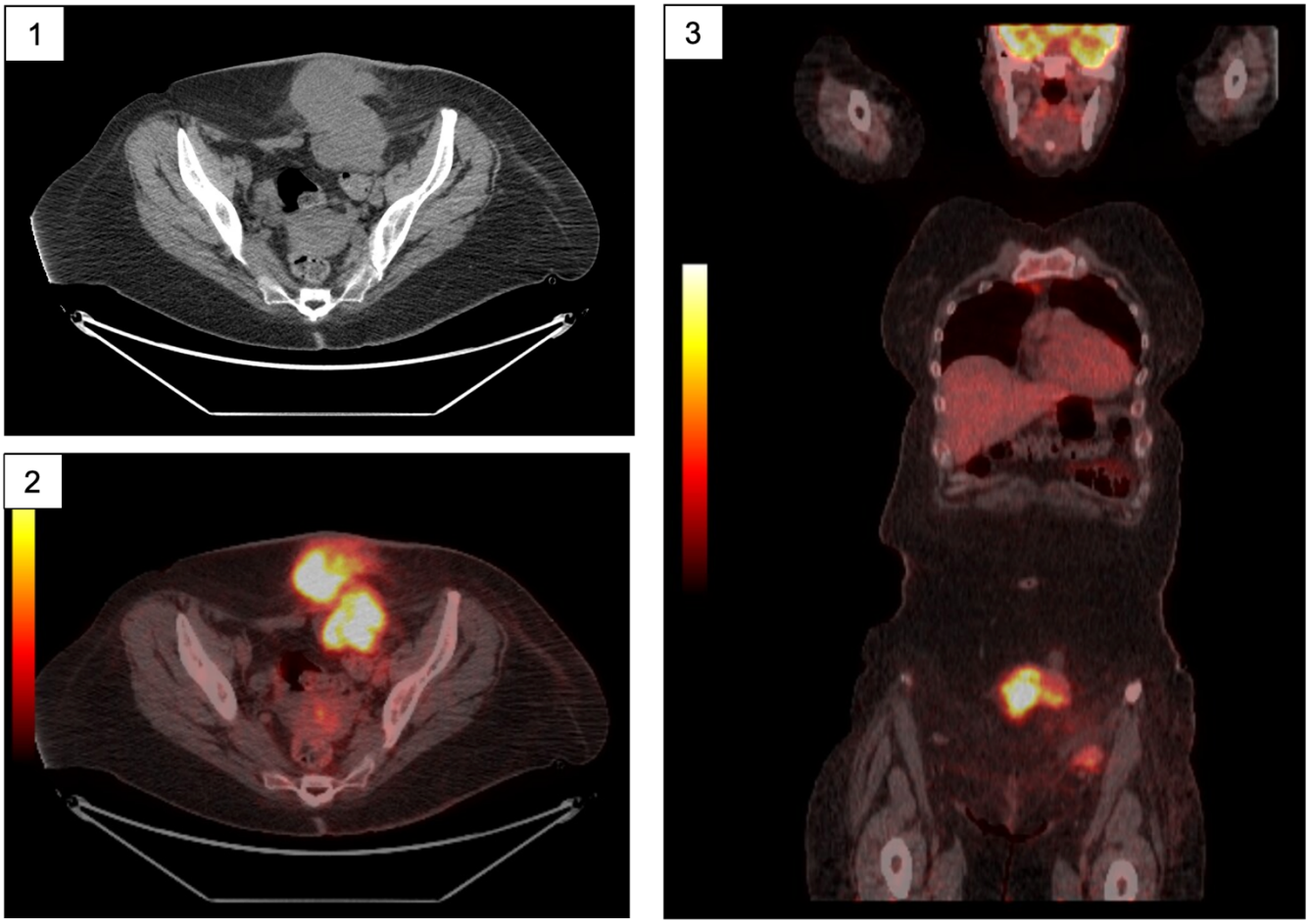

Figure 1: CT imaging revealing complex soft tissue mass in the left ventral abdominal wall.
Figure 2: PET CT of hypermetabolic soft tissue mass from Figure 1, extending through the abdominal wall into the subcutaneous tissue.
Figure 3: PET CT skull-base to mid-thigh revealing the hypermetabolic soft tissue mass of the left ventral abdominal wall.

The patient underwent an exploration and evacuation of the abdominal wall hematoma. Surgical examination suggested that the mass was arising from the abdominal wall itself, within and on the surface of the rectus sheath, which was consistent with CT findings. An abdominal wall incisional biopsy of the mass revealed soft tissue that was consistent with endometrial carcinoma with positive immunostains for CA-19-9, CA125, and increased P53 expression. The next step was to determine if the mass was primary, arising in endometriosis or metastasis from an ovarian or uterine primary cancer. A follow-up PET scan revealed a large lobulated and markedly hypermetabolic soft tissue mass within the left anterior pelvis that extended through the abdominal wall to the subcutaneous soft tissues, consistent with a primary malignancy. There was also a soft tissue mass at the apex of the right adrenal gland with hypermetabolic activity and a Standardized Uptake Value (SUV) of 12.03 concerning for adrenal metastatic disease. Final pathology reports confirmed a diagnosis of aggressive clear cell carcinoma. Furthermore, cytology from cervical swab specimens revealed atypical squamous cells of undetermined significance.

The patient followed up with Gynecology/Oncology and was agreeable to 3-6 cycles of chemotherapy (carboplatin + taxol) with consideration for surgery thereafter.

Discussion:

One of the rarest forms of endometriosis is that of the abdominal wall; this includes cesarean scar endometriosis. It remains overall a challenging condition, and the increasing number of cesarean sections and laparotomies will likely increase the rate of abdominal wall endometriosis. Even further, a synchronous development of endometrioid-type endometrial carcinoma originating from the foci of an abdominal wall endometriosis is an extremely rare phenomenon, with only ~50 cases of endometriosis-associated abdominal wall cancers recorded as of 2021. A study by Mihailovici et al. analyzed data from 48 cases with endometriosis-associated abdominal wall cancers [3]. All patients had undergone uterine surgery of some form, mostly C-sections. The data showed that the average time between the initial surgery and the diagnosis of cancer was roughly 19 years with a confidence interval of about 8 years. The patient in our case study had undergone her C-section roughly 25 years ago, which is within the average range of the study above. Similarly, the study also revealed that while the surgery occurred nearly 2 decades ago on average prior to diagnosis of carcinoma, symptoms only began within 6 months of diagnosis, which was also the case in our case study as our patient had only begun to experience her symptoms within a week. An important thing to point out is that only this, and at least one other study, report the development of endometrioid-type endometrial cancer that originates from the foci in scar tissue of the abdomen likely secondary to seeding of tissue from prior uterine surgery as what was documented. Malignant transformation of an endometriosis associated with surgical scars is extremely rare, with an estimated incidence of less than 0.3% [4]. Given the rare nature of this event, with only very few numbers of cases recorded in literature, there is no standardized treatment. Adjuvant therapy can be beneficial, which is what our patient had begun. Further reports show that in addition to adjuvant chemotherapy and radiotherapy, done in 74% and 30% of cases respectively, surgical treatment is common [5]. Some studies suggest that the recorded prognosis of this condition is poor, however, it is unclear if this is in regards to more common conditions where there was a metastasis from primary uterine carcinoma to the abdominal wall.

Conclusion:

Given the rare nature of this condition, more literature and investigation of recorded treatment approaches and outcomes are needed to specify a favorable treatment plan. The exact mechanism of abdominal wall endometrial carcinoma can usually be explained by hematogenous dissemination from the site of trauma, with seeding of neoplastic cells after direct contact between the tumor and the wound. However, in this case study, the primary tumor is believed to be the site of the abdominal wall itself, with negative findings of cancer in the uterus itself. Further studies with long-term results are needed to determine an optimal approach to this rare condition.

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A Case of Emphysematous Cystitis in an Elderly Male Diabetic Patient with Benign Prostatic Hyperplasia treated with an SGLT2-inhibitor

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Abstract:

Emphysematous cystitis is a rare and complicated urinary tract infection associated with gas formation in the bladder wall. This is commonly associated with poorly controlled diabetes mellitus in elderly women. The case presented involves a male diagnosed with emphysematous cystitis while being treated with empagliflozin, a sodium-glucose-cotransporter-2 inhibitor (SGLT2i), for type-2 diabetes mellitus (T2DM). He was noted to have a past medical history of symptomatic benign prostatic hyperplasia, for which he was prescribed tamsulosin. Treatment was non-operative, and he fully recovered with no long-term sequelae. SGLT2i medications have been beneficial in improving glycemic control for patients with T2DM, though the risk for severe urinary tract infections remains controversial. After reviewing the literature, other cases of genitourinary infective complications have been reported.

Introduction:

Emphysematous cystitis (EC) is a gas-forming infection of the bladder wall that is most commonly caused by *Klebsiella pneumoniae* and *Escherichia coli* [1]. This most commonly afflicts elderly diabetic women, with cases approximately 2:1 women to men [2]. Type-2 diabetes mellitus is a significant risk factor, reported to include nearly 70% of patients diagnosed with EC [2]. One case reported that the average hemoglobin A1c was 9.9% or an average serum glucose level of 293 mg/dL [3]. Other significant risk factors include chronic urinary retention due to neurogenic bladder or bladder outlet obstruction and glycosuria, which provides a ripe environment for fermentation by opportunistic pathogens. EC is considered a complicated urinary tract infection (UTI) and is associated with a mortality of 3-12% [2].

Clinical Course:

A 73-year-old male with T2DM, hyperlipidemia, coronary heart disease, chronic kidney disease, cirrhosis of the liver, and benign prostatic hyperplasia (BPH), presented to the emergency department for evaluation of urinary frequency and dysuria, which developed two days before his presentation. He was prompted to report to the emergency department by his primary care provider after routine blood work revealed an acute elevation in his creatinine to 1.70 mg/dL from a baseline of 1.30 mg/dL. He was treated with tamsulosin for chronic BPH with historical nocturia, urinary frequency, hesitancy of his urinary stream, and a weakened urinary stream. His diabetes was historically treated with metformin, alogliptin, and glargine. Despite this treatment, his hemoglobin A1c continued to rise. The highest value documented was 13.2%. It was at this point

he was started on empagliflozin (an SGLT2i) 10mg by mouth daily. He continued this medication for approximately 2 months, and his hemoglobin A1c improved to 8.9% on repeated blood work. His serum creatinine was elevated on his repeated blood work at 1.70 mg/dL (baseline was 1.30 mg/dL). This, along with acutely worsened lower urinary tract symptoms, prompted his primary care physician to have him report to the emergency department.

On evaluation, he complained of reduced urinary force, urinary frequency, sensation of incomplete voiding, and dysuria for two days. He admitted to lower abdominal pressure but denied any fevers, chills, rigors, nausea, vomiting, or flank pain. On examination, his vitals revealed a temperature of 98.0°F, pulse of 98 beats per minute, respirations of 17 breaths per minute, blood pressure of 163/77 mmHg, and pulse oximetry of 99% on room air. His abdomen was soft and non-tender, though he reported suprapubic pressure with palpation. He had no costovertebral tenderness to percussion. A urine specimen was collected for urinalysis, urine culture, and sensitivity. The urinalysis revealed a specific gravity of 1.025, 2+ protein, 4+ glucose, 1+ ketones, negative nitrites, 2+ leukocyte esterase, 3+ blood, 103 WBCs on high power field (HPF), 65 RBCs on HPF, and 4+ bacteria. Other laboratory values revealed a WBC count of 17,800 mm^3 with a neutrophil count of 16,900 mm^3, hemoglobin of 14.0 g/dL, blood urea nitrogen of 37 mg/dL, creatinine of 1.69 mg/dL and serum glucose of 290 mg/dL. The working diagnosis was a urinary tract infection. He was given ceftriaxone 1g IV while in the emergency department. He was imaged with non-contrast computed tomography (CT), which revealed prostatomegaly, marked bladder distension, emphysematous changes of the bladder wall consistent with emphysematous cystitis, and bilateral perinephric streaking consistent with pyelonephritis (Figure 1A & 1B). He was unable to urinate well and had a post-void residual greater than 650 mL. He had a 3-way Foley catheter placed with 800 mL of turbid urine return. Continuous bladder irrigation was initiated to lavage the bladder. He was subsequently admitted to the hospital.

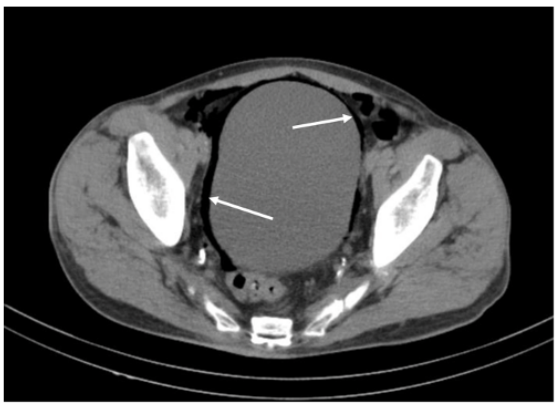

Figure 1A: The axial imaging from the initial CT scan of the abdomen and pelvis revealing emphysematous changes within the bladder wall.

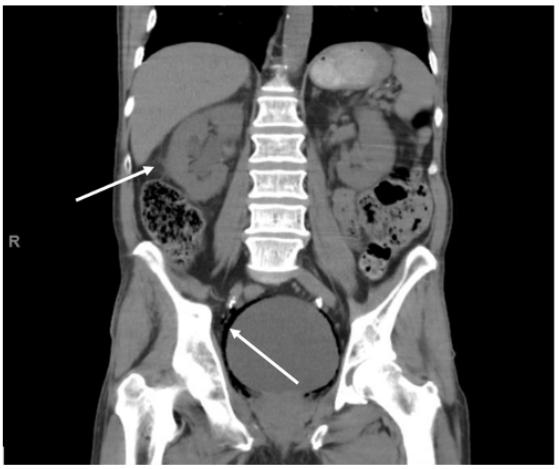

Figure 1B: The coronal imaging from the initial CT scan of the abdomen and pelvis revealing emphysematous changes within the bladder wall and perinephric fat stranding.

During his hospital stay, the urine culture grew >100,000 colonies/mL of *Klebsiella pneumoniae* which was sensitive to piperacillin-tazobactam. He was changed to piperacillin-tazobactam 3.375 g IV every six hours by the inpatient team and was continued on continuous bladder irrigation. His white blood cell count normalized over the first two days of his hospital stay. Tamsulosin was increased to 0.4mg by mouth twice daily, and finasteride 5mg by mouth daily was started to optimize the pharmacologic management of his lower urinary tract symptoms. He failed a voiding trial as an inpatient and was discharged with a Foley catheter. A non-contrast CT of the pelvis was obtained prior to discharge and revealed interval resolution of the emphysematous changes of the bladder wall (Figure 2A & 2B). On outpatient follow-up, he was liberated from the Foley catheter approximately three weeks after discharge and was continued on tamsulosin and finasteride. He recovered well without any sequelae.

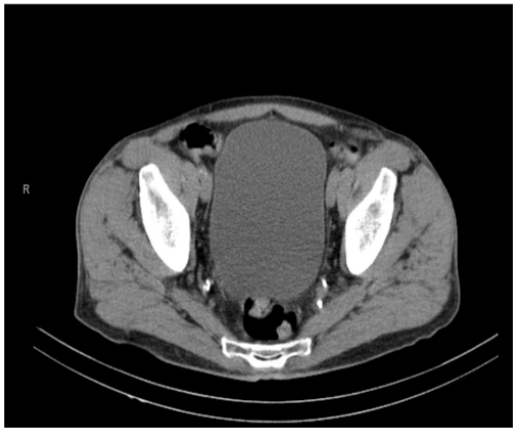

Figure 2A: Axial imaging from the repeat CT scan of the pelvis before discharge shows resolution of the surrounding emphysematous bladder wall changes.

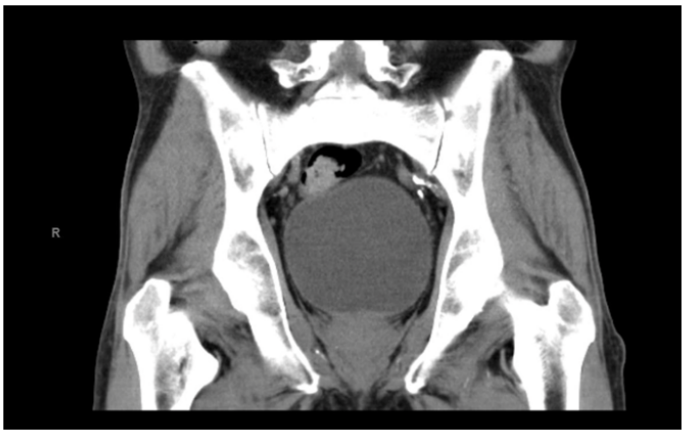

Figure 2B: A coronal image from the repeat CT scan of the pelvis before discharge shows resolution of the surrounding emphysematous changes of the bladder wall.

Discussion:

EC is a rare and complicated urinary tract infection, and if not appropriately identified and treated, it may be fatal [4,5]. The presenting clinical scenario is variable, ranging from incidental diagnosis from abdominal imaging studies to severe sepsis and even septic shock [6]. For those patients who present without symptoms, a diagnosis is made on imaging results alone [7,8]. Many cases have been diagnosed incidentally based on radiographic results. Though EC may be identified on plain radiography, typically showing a translucent ring around the bladder, CT has been generally accepted as the gold standard for diagnosis [9]. The value of a CT scan for initial diagnosis has been noted in the literature [7-9]. While most cases of emphysematous cystitis are treated medically, there are instances where the infection progresses, and surgical intervention is necessary [9].

Symptomatic patients typically report irritative voiding symptoms, including urinary frequency, urgency, and dysuria [6,9]. Pneumaturia has been documented, though the literature notes this as an increasingly rare symptom [7]. A trifecta of occurrences thought necessary for EC was previously described as the presence of gas-forming bacteria, high glucose content of the local tissues, and impaired tissue perfusion [8]. This was thought to provide the perfect environment

for EC to develop. Conditions that are significant risk factors include recurrent UTIs, retained urine due to bladder outlet obstruction, chronic urinary catheter use, immunosuppression, and diabetes mellitus [5,6,9].

SGLT2i medications have been associated with a higher risk of urinary tract infections in patients with diabetes mellitus in some literature, though this remains controversial [10,11]. Through meta-analysis, Li et al. found that a higher risk of complicated UTIs is associated with canagliflozin, dapagliflozin, and empagliflozin compared to placebo [12]. Recurrent UTIs, and even a case of Fournier's gangrene, have been reported after the addition of empagliflozin for improved diabetic control [13,14]. In contrast, studies have shown a low risk of urinary tract infections with the addition of an SGLT2i medication to help improve diabetic control [15,16]. Research has shown improved cardiorenal risk in patients with T2DM [17,18]. One study even reports that empagliflozin slows the progression of end-stage renal disease [19]. When considering clinical guidelines for diabetes management, SGLT2i medications are now indicated for those patients who have concurrent comorbidities of established atherosclerotic cardiovascular disease, heart failure with reduced or preserved ejection fraction, and/or chronic kidney disease (defined as GFR < 60 mL/minute) [20].

In this case, the patient's hemoglobin A1c improved after adding the SGLT2i medication. However, due to his complication of emphysematous cystitis, this was stopped. One similar case was discovered during the literature review [21]. Though SGLT2i medications have proved efficacious for improving T2DM and the associated cardiorenal impacts, it remains uncertain as to the degree of caution needed to be exercised in patients with a history of benign prostatic hyperplasia with lower urinary tract symptoms (LUTS).

Conclusion:

The case presented documents a case of symptomatic acute urinary retention and EC in a male with T2DM with a history of BPH with LUTS who was initiated on empagliflozin. His treatment was nonoperative. He ultimately had no sequelae after successful medical treatment of EC upon follow-up at three months post-discharge. Overall, the literature favoring SGLT2i medications outweighs the noted risks in the reviewed and presented cases. Clinicians may exercise caution and have an informed discussion with patients when contemplating initiation of an SGLT2i medication with symptomatic BPH or a history of UTIs. Appropriate patient education and close follow-up with these patients is recommended.

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A Case of Daptomycin-Induced Acute Eosinophilic Pneumonitis

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Abstract:

Daptomycin is currently an FDA-approved treatment for various infections, whether they be blood or skin-related. One noted complication is the development of acute eosinophilic pneumonitis which can lead to worsening respiratory complications. Mainstay treatment is to discontinue the offending agent, administer steroids, and conservative management to target respiratory symptoms. We present a case of a patient experiencing increasing oxygen requirements, ultimately requiring intubation, after initiating Daptomycin for a prosthetic joint infection. The antibiotic was discontinued, he was treated with IV steroids and was eventually able to be weaned off the ventilator. Care should be taken when initiating such antibiotics in patients with compromised health. Vitals and respiratory status should be closely monitored and there should be a low threshold for discontinuing the medication should they worsen.

Introduction:

Daptomycin is a cyclic lipopeptide antibacterial agent derived from the fermentation of *Streptomyces roseosporus*. It binds to bacterial membranes and causes a rapid depolarization of membrane potential. This loss of membrane potential causes inhibition of protein, DNA, and RNA synthesis, which results in bacterial cell death [1]. Daptomycin was approved in 2003 by the Food and Drug Administration (FDA) for treating complicated skin infections, bloodstream infections, and endocarditis. After the first case of Daptomycin-induced acute eosinophilic pneumonitis (AEP) was published in 2007, pulmonary eosinophilia was added to the “Adverse Reactions, Post-Marketing Experience” section of the drug as a rare complication [1,2].

Clinical Couse:

A 62-year-old male with a past medical history of Crohn's disease and obstructive sleep apnea (on BiPAP) underwent a total right hip replacement in January 2024 secondary to an infection in the hip joint in 2018. The patient, unfortunately, developed a prosthetic joint infection (PJI) in February 2024 of the right hip and underwent incision and drainage with joint fluid cultures growing *MSSA* and *S. agalactiae*. The patient was planned to be treated with high-dose intravenous Daptomycin 900 mg (approximately 8 mg/kg/dose) for six weeks, followed by oral Cefadroxil 500 mg twice daily. Within three weeks of initiating treatment, the patient presented to the hospital with dyspnea associated with weakness and cough.

Vitals in the emergency department revealed a heart rate of 102 beats per minute, respiratory rate of 22 breaths per minute, blood pressure of 119/67 mmHg, Temperature 101.2°F, and oxygen saturation at 97% on 6 L of oxygen via nasal cannula. Physical examination revealed crackles in bilateral lung bases. His blood gas analysis on arrival showed pH 7.50, pCO2 25 mmHg, and pO2 61 mmHg with bicarbonate of 20 mEq/l suggestive of respiratory alkalosis. The respiratory panel was unremarkable, and the complete blood count showed a white blood cell count of 10.5K/µL

with eosinophils at 4.1%. His serum chemistry showed mild hyponatremia (130 mmol/l) and mild elevations in AST (132 U/L) and ALT (101 U/L). Chest x-ray (Figure 1) showed severe bilateral pulmonary opacities, suggesting multifocal pneumonia. CT chest (Figure 2 & 3) showed bilateral ground glass mosaic attenuation in the lower lobes with attenuation. CT Abdomen/Pelvis demonstrated right hip prosthesis with a subcutaneous collection suggestive of an underlying infection.

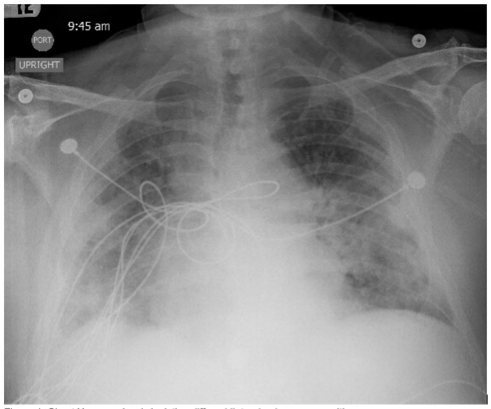

Figure 1: Chest X-ray on day 1 depicting diffuse bilateral pulmonary opacities.

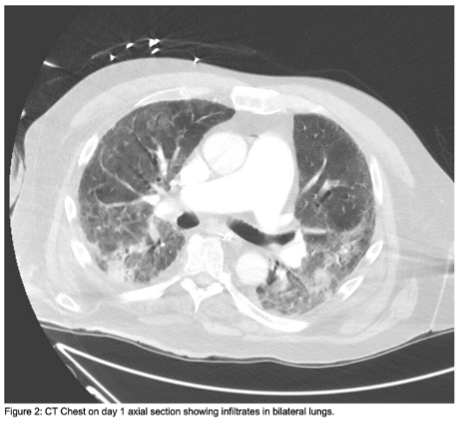
Figure 2: CT Chest on day 1 axial section showing infiltrates in bilateral lungs.

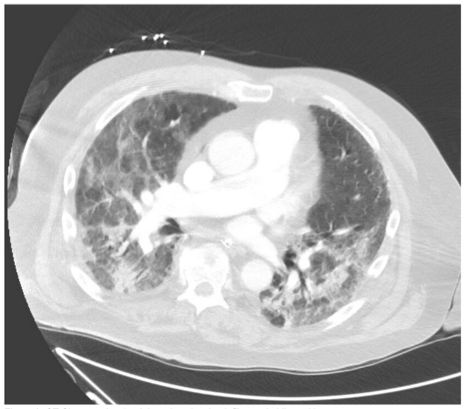
Figure 3: CT Chest on day 1 axial section showing infiltrates in bilateral lungs.

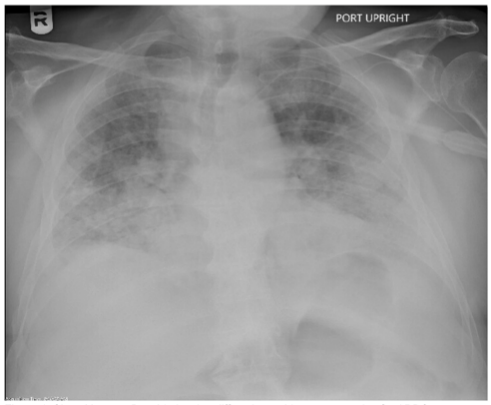

Figure 4: Chest X-ray on Day 14 showing diffuse lung whiteout concerning for ARDS.

Empiric treatment was initiated with Piperacillin/Tazobactam (Zosyn) for concern of multi-lobar pneumonia. Given the lack of response to antibiotics, his increasing oxygen requirements, the presence of fever, lack of viral/bacterial/fungal infection, and new pulmonary infiltrates on chest imaging, the patient met the diagnostic criteria for Daptomycin-induced AEP. Daptomycin was discontinued, and the patient was started on intravenous Methylprednisolone 60 mg daily and intravenous Vancomycin for the PJI. Despite being off Daptomycin for more than 10 days & receiving intravenous Methylprednisolone with doses adjusted daily based on clinical status, his respiratory status continued to deteriorate.

The level of care was escalated, and the patient was transferred to the ICU in anticipation of mechanical ventilation. A bronchoscopy could not be performed due to the severity of his AEP and the patient being highly unstable with increasing supplemental oxygen requirements. He subsequently went into ARDS (Figure 4). IV Methylprednisolone was continued and the patient was diuresed. Ultimately, he required intubation and began mechanical ventilation for which he was on for 12 days.

The patient developed deep vein thrombosis, bilateral pulmonary embolism, and cardiac rhythm abnormalities during the hospital course. The patient was monitored, his respiratory status improved significantly & was eventually able to be discharged to LTAC. Per ID recommendations, he was to continue on chronic oral Cefdinir 300 mg BID for his PJI.

Discussion:

Epidemiology:

The first case of AEP was first noted in 2007 secondary to a case of *MSSA* endocarditis treated with Daptomycin [2]. Other differentials of eosinophilic respiratory complications can include infections from helminths, Allergic Bronchopulmonary Aspergillosis (ABPA), Churg-Strauss syndrome, as well as reactions to other medications/toxins [3]. AEP has a seemingly male predominance, and the severity of the pneumonitis depends on the time exposed to the drug as compared to the dose the patient receives [4].

Pathophysiology:

Several mechanisms have been proposed to explain Daptomycin-induced AEP.

1. Conformational changes of membrane ion channels that allow for altered ion exchange.
2. A higher drug concentration on alveolar epithelium due to surfactant-binding, causing cellular injury.
3. An increased release of eotaxin and interleukin-5 induced by the drug, leading to an eosinophil migration to the lungs and subsequent pulmonary injury [5][6].

As per West et al., the syndromes of this form of pneumonitis can be divided into 3 categories: peripheral eosinophilia, primary Delayed Eosinophilic Pneumonitis (DEP) (usually occurring about four weeks into therapy), and DEP related to re-exposure [7].

Diagnosis:

For patients to be diagnosed appropriately with Daptomycin-induced AEP, the FDA proposed the following guidelines in 2010: the patient is required to be exposed to Daptomycin for long periods, should present with associated fevers and shortness of breath requiring increasing amounts of supplemental oxygenation or mechanical ventilation, and new pulmonary infiltrates or opacities are witnessed on a chest X-ray or CT. Additionally, a bronchoalveolar lavage (BAL) suggestive of > 25% eosinophils and improvement after Daptomycin withdrawal is warranted for a patient to be diagnosed with AEP. Alternatively, Solomon and Schwartz proposed diagnostic criteria in 2006 that did not include patients requiring to be febrile or have dyspnea. Their criteria alluded to the presence of > 25% eosinophils on a lung biopsy or a BAL, the absence of any fungal, bacterial, or viral infection causing pneumonitis, and all prior FDA criteria mentioned above [8].

However, per a vast literature review, a lung biopsy is not indicated to diagnose AEP, and a bronchoscopy will suffice. Given the instability and severity of pneumonitis, our patient could not have a bronchoscopy. A lung biopsy is indicated to explore differential diagnosis in cases with atypical presentations or insufficient imaging features. Interestingly, peripheral eosinophilia is also not required for diagnosis of AEP. In case of any rare diagnosis, other reversible causes must be identified. A comprehensive medical history and physical examination are warranted, with particular attention to smoking history, exposure to any other drugs that can contribute to AEP, and exposure to any fungal or parasitic infections at the patient's place of residence. If clinical

and radiological contexts are appropriate, additional screening tests for eosinophilic granulomatosis with polyangiitis are also applicable [9].

In a prospective cohort study in Lyon, France, about 4600 patients with bone and joint infections who received Daptomycin, like ours, were studied. Out of the 4600, 17 developed Daptomycin-induced AEP; however, only 1 of those patients had a positive bronchoscopy indicating > 25% eosinophils as per the FDA and Solomon and Schwartz criteria. The study discussed how only a minority of their patient cohort fit the proposed criteria, and the researchers proposed a new Lyon criteria. It was argued that the current criteria are very restrictive, particularly the BAL, which indicates > 25% eosinophils, as it is only sometimes done in clinical practice. Fever is a mandatory requirement per the FDA; however, neither of these patients from Lyon presented with fever. The Lyon criteria emphasized radiologic evidence of AEP on CT scan, including bilateral infiltrates, abnormal eosinophilia (either peripheral or from BAL), and symptom improvement once Daptomycin was discontinued. This would diagnose AEP, as per Truongh-Thanh et al., regardless of whether BAL was performed or inconclusive [10].

Complications:
The most common complication occurring in patients with Daptomycin-induced AEP is acute hypoxic respiratory failure requiring mechanical ventilation. In elderly patients, acute renal failure has also been observed in light of receiving higher doses of Daptomycin. Corticosteroids have been primarily used to treat AEP, however, this can exacerbate underlying infections in patients in the critical care setting [11].

Treatment:
Treatment of Daptomycin-induced AEP begins with stopping the offending agent, followed by the mainstay treatment with corticosteroids. The dose of corticosteroids is tailored to the severity of the disease. In hospitalized patients, intravenous Methylprednisolone starting at 60-125 mg every 6 hours is appropriate, followed by oral Prednisone 40 to 60 mg daily tapered over 2- 6 weeks once respiratory status stabilizes, and the patient is extubated [9].

Unlike our patient, clinical improvement is seen within 24 hours to one week of beginning corticosteroid therapy. The duration and dose of steroid therapy are very sparsely studied when it comes to treating Daptomycin-induced AEP. In a retrospective study with prospectively collected data in a Korean military hospital, the efficacies of two groups, being a 2-week versus 4-week course of corticosteroids, were analyzed by Rhee et al. Interestingly, both groups showed similar efficacy in terms of clinical improvement and resolution of radiological findings of AEP. The frequency of adverse effects between the two groups was also comparable. The results of the study indicated that high-dose steroids could be tapered to as close as ten days for treatment of AEP [12].

Conclusion:

AEP is a rare but severe compilation associated with the initiation of Daptomycin. Patients can experience increasing oxygen requirements which can ultimately require intubation. Currently, initial discontinuation of the medication, as well as steroid and conservative respiratory care, are mainstays of management, but further exploration is needed regarding more definitive strategies. Healthcare providers must be mindful of this complication in treating AEP.

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A Case Report on the Presentation of Pulmonary Langerhans Cell Histiocytosis

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Abstract:

Pulmonary Langerhans Cell Histiocytosis (PLCH) is a rare disorder of the lungs characterized by the accumulation of CD1a+ cells in loosely formed granulomas in small airways. A patient with PLCH commonly presents with a smoking history with peak onset between 20 to 40 years of age. PLCH outcomes show a shorter survival rate than the general population and require lung transplantation for survival. In this report, we describe a 42-year-old Caucasian female who presents with a unique episode of bilateral spontaneous pneumothorax and shortness of breath. Pathological samples of the pulmonary biopsy showed Langerhans cells stained positive for CD1a and S100, consistent with the diagnosis for PLCH. The patient was further counseled on smoking cessation with eventual symptom improvement.

Introduction:

Pulmonary Langerhans Cell Histiocytosis is characterized by the accumulation of CD1a+ cells in granulomas of the small airway leading to the destruction of respiratory bronchioles and affecting individuals between the ages of 20 to 40 years old [1,2]. Patients with PLCH may present with respiratory symptoms, including nonproductive cough, dyspnea, fatigue, fever, weight loss, and pleuritic chest pain. Further, approximately 30% to 45% of patients with PLCH presented with spontaneous pneumothorax [3,4]. In addition, patients with PLCH in the early stages may present with nodules between 1 mm to 10 mm on chest radiography and eventually thick-walled or thin-walled cysts in a later stage of PLCH [5]. In this report, we will discuss the case of a middle-aged woman who spontaneously developed a pneumothorax, later discovered as secondary to Pulmonary Langerhans Cell Histiocytosis (PLCH).

Case Presentation:

A 42-year-old Caucasian female with no significant past medical history, except for being a 25-pack-year smoker, presented to her local urgent care with shortness of breath, chest pain, and cough. She was later prescribed Keflex (Cephalexin) under the impression of bacterial pneumonia. However, after two weeks, the patient still presented with her initial symptoms with no improvements from her antibiotics. She was advised to go to her nearest local emergency department when she presented at her urgent care facility a second time. At the emergency department, she was discovered to have a left-sided pneumothorax via chest radiograph and was eventually placed on nebulizer treatment (Albuterol-Ipratropium) along with a left-sided chest tube placement. The patient was later transferred to a higher care facility for further assessment.

Upon further management, the patient was later discovered to have another spontaneous pneumothorax occurring on the right side for which a chest tube was appropriately placed. The patient underwent further surgical biopsy of the left upper lobe, left lingula wedge, and left pleura peel preserved in a formalin container. On microscopic examination, there was the presence of

cellular proliferation composed of Langerhans cells admixed with eosinophils, macrophages, and lymphocytes. With immune histochemical staining, the Langerhans cells were highlighted by CD1a (Figure 1), and S100 markers (Figure 2), directing the diagnosis of PLCH. Further inspection presented no evidence of Lymph Angioleiomyomatosis (LAM) due to negative HMB45 staining. Eventually, the patient was stable enough to have the left-sided chest tube removed while the right-sided pigtail catheter remained in place for drainage of serosanguineous fluid.

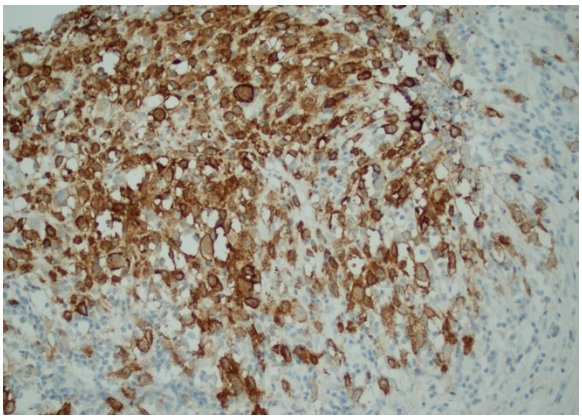

Figure 1: 20X CD1a staining.

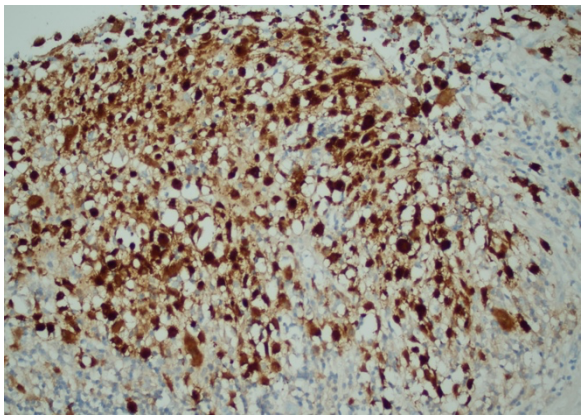

Figure 2: 20X S100 staining.

Upon diagnosis and stabilization, the patient was discharged on supplemental oxygen, albuterol-ipratropium, and guaifenesin for symptomatic management of dyspnea and cough. She was further provided nicotine patches with the aim of smoking cessation to prevent the further progression of her PLCH diagnosis. After discharge, the patient had her right-sided pigtail catheter removed from the outpatient surgical center. During follow-up in the outpatient center, the patient had stopped smoking and was slowly weaning off oxygen supplementation with significant improvement from her initial symptoms.

Discussion:

PLCH commonly presents with nonproductive cough, dyspnea, fatigue, fever, weight loss, and pleuritic chest pain [4]. In one case-series study including 7 individuals, it was found that all had presentations of shortness of breath, and 4/7 had a productive cough. One individual was found to have rales upon auscultation [6]. The initial presentation of shortness of breath and rales on physical examination may explain why our patient initially may have been suspected of a pulmonary infection which led to her being treated with cephalexin from the beginning. Further, it has been reported that pneumothorax complication was seen in 16 of 102 patients with confirmed PLCH [7]. However, what made the presentation of pneumothorax in our case interesting is the occurrence of bilateral pneumothorax, which has been shown to be rare and fatal [8].

The current prevalence of Langerhans Cell Histiocytosis (non-pulmonary) is 12/1,000,000. However, the prevalence of PLCH is unknown due to asymptomatic presentation. In Japan, it has been reported that PLCH prevalence is 0.07/100,000 in women and 0.27/100,000 in men [1,9].

Pulmonary biopsy, whether from surgical or bronchoscopy, is required to make a definitive diagnosis for PLCH [1]. Diagnosing PLCH requires immune histochemical staining with monoclonal antibodies against CD1a or with electron microscopy with a presentation of Birbeck

granules [2]. In the case of our patient, her PLCH diagnosis was confirmed by surgical pulmonary biopsy with positive immune histochemical staining for CD1a along with S100.

Smoking causes Langerhans cells to accumulate in the lungs, eventually leading to PLCH [10]. Therefore, it is important to encourage smoking cessation as a part of therapy management. Further treatment should include Prednisone 0.5-1.0 mg/kg daily for progressive PLCH disease, although the efficacy remains unclear [1]. In patients with PLCH and reactive airway disease, a trial of inhaled corticosteroids along with long-acting β2 agonists may provide some benefit [11]. However, in the case of our patient, she was treated with albuterol-ipratropium, a short-acting β2 agonist and short-acting muscarinic antagonist, which has provided symptomatic relief. Aside from smoking cessation and steroid use in the management of PLCH, Cladribine, a purine analog that reduces DNA synthesis via inhibition of DNA polymerase, has been shown to improve dyspnea in 4 of 5 patients with PLCH [12]. Arguments have been made regarding PLCH as rather neoplastic; especially due to the BRAFV600E mutation noted in Langerhans Cell Histiocytosis. This has led to the use of BRAF inhibitors as a tactic for the stabilization of PLCH [1]. Specifically, a study showed 14 individuals with LCH with BRAFV600E mutation treated with Vemurafenib resulted in 6 of 14 treatment responses [13].

Conclusion:

In this case report, our patient presented with the initial impression of bacterial pneumonia. She was subsequently started on antibiotics, her symptoms, however, had worsened. Eventually, on workup, she was found to have bilateral pneumothorax. On further pathologic biopsy, our patient was diagnosed with PLCH based on positive CD1a and S100 immunohistochemical staining. The initial clinical features of PLCH may include cough, dyspnea, and fever which can be mistaken as possible pneumonia from initial impression, as in the case of our patient. This shows how PLCH can initially be mistaken for pneumonia. PLCH still remains rare in its prevalence and diagnosis is rather made based on incidental findings from images or the presentations of spontaneous pneumothorax which require further investigation with pulmonary biopsy. This case shows the importance of having a broader differential when presented with symptoms of pneumonia and how; although rare, PLCH should still be considered a part of differential diagnosis when presented with pneumonia.

Acknowledgment:

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A Systematic Review of Air Quality Levels and SLE Rates Among Developed and Developing Countries

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Abstract:

Research on the impact of air pollution on Systemic Lupus Erythematosus (SLE) patients worldwide has consistently shown a correlation between high pollution levels and increased health complications. This includes more hospitalizations and disease activity in SLE patients, particularly in areas with poor air quality management practices.

The presence of harmful substances (i.e. particulate matter, nitrates, lead, carbon monoxide, and ozone) in the air pose health risks for SLE patients. Prolonged exposure to air pollution can trigger inflammation and oxidative stress, exacerbating conditions like SLE and impacting various organs.

Developing countries tend to have higher SLE incidence rates due to elevated gas and particle levels in the air, emphasizing the need for protective measures. Exposure to pollutants, such as PM2.5, PM10, SO_2, NO_2, and ozone, is associated with increased inflammatory markers and disease activity in SLE patients.

Overall, this research highlights the importance of monitoring and improving air quality to reduce the health risks and mortality rates associated with SLE, particularly in developing countries facing economic challenges in managing pollution levels.

Introduction:

Prolonged exposure to air pollution has been correlated with an increased susceptibility to autoimmune diseases, with research indicating that concentrations exceeding specific thresholds are linked to a heightened risk of autoimmune disease development [1]. Consequently, there is a critical imperative to delve deeper into the threshold levels that may precipitate the onset of one particular disease: SLE.

Air quality is typically evaluated using the air quality index (AQI), which serves as a metric to gauge the level of pollution present or anticipated in a specific area. Air pollution, characterized by the introduction of harmful foreign substances, poses significant risks to human health. Particulate matter (PM10 or PM2.5), nitrates (NO), lead, carbon monoxide (CO), sulphur dioxide (SO_2), ozone (O_3), as well as potentially harmful byproducts from cigarette and tobacco smoke, collectively contribute to air pollution [2].

Particulate matter encompasses a mix of hazardous chemical compounds containing pollutants like sulfates, metals, ions, and harmful organic substances, with varying diameters of 2.5 micrometers or 10 micrometers, both posing health hazards. Urban areas often witness the

emission of these particles from automobile tailpipes. Fine particles, with a diameter of 2.5 mm or less, and ultrafine particles, with an average diameter below 0.1 mm, are of particular concern [3]. The adsorption molecules of particulate matter can contain significant quantities of sulfates, nitrates, metals, hydrocarbons, and other compounds [4].

Extensive global research has highlighted the detrimental impact of air pollution on the mortality and morbidity rates of chronic diseases, underscoring its severe consequences on human health [5]. Air pollution is recognized as a key environmental factor contributing to inflammation and autoimmune diseases, primarily due to its pro-inflammatory effects. Inhaled pollutants have the potential to trigger inflammation and oxidative stress, linked to both short-term and long-term respiratory conditions, systemic inflammation, and immune-mediated disorders [2].

SLE is an autoimmune rheumatic condition characterized by immunological complex depositions and impaired immunological modulation [6]. Investigation indicated that environmental variables, such as air pollution, could trigger the genetic component of SLE to develop, causing devastating consequences on numerous organs, including joints, the skin, the central nervous system, and kidneys [7].

Study Rationale:

Investigate the potential correlation between elevated pollutant levels and the incidence of SLE in both developed and developing countries by analyzing SLE cases during and post periods of heightened pollution.

Methods:

This study used an integrated cohort and observational approach to examine the occurrence of SLE across diverse geographical regions and its correlation with air quality. The literature review adhered to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) methodology [8].

Inclusion criteria for the study encompassed factors such as the incidence ratio and prevalence of SLE, with a focus on markers like hospitalization and clinic visits following increases in air pollutants. Participants of any sex, ethnicity, or national background were considered eligible for inclusion, provided that the studies offered detailed information on air pollutants and their concentrations in the atmosphere. Studies failing to meet these specified parameters were excluded.

Exclusion criteria involved filtering out papers published before 2000, publications that referenced autoimmune conditions without explicit mention of SLE, duplication of prior studies, limited accessibility, non-English articles, and studies that did not align with the predefined inclusion criteria.

Electronic searches on PubMed Online and Scopus utilized key terms and combinations such as “SLE”, “lupus”, “systemic lupus erythematosus”, “autoimmune disorders”, “air quality”, “developing nations”, “developed countries”, “SLE incidence”, “environment and SLE”, and “air and SLE”. The search spanned up to the summer of 2022, resulting in the identification of 119 papers, with duplicates removed to yield 87 articles. Inaccessibility due to paywalls or non-English publications further reduced the total to 18 articles. Subsequent refinement steps involved filtering out studies

that conflated other autoimmune conditions with SLE and publications predating 2000, culminating in a final selection of 6 articles for analysis with 3 from developing countries (Brazil, Chile, and China) and 3 from developed countries (Taiwan, Canada, and USA) with the classification defined by World Bank's economic categorization of developed and developing economies. Figure 1 visually displays the process.

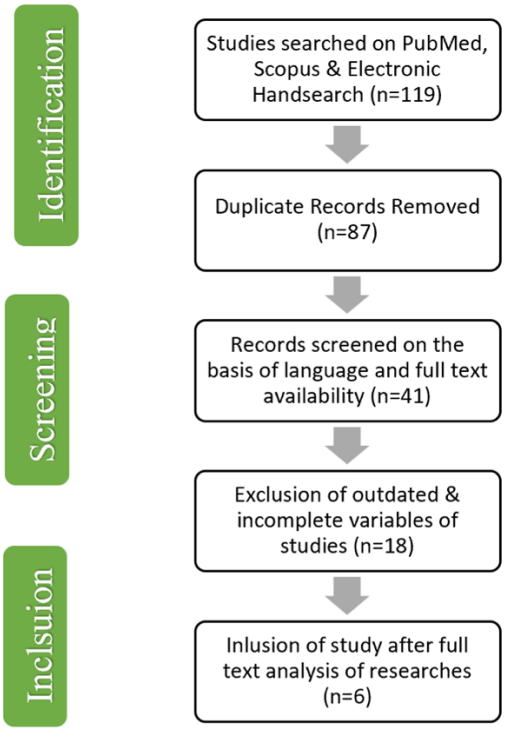

Figure 1: Study identification & selection layout.

This review encompassed data from 6,259 participants across research studies conducted in both developing and developed nations, exploring the impact of air quality on SLE rates. The study predominantly features female participants, with a distribution of 89% female and 11% male. Figure 2 visually illustrates the distribution of study participants across various research studies and their corresponding countries.

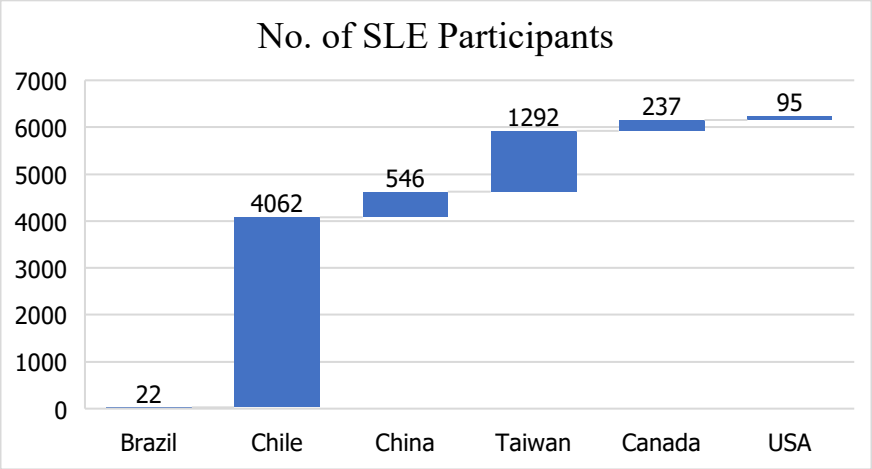

Figure 2: Number of study participants.

Analysis:

The overall analysis indicates a correlation between increased pollution levels exceeding the WHO's recommended annual average and a rise in SLE incidence. Elevated exposure to particulate matter and pollutants, like SO_2 and NO_2, heightens the risk of developing SLE. Across all countries studied, the incidence ratio averages during states of high pollution were 3.57 ± 3.28%. Notably, developing countries exhibit a significantly higher incidence rate of 5.75 ± 2.77% compared to developed countries at 1.39 ± 2.2%. This disparity is attributed to the elevated levels of gases and particles present in developing nations, emphasizing the need for protective measures for affected individuals during periods of heightened pollution. Further examination will delve into age-specific trends and the impact of various gases and particles in both developed and developing countries.

PM2.5 & PM10:

Elevated exposure levels have the potential to induce an increase in inflammatory markers [9]. The WHO guidelines stipulate an annual average concentration threshold of 5 µg/m³ for PM2.5 and 15 µg/m³ for PM10. Excessive levels of particulate matter can serve as a catalyst for heightened leukocyte infiltration, elevated levels of IgG, anti-dsDNA, and anti-nuclear antibodies, leading to significant inflammation [10]. The average PM2.5 concentration across the six studies was recorded at 33.58 ± 2.95 µg/m³, with figures of 44.96 ± 22.39 µg/m³ in developing countries and 22.2 ± 17.25 µg/m³ in developed nations. These values surpass the WHO recommendations, with levels in developing countries being double those in developed countries [11]. PM10 levels were measured at 66.26 ± 27.99 µg/m³ in developing countries, while data for developed countries on PM10 concentrations was not available.

NO_2:

Elevated levels of CRP and Interleukin-17 have been documented following exposure to NO_2, both of which are significant in the pathophysiology of SLE [12]. Furthermore, NO_2 has been associated with an escalation in the SLE Disease Activity Index (SLEDAI) score among SLE patients [12]. The WHO guidelines recommend an annual average NO_2 concentration not exceeding 10 µg/m³ [11]. Our analysis of air quality parameters extracted from the research

articles revealed an average NO concentration of 59.91 ± 24.69 μg/m³. Specifically, developing countries exhibited higher average NO_2 levels at 66.22 ± 26.0 μg/m³, while Taiwan reported a lower concentration of 40.98 ± 12.42 μg/m³. The studies from the USA and Canada did not provide NO_2 data.

SO_2:

SO_2 has the potential to irritate the respiratory tract, exacerbate inflammation, and potentially lead to lung complications such as pleuritis, lupus pneumonitis, and pulmonary hypertension in SLE patients. WHO guidelines specify that the annual average concentration of SO_2 should not surpass 20 μg/m³ [11]. Both China and Chile have recorded levels exceeding this recommendation. Data on SO_2 concentrations in the USA and Canada were not available.

Ozone:

An analysis conducted by Thompson et al. demonstrated a significant and positive association between ambient air pollution, interleukins, and fibrinogen, with O_3 levels being linked to increased interleukin 6, a pro-inflammatory cytokine [13]. According to WHO guidelines, the annual average concentration of ozone should not exceed 100 μg/m³ over an 8-hour period [11]. In our study, the total data showed O_3 levels of 73.20 ± 32.67μg/m³. Developing countries exhibited a mean of 90.54 ± 31.7μg/m³, while developed countries had levels at 47.19 ± 0.72μg/m³.

CO:

CO is a potent and hazardous component of air pollutants that can trigger a rapid and excessive immune response via nitrosative stress, oxidative stress, and systemic inflammation [14]. The WHO recommends that CO should not exceed 10 μg/m³ (or 3.82 ppm) for a maximum daily of 8 hours [11]. Our study revealed the total carbon monoxide level to be under the recommended levels for all countries.

Age:

The mean age of the study cohort was calculated to be 31.96 ± 10.88 years (95% CI: 18.45-45.47). The study by Chakmak et al. highlighted a higher incidence of SLE and SLE-related hospitalizations among individuals aged over 30 years, particularly in females [15]. Similarly, the research by Jung et al. indicated a greater prevalence of SLE in older females (HR = 6.34; 95% CI: 5.42-7.42). Additionally, a significant association between SLE comorbidities and an age of 49 years or older was observed [16]. These findings suggest that advanced age may render individuals more vulnerable to environmental pollution and the onset of SLE.

Table 1: Table depicting various characteristics of the research articles reviewed.

Study	Year	Location	SLE patients	M/F	Age	IR	NO_2	SO_2	O_3	CO	PM 2.5	PM10
		Country	n		Years	%	µg/m³	µg/m³	µg/m³	ppm	µg/m³	µg/m³
Developing												
Fernandes [3]	2015	Brazil	22	2/20	15.3	5.37	80.87 ± 18.30	8.72 ± 1.95	80.85 ± 14.64	1.41 ± 0.47	-	38.02 ± 10.96
Chakmak [15]	2020	Chile	4062	475/3587	-	8.7	81.59	23.10	125.98	0.96	29.13	66.78
Zhao CN [6]	2019	China	546	45/501	38.4	3.2	36.20 ± 14.60	21.60 ± 7.69	64.80 ± 26.70	0.0009	60.80 ± 33.60	94.0 ± 47.50
Developed												
Jung [16]	2019	Taiwan	1292	182/1110	30.8	0.18	40.98 ± 12.42	15.30 ± 5.13	46.68 ± 11.0	0.59 ± 0.14	34.4 ± 7.6	-
Bernatsky [17]	2011	Canada	237	14/237	31.0	0.004	-	-	47.7 ± 23.7	-	10.0 ± 7.8	-
Finchk [18]	2006	USA	95	0/95	44.3	4.0	-	-	-	-	-	-

Results and conclusion:

There exists a consistent correlation between air pollution and heightened SLE-related health complications across diverse geographical regions. The study indicates that air pollution levels exceeding the WHO's recommended averages, stemming from sources like traffic/ factor emissions or ambient particulate matter, may be linked to increased hospitalizations and disease activity in SLE patients.

As pollution levels escalate, so do the occurrences of adverse health events. Furthermore, these pollutants likely contribute to a higher frequency of hospital admissions among SLE patients, exacerbating the negative impacts associated with the condition. Notably, developed nations demonstrate lower incidences and impacts of SLE during periods of heightened air pollution, attributed to air quality management practices through equipment and regulations, in contrast to developing countries facing economic challenges. Consequently, these concentrated pollutants have resulted in unfavorable outcomes, including elevated mortality rates among SLE patients.
With the escalation of global warming and the increasing frequency of fires and natural disasters that can cause increased air pollution, the risk of poor air quality will increase [19]. Therefore,

implementing strategies such as indoor air filtration or the utilization of respiratory devices may be imperative to mitigate the incidence and reactivation of SLE. Promising studies indicate the efficacy of HEPA filter masks, including N95 respirators, in reducing the cardiovascular effects of air pollution by limiting exposure to fine particles [20]. However, current research does not yet demonstrate a direct correlation between air pollution filters and a reduction in SLE incidence during periods of high pollution levels.

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A Case of Multisystem Degeneration of the Autonomic Nervous System

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Introduction:

Shy-Drager Syndrome (SDS), now called Multiple System Atrophy (MSA) is a rare, degenerative neurological disorder that affects autonomic, pyramidal, parkinsonian, and cerebellar functions [1]. This condition was initially classified in 1960 for cases of hypotension of unknown etiology from neurologic disorder. Depending on predominant clinical features, MSA is categorized as MSA-P for parkinsonian and MSA-C for cerebellar. Brain atrophy, primarily on the cerebellum, pons, and putamen, is the anatomical hallmark of MSA [2].

Several hypotheses have been proposed for the etiology of MSA, but its exact cause is yet to be discovered. Pathology ranges from intracellular alpha-synuclein accumulation to mitochondrial dysfunction and inflammation. In contrast to Parkinson's disease, which has an accumulation of alpha-synuclein intracellularly, alpha-synuclein accumulates in oligodendrocytes in MSA [2]. Several areas of the CNS are found to have neuronal loss and gliosis. Aggregates of misfolded alpha-synuclein in oligodendrocytes are the hallmark of MSA [3].

MSA usually manifests in the sixth decade of life with the incidence rate approximated between 0.6 - 0.7 per 100,000 people each year. Geographic distribution is observed for each subtype. Japan has largely MSA-C cases, while Western countries mostly have MSA-P [2].

Case Presentation:

Our patient was a 60-year-old African American male with a past medical history significant for Shy-Drager Syndrome, Benign Prostatic Hyperplasia (BPH), Vitamin D deficiency, sickle cell, seizures, asthma, CKD Stage 2, and hypertension. He had been residing in a nursing home for about 10 months. The patient was being followed by the medical team for his monthly visit at the nursing home. During a follow-up visit, he noted: "neck stiffness when straining to defecate".

The neck stiffness was associated with constipation and bowel movements, described as pellet-like in small amounts. He was prescribed a stool softener but refused as he was afraid of incontinence episodes. He was also prescribed a muscle relaxant for neck pain but refused it because he thought this medication would cause his rectal sphincter to relax and lead to incontinence episodes. He also reported nighttime urinary incontinence. As for his BPH, he was being followed by a Urology team; the Prostate-Specific Antigen (PSA) checked roughly 1 month prior was within normal limits. He also reported chronic right shoulder pain, without improvement seen with physical therapy. He noted a history of trauma when a motor vehicle hit him and dragged him across the road approximately 10 years ago. At that time, he was told that his shoulder could not be fixed because he had nerve damage in the area.

The patient mentioned multiple episodes of lightheadedness and dizzy spells when standing and straining. In the past, this has resulted in multiple falls and seizures that were determined to be caused by hypotension. He follows up with a cardiologist for these episodes of bradycardia and syncope. A recent cardiology visit about 2 months prior for profound dysautonomia and orthostatic hypotension which resulted in falls and syncopal episodes. He endorses fluctuations of blood pressure with elevations as high as 170/110 mmHg. Per his Cardiology team, he had not tolerated any scheduled antihypertensive regimens due to low blood pressure fluctuations, as low as 80/50 mmHg. Hydralazine was offered to him on an as-needed basis for episodes of systolic blood pressure greater than 160 mmHg. They recommended further evaluation at a dysautonomia center or by neurology at a tertiary care center. These episodes of syncope and seizures had led to many hospitalizations. About 2 years ago during a hospitalization for seizures and syncope, a CT scan of the head was done that showed chronic cerebellar atrophy without any evidence of acute stroke, hemorrhage, hydrocephalus, or mass. Neurology was consulted at that time and the patient was placed on Levetiracetam (Keppra) 500 mg tablet twice daily for seizures. The patient did not follow up with the neurologist thereafter.

The patient's current medications include Polyethylene glycol (MiraLAX) for constipation, vitamin D supplements, Bisacodyl 10 mg for when the patient has not opened bowels in 4 days, Hydralazine 25 mg as needed for elevated systolic blood pressure, Magnesium Hydroxide for constipation at bedtime, Acetaminophen 325 mg for pain as needed, Finasteride 5 mg QD, fleet enema, Albuterol Sulfate as needed for asthma, Carboxymethylcellulose Sodium ophthalmic gel for dry eyes.

Discussion:

Diagnosis:

MSA is primarily a clinical diagnosis and great care should be taken to differentiate it from other, more common neurological disorders. Classically, the disease presents with two variants: MSA-P which presents with primarily parkinsonian features, and MSA-C which presents primarily with cerebellar features [4]. An important feature distinguishing MSA from purely parkinsonian or cerebellar pathological processes is concurrent autonomic dysfunction, most frequently manifesting as orthostatic hypotension or urinary incontinence. In practical terms, the concurrent presence of autonomic dysfunction with signs of parkinsonian or cerebellar degeneration should alert the clinician to the possibility of a diagnosis of MSA.

For these reasons, history and complete neurologic examination are central in the diagnosis of SDS. Accurate timing should be elicited from the history since SDS begins at an earlier age and progresses more rapidly when compared to Parkinson's disease; this would be a strong differential diagnosis for our patient.

Also, it should be noted, that SDS presents with ambulatory dysfunction and risk for falls. Tilt table tests can be done to confirm autonomic instability, such as orthostatic hypotension. Additionally, levodopa response assessment could distinguish Parkinson's Disease (PD) from SDS. Excellent response is associated with the former and poor and un-sustained response is for the latter [5]. Since urological symptoms are often present as well, it may be helpful to elicit a history of urinary urgency, frequency, nocturia, and urge incontinence. A Point of Care Ultrasound (POCUS) bladder scan may also be helpful in eliciting post-void residual.

Although not strictly necessary for diagnostic purposes, imaging can help confirm the diagnosis of MSA. A sensitive but not specific finding for MSA on MRI is the “hot-cross bun sign,” a cross-shaped hyperintensity visualized on T2-weighted pontine axial imaging which is said to resemble the pastry traditionally on Good Friday in much of the Anglosphere [6]. Imaging can also help confirm the diagnosis of MSA by demonstrating atrophy of the olivopontocerebellar system (MSA-C) or the striatonigral system (MSA-P).

Treatment:
The treatment for SDS is mainly symptomatic management, as there is no currently recognized definitive cure for the underlying cause of the condition [7]. Consequently, clinicians should work closely with the patient to identify symptoms most responsible for patient distress and take steps to alleviate them directly.

Parkinsonian symptoms can be treated in much the same way as Parkinsonism, primarily through the use of dopamine agonists such as Levodopa. Levodopa is used primarily as a diagnostic way to differentiate SDS from PD; for those with probable SDS, MSA patients may respond better to Levodopa than when not on it, especially if diagnosed with the MSA-P variant [8]. More so, the role of dopamine agonists are limited. Patients who do not respond to Levodopa would unlikely respond to dopamine agonists.

Botulinum toxin can be used for focal dystonia associated with the disease. For urologic symptoms such as overactive bladder, lifestyle modification such as reducing consumption of caffeine at night or fluids at bedtime is reinforced. A beta adrenergic-3 agonist, such as Mirabegron, can be used if the former fails. For urinary retention, self-catheterization can be performed as needed if there is residual volume of more than 100 mL. For autonomic dysfunction with wide swings in blood pressure, Midodrine can be used to improve blood pressure. More conservative measures such as compression stockings or careful control of salt intake may also be helpful.

Finally, depending on the details of the disease progression, patients may benefit from physical, occupational, and speech therapy as supportive care for these patients. As with all chronic diseases, clinicians should work closely with patients to determine their treatment goals and design appropriate interventions accordingly.

Conclusion:

SDS is a condition that affects the functions of the autonomic nervous system in an unpredictable manner. Management of this condition becomes difficult because of this uncertainty in the pattern of symptoms and outcomes. Providers must be extremely careful when managing symptoms of this condition, as the combination of the disease process and medications can lead to the exacerbation of health problems. Close follow-ups in a timely manner of small increments are essential to allow the patient to lead close to normal lives as the disease only progresses further toward disability. Helping the patient determine their needs and setting up assistance is important for the safety of the patient.

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