Volume by Ahmed A Salahudeen MD

*Volume* is in reference to intravascular volume resuscitation. The imagery is intentionally dramatic, fantastical and horrific in its attempt to capture the clinical magic of administering IV fluids— a very simple treatment that can save lives. On the other hand, the imagery might invoke the sensation of drowning. This sinister perspective might make volume overload, a clinical condition in which excessive intra/extravascular fluids can literally drown the patient from within, a more apt title reference. The picture isn't always clear in medicine...
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Incidental Detection of a Thrombosed Coronary Aneurysm by Cardiac Magnetic Resonance Imaging Following Myocardial Infarction

Gabriela Sanchez Petitto, MD, Daniel Ocazionez-Trujillo, MD, Jason Au, MD, Salman A. Arain, MD.

Fig 1. Panel A. Cardiac MRI, coronal axial black blood sequence demonstrating saccular aneurysm in the proximal LAD (arrow). Note the lack of intraluminal flow void and circumferential edema of the vessel wall indicative of acute thrombosis. Panel B. Bright blood cine sequence of Cardiac MRI, showing a thrombus in the apex of the left ventricle (arrow). Panel C. Delayed post contrast imaging of Cardiac MRI, showing transmural delayed enhancement from anterior wall infarct (arrow).
A 31-year-old woman with hypertension presented to the hospital with an anterior wall myocardial infarction (MI). Angiography revealed occlusion of the mid left anterior descending artery (LAD) that could not be crossed despite multiple attempts. The patient made an uneventful recovery, and was discharged on optimal medical therapy for the coronary artery disease (CAD) and new left ventricular dysfunction. Two weeks later she presented to our hospital with a non-ST elevation myocardial infarction. Repeat angiography showed persistent LAD occlusion without a new coronary stenosis or occlusion. Cardiac magnetic resonance (CMR) imaging was performed to determine anterior wall viability and it revealed a thrombosed saccular aneurysm of the LAD at the site of the occlusion not seen during angiography. The study also demonstrated delayed transmural enhancement of the anterior and septal wall segments consistent with poor myocardial viability. The patient was discharged after adjustment of her medical therapy.

Coronary artery aneurysms (CAA) are focal or diffuse dilatations within the coronary artery that exceed the diameter of the adjacent normal segments by at least 1.5 times. The entity was first described by Morgagni in 1761. The incidence of CAA varies from 0.3% to 5.3% in the general population. The diagnosis is usually made by cardiac computed tomography angiography (CCTA), MRI, or traditional catheter based coronary angiography. Our patient had a thrombosed CAA within the LAD that was not identified at the time of angiography but was subsequently detected incidentally by CMR. The location of the aneurysm was fundamental for its detection because CMR is better suited to evaluate the proximal coronary artery segments in most cases. In this case CMR was used to determine cardiac function as well as stress perfusion. The patient was determined to be unsuitable for single vessel coronary artery bypass surgery on account of the lack of viability in the anterior wall. Although CCTA allows higher spatial resolution than MRI for coronary
aneurysms, our patient benefited from MRI in terms of viability evaluation and avoided unnecessary exposure to ionizing radiation.

References


Not All Megacolon is Toxic.

Manoj Thangam, MD, Jeremy A. Ross, MD, Amit J. Patel DO.

Figure 1. Patient in supine position.

Figure 2. Supine abdominal radiograph displaying dilation of large intestine.
Figure 3. Computed tomography scan of the abdomen. Distended large intestine in transverse plane.

Figure 4. Computed tomography scan of the abdomen. Distended large intestine in sagittal plane.
A 42-year-old man presented with fever, abdominal distension, and altered mental status. He had suffered ballistic trauma to the cervical spine 22-years prior resulting in quadriplegia as well as neurogenic bladder and bowel. Physical examination revealed a distended, non-rigid abdomen (Figure 1) with normal bowel sounds and hard stool in the rectal vault. An abdominal radiograph was obtained showing dilation of the transverse colon measuring 19.1 cm (Figure 2). Computed tomography scans of the abdomen and pelvis revealed colonic dilation in the transverse plane measuring 20.0 cm (Figure 3) and sagittal plane measuring 18.7 cm (Figure 4). Initial concern for toxic megacolon prompted the patient’s admission to the medical intensive care unit. Later, the patient was found to have pyuria and gram-negative bacteremia that was treated with intravenous antibiotics. His neurogenic bladder was likely the predisposing culprit for urosepsis.

Gastroenterology and general surgery were consulted to evaluate for colonic decompression or partial colectomy for recurrent constipation in our patient. Conservative management was deemed the best option since constipation resolved with an improved bowel regimen and scheduled saline enemas. Surgical management with subtotal colectomy in spinal cord injury (SCI) patients is usually reserved for patients with toxic megacolon, bowel perforation, constipation refractory to intensified bowel regimens, or those with sacral ulcers concerning for excremental contamination. Megacolon occurs in up to 72% of patients with SCI. It is often difficult to manage due to reduced responsiveness to laxatives and manual intervention. Age over 50 years, use of 4 or more laxative doses per month, and greater then 10 years post SCI have been shown to be independent correlates of megacolon. In most cases, medical management is preferred if adequate symptom control can be achieved. Therapy is targeted to cleanse the colon, prevent impaction, and minimize stool volume and gas accumulation.
References


A 60-year-old Hispanic female with a past medical history of Rickets, osteoporosis and hypothyroidism presents with unilateral severe hip pain after falling from a standing position. She was out of the country when she fell, traveled back home via airplane, and presented immediately to the emergency room. Bilateral hip radiographs (Figure 1) show left sided complete femoral neck fracture with associated soft tissue inflammation. The radiograph is also significant for bilateral bowing with the left worse than right. This is consistent with severe rickets. The patient was diagnosed with rickets as an adult and
began on vitamin-D supplementation after the deformity had occurred. Her osteoporosis was severe with a T-score of -3.3 on DEXA scan. Orthopedic surgery was consulted and took the patient to the operating room for femur repair. However, she was found to be a poor candidate for reaming or broaching, even with osteotomy. The decision was made in the operating room to perform a unilateral Girdlestone procedure to provide her with pain relief and to limit her risk for future complications.
A 21-yr-old Hispanic male with no known past medical history except remote trauma to his right elbow one year prior presented to the emergency department with swelling of his right arm (Figure 1) and pain beginning three weeks prior. The mass was biopsied for concern of malignancy. Pathological evaluation suggested a diagnosis of biphasic synovial sarcoma. The patient was referred to oncology and surgery for treatment.

Synovial sarcoma is a soft tissue tumor that consist of epithelial and/or spindle cells. The differential diagnosis includes malignant peripheral nerve sheath tumors, muscle-derived sarcomas, and biphasic mesotheliomas. The reported incidence of synovial...
sarcomas ranges from 5.6% to 10%. Ninety percent of these tumors are associated with a chromosomal translocation, t(X;18)(p11.2;q11.2). The 5-year and 10-year survival rates in patients with synovial sarcoma are 50% and 20% respectively. Treatment consists of local excision with wide margins, followed by high dose radiation therapy. Adjuvant chemotherapy can also play a role.
A Dying Patient With No Advocate

Collard K MS, De Cicco IA MD, Liras IN MS, Smith BD MS, Aisenberg G MD.

Story from the front lines

An 86-year-old man with history of dementia came to the hospital with an anterior shoulder dislocation after being assaulted in his group home. He was barely responsive, even to noxious stimuli, but was able to protect his airway. He seemed uninterested in food and was only able to mumble a few unintelligible words. Personnel from the group home were contacted, and reported that the patient had been at a similar baseline for the last several months. About twelve hours later the patient was more alert, responsive, and able to feed himself. His ability to make complex decisions was impaired. His vital signs were normal, and he had no focal motor deficit, or impaired cranial nerve function. The remainder of the examination was normal. A computed tomography of the brain, and routine laboratory tests were normal, while RPR and HIV serology were negative. Reassured by personnel at his usual household, a lumbar puncture was withheld. The patient had no family or an established surrogate decision maker. The following day the patient returned to the group home, without having appointed a guardian, or modified his full-code status. Within 48 hours he had returned in apparent septic shock which progressed into cardiopulmonary arrest, requiring 20 minutes of resuscitation. Ten days after the arrest, the patient had visible ischemia of three of his limbs, elevated creatinine, and was only able to open his eyes with no interaction with his surroundings.

Teachable moment

This patient was first identified as having dementia. Provisions should have been made to ascertain the patient’s wishes and obtain advanced directives or find a family
member or friend to serve as a surrogate decision maker in the event that the patient could no longer make decisions for himself. However, as black and white as that process may sound, the reality is quite gray. In eight states and the District of Columbia, guardians may not make decisions regarding end-of-life care (although some states have exceptions), and thirty-seven states have no language in their guardianship policies regarding end-of-life care. More specifically, when the issue on target is the decision to apply or withhold advanced cardiac life support (respectively described as being full code, or “Do-Not-Resuscitate” or DNR), not uncommonly the guardian may not be willing to implement or change either. While such decisions should not be made lightly, often the process is complicated by long legal battles that only serve to prolong care that may inadvertently cause harm to the patient.

We believed that a DNR order was appropriate given our patient’s apparent advanced dementia, as later confirmed at the group home in which he resided. However, there was no known guardian nor any known family or friends for us to contact. Appointing a court-designated guardian is an arduous process, and doesn’t ensure adequate outcomes. To referee in this type of situations, most hospitals have an ethics committee that help guide decisions but can only replace a legitimate surrogate decision-maker in extreme conditions. Moreover, timeliness is an obstacle to this option because assembling this usually multidisciplinary committee often takes a long time. Additionally, the majority of the members of these committees are physicians, which introduces potential conflicts of interest to continue providing care in a pay-for-service system. Another danger is that the physician, who often does not know the patient, will not act on the patient’s behalf.
In conclusion, the medical system is flawed when it comes to end-of-life care of those who have no advocate. Currently, we must muddle through the legal system as best as we can while providing treatment we consider futile or even harmful.

References


Anti-Neutrophil Cytoplasmic Antibodies (ANCA) positive serology in a patient with Ulcerative Colitis.

Anju Mohan, MD

Introduction

The ANCA Associated Vasculitides (AAVs) include Granulomatosis with Polyangiitis (GPA), formerly Wegener’s granulomatosis; Microscopic Polyangiitis (MPA) and Eosinophilic Granulomatosis with Polyangiitis (EGPA), formerly Churg-Strauss syndrome. These primary systemic vasculitides are multi-system diseases characterized by a pauci-immune necrotizing vasculitis of small to medium sized blood vessels with an associated serologically detectable ANCA in a majority of the cases. ANCAs are a family of autoantibodies directed against cytoplasmic antigens, mainly lysosomal enzymes in polymorphonuclear neutrophil leukocytes [West 224]. In making a diagnosis of AAVs, the utility of ANCAs depends on the clinical setting and on the assay used. Indirect immunofluorescence is used to detect ANCA patterns. Three common patterns are perinuclear (p-ANCA), cytoplasmic (c-ANCA) or atypical (not clearly p-ANCA or c-ANCA). Positive immunofluorescence should be followed by ELISA for ANCAs specifically directed against proteinase 3 (PR3) or myeloperoxidase (MPO), which are associated with GPA and MPA, respectively, in greater than 80% of cases [Lally & Spiera, 3].

Apart from the occurrence in primary systemic vasculitides and rapidly progressive glomerulonephritis, p-ANCA may be seen in other disease states, for example rheumatoid arthritis without signs of vasculitis and inflammatory bowel disease [Peen et al., 1].

Case Presentation

A 41-year-old African-American woman with ulcerative colitis for over ten years that is treated with sulfasalazine presented to clinic with a perivaginal rash. Her labs were significant for anemia (hemoglobin 10.6) and thrombocytopenia (platelets 121). She had
worsening watery diarrhea and her perivaginal rash began to ulcerate. She sought care in the emergency department and was found to have hemoglobin of 4 and macroscopic hematuria. Subsequent cystoscopy revealed a necrotic bladder mass as well as necrotic vulvar and vaginal walls on biopsy. She underwent transurethral resection of the bladder mass and debridement of the perineal wound. The bladder biopsy revealed leukocytoclastic vasculitis with fibrinoid necrosis, multifocal acute and organized thrombi, and acute inflammation of bladder wall. She was transferred to our hospital for higher level of care. On examination, the patient appeared to be ill. The genital exam revealed induration of entire mons pubis, hyperpigmentation, exposure of subcutaneous tissue, signs of chronic inflammation of the inner thighs with erythema, sloughing, and malodorous liquid discharge. The vagina was narrowed with no inguinal lymphadenopathy. Nasal and oral cavity exam did not reveal any crusting or ulcers. Her eye and lung exams were also normal.

Laboratory data revealed a leukocytosis of 13,000 cells per mcL, hemoglobin of 8 g/dL, creatinine of 1 mg/dL, positive ANA (1:160 titer), positive p-ANCA (1:40 titer), and positive MPO. The evaluations for c-ANCA, SSA/B, RNP, anti-sm and ds DNA were negative. Serum electrophoresis and immunofixation indicated chronic inflammation with polyclonal gammopathy. HIV and hepatitis panels were negative along with erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Bacterial, viral and AFB cultures from the ulcer sites failed to identify any organisms. Also, urine cytology was negative for malignancy. Computed tomography (CT) scans of the abdomen and pelvis was did not reveal any abnormalities.

General surgery, urology, colorectal surgery and gynecology were consulted. With their assistance, the patient underwent extensive perineal debridement with wound vacuum placement and numerous biopsies. The repeat biopsies showed acute necrotizing
inflammation and areas with granulation tissue (see figure 1). Pathology revealed no evidence of vasculitis.

Broad-spectrum antibiotics including vancomycin and piperacillin-tazobactam were started. Sulfasalazine was restarted after her past colonoscopy reports showing ulcerative colitis were verified. She was continued on prednisone 60 mg daily that was started at the outside institution. Rheumatology ruled out MPA based on the clinical presentation but was concerned about Pyoderma Gangrenosum (PG). Although dermatology was consulted, the patient had undergone vast debridement prior to consultation and a definitive diagnosis could not be made. However, the likely diagnosis was believed to be pyoderma gangrenosum. Hence, the diagnosis of Inflammatory Bowel Disease (IBD) with Pyoderma Gangrenosum was made. The patient underwent a diverting loop sigmoid colostomy. Post surgical intervention, her wound healing progressed gradually and a steroid taper was initiated. After a prolonged stay, she was discharged home with home health.

Discussion

Patients with IBD (60-80% with ulcerative colitis and up to 25% with Crohn’s disease) are positive for p-ANCA [West 234]. Although MPO positivity is rare, it is not unprecedented [Peen et al., 57]. Our patient may have had a flare of her IBD consisting of worsening diarrhea that preceded the onset of other symptoms. IBD is also known to be associated with several skins manifestations including erythema nodosum and PG. In our case, PG was believed to the most likely diagnosis. Nevertheless, she received treatment with systemic steroids for two weeks followed by a taper which in effect is the treatment for PG.

While MPA is associated with p-ANCA (60%), the serology is only supportive of the diagnosis. The definitive diagnosis is made on the basis of a characteristic clinical presentation along with a renal biopsy showing necrotizing glomerulonephritis without
immune deposits [West 231]. Even though our patient had positive serologies, it was insufficient to make a diagnosis of MPA. Moreover, many patients with MPA present with acute onset of rapidly progressive glomerulonephritis (100%) and up to 50% have pulmonary infiltrates. Nonspecific symptoms like fever (50-70%), arthralgias (65%) and purpura (40%) are commonly seen [West 231, Guillemin et al., 424]. This patient did not have any of the above mentioned clinical symptoms including normal renal function.

A literature review revealed only nine previous reports of vasculitis involving the urinary bladder including PAN (6 cases), GPA (2 cases) and SLE (1 case) [Fisher et al., 903] and is extremely rare. The patient’s repeat biopsy, however, did not report leukocytoclastic vasculitis. The histology of PG is non-specific, but it facilitates the diagnosis. Additionally, it aids in the exclusion of other underlying diseases. Inflammatory infiltrates consisting mainly of pandermal neutrophil accumulation can be observed along with abscess formations and necrosis. Several studies have demonstrated that the unaffected-appearing tissue around the PG lesions actually has a perivasculitic necrotizing picture, which can be classified as leukocytoclastic vasculitis in 40% of PG patients [Ehling 3077, Crowson et al., 101]. This patient did have a biopsy reading of leukocytoclastic vasculitis which can be explained by the diagnosis of PG.

Conclusion

This case is illustrates how serology can point towards one particular diagnosis, MPA, while the clinical picture points elsewhere. It also reiterates the fact that positive ANCA s do not necessarily indicate vasculitis.

In the setting of GPA, MPA or EGPA, P-ANCA is usually due to anti-MPO antibodies. In other disorders p-ANCA positivity is not very well characterized. Goodpasture syndrome, IBD, autoimmune liver disease, cystic fibrosis and infections (HIV, subacute
bacterial endocarditis and acute parvovirus B19) are some of the other disorders associated with p-ANCA [West 234].

IBD is known to cause various skin manifestations including PG with positive p-ANCA serologies. Nodules, pustules, and/or papules combined with severe pain mark PG with sudden onset. The initial skin ulcers develop into large lesions reaching diameters of five to ten centimeters within a few weeks [Ehling 3076]. In ongoing active disease, they present as a necrotic, hemorrhagic, suppurative erosion with deep, purple-red, irregular, undermined borders and an erythematous halo. In very aggressive, rapidly progressing forms, the PG lesions can even affect fascia, muscles, and tendons. The diagnosis of PG is generally based on clinical symptoms and histologic diagnosis.

A previous study, which examined 1132 patients with ulcerative colitis, interestingly noted that 20% of patients with PG had inactive disease [Mir-Madjlessi 615]. Treatment includes systemic steroids and sometimes pulse dose steroids. If refractory, then cytotoxic options including cyclosporine, azathioprine, mycophenolate mofetil may be considered. Also, anti-TNF biologics are increasingly being utilized [Ehling 3077, Crowson et al., 103].

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Coronary Artery Thrombosis Associated with Energy Drink Consumption

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Abstract

Energy drinks have become readily available and are being utilized globally. However, the potential side effect of their use is not well understood. Most consumers use these beverages with the goal of increasing stamina. However, unintended ramifications of energy drinks may include increased sympathetic drive, endothelial dysfunction, and mitigation of coronary blood flow. A few reports have brought to light the rare phenomenon of myocardial infarction occurring secondary to energy drink consumption. We present this case of a young healthy man who suffered a myocardial infarction requiring emergent coronary intervention to contribute to the limited literature available on this topic. The increasing popularity and use of energy drinks necessitates further investigation into their unintended cardiac consequences.

Introduction

Worldwide, consumption of energy drinks (EDs) has become exceedingly popular and beverage sales have evolved into a multi-billion dollar industry.\textsuperscript{1} Regular consumption of EDs has been reported as high as 68\% in adolescents and 30\% in adults.\textsuperscript{1} The safety of ED consumption is being questioned due to associations with cardiovascular complications.
including: elevated arterial pressure, QTc interval prolongation, arrhythmias, coronary artery spasm, coronary artery thrombosis, Takotsubo cardiomyopathy, myocardial infarction, aortic dissection, and sudden cardiac death.\textsuperscript{2-4} Rising heart rate, elevated systolic blood pressure, endothelial dysfunction, increased platelet aggregation, and increased blood viscosity are all proposed mechanisms of ED’s potential side effects.\textsuperscript{2, 5} This report describes a case of a healthy young man with no past medical history presenting with a ST-segment elevation myocardial infarction (STEMI) secondary to thrombosis of the right coronary artery after consuming numerous energy drinks.

Case Description

A 28-year-old man with no past medical history had been drinking an average of four to five energy drinks per evening for several weeks. After exercising at the gym, he experienced acute retrosternal chest pressure and shortness of breath. He contacted emergency medical services and was brought to our emergency center.

On arrival, the electrocardiogram (ECG) showed sinus rhythm with hyper-acute T waves in leads II, III, aVF, and ST-segment depression in leads I, aVL, V1, and V2 (Figure 1A). Cardiac enzymes revealed a mildly elevated creatinine kinase and normal troponin levels. He received aspirin 325 mg, clopidogrel 600mg, atorvastatin 80 mg, and was started on intravenous unfractionated heparin therapy. A transthoracic echocardiogram demonstrated basal inferior and inferior septal hypokinesis with a preserved left ventricular ejection fraction of 60%. A repeat ECG showed 3 mm ST-segment elevations with tombstone morphology in leads II, III, aVF along with ST-segment depression in I and aVL (Figure 1B). The patient underwent emergent coronary angiography. The left coronary system was normal. However, a complete occlusion of the mid right coronary artery (RCA) was observed with TIMI 0 flow in the mid and distal portions of the vessel (Figure 2A). Aspiration thrombectomy was performed with removal of a substantial amount of
thrombus (Figure 3). Residual 20-30% stenosis was noted in the mid RCA with the aid of intravascular ultrasonography. Post intervention angiography showed good distal runoff with TIMI 3 flow (Figure 2B). Neither angioplasty nor stenting were performed due to the quality of flow, patient’s age, and paucity of comorbidities. The patient was continued on dual antiplatelet therapy and monitored in the coronary care unit. His creatinine kinase levels peaked at 3,940 U/L, troponin T at 5.27 ng/mL, and troponin I at > 40 ng/mL. Repeat echocardiogram was performed after catheterization and remained unchanged. The remainder of his lab work including urine drug screen was unremarkable. The patient did not develop any further chest pain throughout the hospitalization and was discharged home in stable condition on dual antiplatelet therapy. He has remained free of chest pain for over six months after discharge and continues to abstain from energy drink consumption.

Figure 1: A: Initial electrocardiogram (ECG) with peaked T waves and convex ST-segment elevation in leads II, III, aVF, as well as ST-segment depression in leads I and aVL. B: Repeat ECG with 3 mm ST-segment elevation with “tombstone” appearance in leads II, III, aVF and ST-segment depression in I and aVL.
Figure 2: A: Coronary angiography revealed complete occlusion of the middle right coronary artery. B: Coronary angiography after thrombectomy revealed TIMI 3 flow distally.
Figure 3: Post aspiration thrombectomy showing a substantial amount of clot removed.

Discussion

EDs differ greatly from traditional soft drinks, coffee, and tea in that every ED exceeds the official FDA caffeine concentration limit of 71 mg/12 fl oz. Case reports have established rare instances of EDs being linked with STEMI. At least four reports of coronary
artery thrombosis triggering STEMI patients in the setting of ED consumption have been described in the literature. Given that the only available evidence linking coronary artery thrombosis with ED consumption is in the form of case reports, a definitive causal relationship cannot be established.

Our patient in our report developed chest pain shortly after exercising. One possible explanation may be acute endothelial dysfunction. In healthy subjects who consume caffeine prior to exercise, myocardial blood flow may be significantly reduced. In two studies using positron emission tomography (PET), exercise induced myocardial blood flow following caffeine consumption was found to be decreased by 14% (P < 0.05) and 22% (P < 0.01). Furthermore, studies utilizing brachial artery dilation as a surrogate for coronary artery endothelial function demonstrate that caffeine consumption prior to exercise attenuated the expected increase in blood flow by as much as 53%. The underlying mechanism for these findings may be caffeine’s inhibition of adenosine mediated vasodilation triggered by increased cardiac work during exercise.

A study was conducted on 50 healthy subjects with a median age of 22 years. The study group consumed 250 mL of sugar-free energy drink and the control group consumed 250 mL of carbonated water. Platelet aggregation, endothelial function, and mean arterial pressure were tested before and one hour after consumption of the respective beverages. In the ED group, there was a significant increase of 13% in platelet aggregation by adenosine diphosphate-induced optical aggregometry. Endothelial function assessed by peripheral artery flow mediated dilation was acutely decreased after ED consumption and mean arterial pressure was significantly increased.

The increased prevalence of ED consumption in recent years, has seen a rising incidence of emergency room visits and serious cardiovascular events. There is growing evidence suggesting that these beverages are not innocuous performance enhancers and
may harbor significant risks to healthy young people. More research in this field is vital to developing a better understanding of the cardiovascular risk associated with ED consumption.

References


Mycobacterium fortuitum infection of the scalp after a skin graft.

Smith BD MS, Liras IN MS, De Cicco IA MD, Collard K MS, Aisenberg G MD.

Abstract

Mycobacterium fortuitum (MF) is a non-tuberculous mycobacterium found in the soil and water of most regions of the world, and has been reported to cause disease in both immunocompetent and immunocompromised hosts. We present a 52-year-old man who developed a scalp abscess under a free flap for cranium coverage after a motor vehicle accident. Culture of material drained from the abscess grew MF.

Introduction

Mycobacterium fortuitum (MF) is a non-tuberculous mycobacterium characterized by its rapid growth in culture media. This bacterium can be found in the soil and water of most regions of the world, and has been reported to cause disease in both immunocompetent and immunocompromised hosts. Disseminated infection is more common among the latter, whereas soft tissue, especially post-surgical wound infections, do not correlate with immune status.

We present a 52-year-old man who received a free flap with split-thickness skin graft for cranium coverage after a motor vehicle accident, and subsequently developed a scalp abscess. Culture of material drained from the abscess grew MF. To our knowledge, this is the first case of MF infection causing a flap-related scalp abscess reported in the literature.

Case Report

A 52-year-old African American man with a history of hypothyroidism, schizophrenia and hypertension presented to Lyndon B Johnson Hospital with a two-month history of scalp pain and two days of purulent discharge from a scalp wound. The patient was involved in a motor vehicle accident three months prior, at which time he
sustained a scalp injury that resulted in a significant area of exposed cranium. Since this
time, the patient has undergone multiple irrigation and debridements as well as a
latissimus dorsi free tissue transfer with split-thickness skin graft in order to achieve
adequate tissue coverage of the area. The night before presentation the patient
experienced swelling and pain in the area of his flap, and noticed bloody and purulent
discharge from the wound.

On presentation, the patient was overall healthy appearing, his temperature was
36.8°C, blood pressure 145/100 mmHg, pulse 82 beats per minute, respiratory rate 18
breaths per minute, and oxygen saturation 98% on room air. On exam, the patient’s scalp
flap appeared viable with no apparent signs of tissue necrosis. An abscess was appreciated
at the superior-most portion of the flap, with purulent material noted to be expressed from
under the free flap. The flap and scalp were non-erythematous. The remainder of the
examination was normal.

His laboratory results showed a white blood cell count of 8.3 K/mL (68.1%
neutrophils, 19.2% lymphocytes), hemoglobin of 12.8 g/dL with a mean corpuscular
volume of 82 fL, and a platelet count of 332 K/μL. His serum electrolytes were normal,
blood urea nitrogen of 17 mg/dL and creatinine of 1.0 mg/dL. Computed tomography (CT)
of the head revealed multiple rim-enhancing lesions associated with the right frontal scalp
flap, the largest of which measured 3.8 cm in diameter. The CT did not demonstrate any
underlying irregularity of the skull.

Empirical therapy with vancomycin was started. The patient underwent irrigation
and debridement the day after admission, which he tolerated well, with no complications.
Cultures from the scalp abscesses were collected during the surgery. The initial Gram stain
reported no organisms. However, ten days after discharge from the hospital, the wound
culture isolated MF (table 1).
TABLE 1 Antimicrobial susceptibility testing of *Mycobacterium Fortuitum*

<table>
<thead>
<tr>
<th>Antibiotic(s)</th>
<th>Interpretation</th>
<th>MIC (mg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>Susceptible</td>
<td>3</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>Intermediate</td>
<td>3</td>
</tr>
<tr>
<td>Imipenem</td>
<td>Resistant</td>
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<td>Linezolid</td>
<td>Susceptible</td>
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<tr>
<td>Moxifloxacin</td>
<td>Susceptible</td>
<td>0.012</td>
</tr>
<tr>
<td>Trimethoprim/Sulfamethoxazole</td>
<td>Susceptible</td>
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Discussion

The reported incidence of non-tuberculous mycobacterial (NTM) cutaneous infections continues to rise, and penetrating wounds or the presence of foreign bodies appear to be predisposing conditions.⁴ MF has been associated with a broad variety of exposures, such as acupuncture, lacerations, body-scrubbing in public baths, chemotherapy, and organ transplants.⁵,⁶ Outbreaks have been reported in nail salons and with the use of electromyograms, ventriculo-peritoneal shunts, and steroid injections.⁷-¹¹ These infections have been described both in immunocompetent and immunocompromised patients.²,¹²-¹⁴

To the best of our knowledge, we are reporting the first case in the literature of MF causing a skin graft-related scalp abscess. Though MF is widely distributed in the environment, it is unclear how the organism reached this patient’s scalp. We hypothesize that this might be a late infection related to his prior surgical graft.

In typical cases of skin and soft tissue MF infections, the lesions develop after an inoculation period of 4 to 6 weeks and can present as painful nodules, abscesses, ulcers, draining sinus tracts, or cellulitis.¹⁵ Histologically, older lesions have a poor infiltrate, whereas acute lesions display suppurative granulomas without caseation, local tissue destruction, and a mixed infiltrate.¹⁶
Antimicrobial sensitivity usually guides the therapy, and using a combination of antibiotics is recommended. For limited skin and soft tissue infections, such as in our case, oral therapy with two agents is recommended. The duration of treatment should be for a minimum of four months. The preferred regimens include clarithromycin or azithromycin combined with ciprofloxacin, levofloxacin, doxycycline, minocycline, or trimethoprim-sulfamethoxazole. For severe or disseminated disease, initial parenteral treatment is recommended with two to three effective antibiotics, followed by oral treatment for 6 to 12 months. Our patient started empiric antibiotic therapy with vancomycin and cefepime and underwent debridement with Jackson-Pratt drain placement. After the procedure, he was discharged on trimethoprim-sulfamethoxazole. When the wound culture grew MF, the regimen was changed to doxycycline and ciprofloxacin. Currently the patient has received two of four months of antibiotic treatment and is progressing favorably.

In conclusion, we describe a case of skin-graft related scalp abscess caused by MF treated with dual antibiotic treatment and extensive surgical debridement. As with other infections caused by uncommon pathogens, this case shows the importance of the microbiological analysis of material drained from skin abscesses.

References


**Hyperesoinophilic Syndrome in a 17-Year Old Female Mimicking Heart Failure**

Danielle Stone, MD, James Stone MD

Abstract

Hypereosinophilic syndrome (HES) is a disease defined as persistent eosinophilia (blood eosinophil count > 1500/μL), for at least six months and organ damage. Myocardial infiltration is the most serious complication and is a major cause of morbidity and mortality in HES. Eosinophilic myocarditis (EM) is a rare form of myocarditis with limited understanding of the underlying etiology. Hypersensitivity to a drug or substance has been identified in various cases, but the majority of EM are idiopathic. The spectrum of clinical presentation varies greatly among patients diagnosed with HES. The following case report describes the presence of HES in a 17 year-old woman presenting with symptoms mimicking heart failure. Although endomyocardial biopsy (EMB) is the gold standard to diagnose EM, cardiac magnetic resonance (CMR) imaging was used to establish the diagnosis as prior upper gastrointestinal biopsies confirmed the presence of HES. With the early induction of corticosteroids, her eosinophilia resolved and her clinical outcome improved dramatically.

Introduction

Early onset eosinophilic myocarditis (EM) presenting with necrosis follows a rapidly deteriorating course. Thus, it is vital to obtain an early diagnosis and initiate treatment with corticosteroids, which has been shown to have an improved overall outcome. In the following case, we discuss the diagnosis and treatment modalities of EM by promptly identifying endomyocardial eosinophilic infiltration to prevent the increased morbidity and mortality associated with necrotizing EM.
Case presentation

On admission, a 17-year old female with known MVP and a 3-year medical history of hypereosinophilic syndrome (HES) presented with mid-sternal chest pain along her sternotomy incision site and shortness of breath with minimal exertion for two weeks. She also complained of paresthesias in her fingertips and toes.

Approximately 6 months preceding this admission, the patient had been admitted to our hospital for a six-day history of shortness of breath and sub-sternal chest discomfort. It was discovered that she had undergone a recent mechanical mitral valve replacement only a few months prior at an OSH. Her post-operative course was complicated by thromboses on her new valve and known residual posterior leaflet dysfunction. She subsequently received catheter directed tPA infusion at that time. After further investigation, it was found on TTE that her mechanical mitral valve was severely stenotic and leaflets were immobile, and thus she underwent a second mechanical valve replacement at our hospital. A post-operative TTE showed a normal functioning mechanical mitral valve prosthesis prior to discharge.

During this admission, the patient was again hospitalized for chest pain and worsening shortness of breath. Her chest pain was mid-sternal along the sternotomy incision site. She described the pain as severe, sharp and stabbing in nature, without radiation, and exacerbated by palpating the site. She also presented with paresthesias in her fingertips and toes. Her vitals were unremarkable. EKG showed no ST segment changes and cardiac enzymes were only slightly elevated (Troponin I 0.70; CK-MB 2.6). Her initial eosinophil count was 10,100 μL. Transthoracic echocardiography (TTE) showed an EF 40-45% with mild global hypokinesis and akinetic mid anteroseptal, mid inferoseptal and apical septal wall segments. Chest computed tomography (CT) imaging showed a
markedly enlarged esophagus with a thickened wall and no disruption of sternal wires from the sternotomy.

While inpatient, the patient continued to have chest discomfort and shortness of breath along with limb paresthesias. She was given morphine to control her pain, and steroids were given once all testing had been completed as to achieve accurate results. Hematology, gastroenterology and rheumatology were consulted to workup the cause of HES in this patient. Peripheral smear and bone marrow biopsy showed marked eosinophilia. Cytogenetic testing and autoimmune workup were negative. EGD with biopsy showed chronic active gastritis, eosinophilic esophagitis and sub-mucosal eosinophilia in the duodenal bulb and second portion of the duodenum.

Cardiac MRI demonstrated apical and mid segments compatible with areas of endomyocardial fibrosis consistent with HES along with mild global hypokinesis with EF of 52%.

In addition to induction of steroids, the patient was started on a beta-blocker, ACEi, and diuretics. Her eosinophil count returned to normal and her shortness of breath and paresthesias resolved as well.

Discussion

Hypereosinophilic syndrome (HES) is a rare disorder of unregulated eosinophilia, which if untreated, may lead to systemic tissue infiltration and inflammation. The causes of eosinophilia are described in the CHINA mneumonic (connective tissue diseases, helminthic infection, idiopathic, neoplasia, allergy). An elevated eosinophil count (>1500/μL) without a secondary cause and evidence of organ involvement are diagnostic of HES. The most common organs affected by HES include the skin, lungs, gastrointestinal tract, and heart. When eosinophilic infiltration causes diffuse myocardial inflammation eosinophilic myocarditis (EM) results. In this case, the patient’s HES affected her GI tract,
skin and heart. With confirmative biopsies showing eosinophilic infiltration involving the stomach, esophagus and duodenum in the setting of profound peripheral eosinophilia (10,100/μL), we suspected EM following CMR imaging. We used high-dose corticosteroids and heart failure medications to reverse the cardiac injury and to improve the clinical outcome.

According to previous reports [1-2], cardiac involvement occurs in 54–82% of cases, and, the prognosis is determined by the extent of the myocardial fibrosis and related complications. The five-year mortality of EM is 30%.

Infiltration of eosinophils into the myocardium causes EM via release of toxic eosinophilic granule proteins such as ECP and major basic protein (MBP), which causes dysfunction of myocyte mitochondria leading to myocardial lesions and necrosis [3].

Myocarditis presents in many different ways from asymptomatic cases to life-threatening conditions such as cardiogenic shock or sudden cardiac death due to malignant ventricular arrhythmias. Common manifestations of EM may be in the form of chest pain, dyspnea, fatigue, palpitations, and/or syncope. Prior to the onset of EM, approximately two-thirds of patients have symptoms of the common cold and one-third of cases suffer from allergic diseases such as bronchial asthma, rhinitis, or urticaria [4].

Diagnosis of EM can be done by CMR imaging [5] prior to endomyocardial biopsy (EMB) to visualize the extent of myocardial involvement. EMB is the gold standard for diagnosing EM. EMB findings are characterized by diffuse myocardial necrosis associated with extensive eosinophilic infiltration of the myocardial interstitium, focal myocyte dissolution, perivascular infiltration and myocardial interstitial fibrosis [6]. However, EMB cannot be performed in all patients suspected of having EM because it may be too invasive. HES may or may not be associated with mutations in the tyrosine kinase receptor gene, but such involvement is important to identify, because treatment with imatinib is
effective in such cases. If HES is not associated with such mutation, treatment with high-dose methylprednisone is the standard of care. We did not use imatinib in this patient as no mutation in the tyrosine kinase receptor gene existed.

The therapy of choice after a diagnosis of EM consists of standard heart failure medication and early treatment with high doses of cortisone [7]. The early initiation of steroid therapy can achieve substantial improvements in clinical outcomes, prognosis and long-term survival. Corticosteroid therapy in HES has been successfully documented in published case reports with induced complete or partial responses at 1 month in 85% of patients following monotherapy; most patients remained on maintenance doses with a median of 10 mg prednisone equivalent daily dose for 2 months to 20 years [7,8,9].

Our patient likely had a subtype of EM known as idiopathic hypereosinophilic syndrome (HES). This syndrome is characterized by absolute eosinophil count greater than $1.5 \times 10^5/L$ lasting for more than six months in the absence of any known cause of hypereosinophilia and with evidence of multi-organ involvement directly attributable to the eosinophilia or otherwise unexplained in the clinical setting [4,10,11].

Conclusion

In summary, myocarditis presents in a variety of ways and EM should be considered in cases with persistent eosinophilia. In this case, the results of relevant laboratory analyses and CMR imaging led to the diagnosis of a subtype of EM known as idiopathic HES. Early diagnosis and initiation of steroid treatment achieved a normal eosinophil count and marked improvement of the patient’s prognosis. In addition, optimization of heart failure therapy demonstrated to improve hemodynamics and symptoms.

References


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Biventricular failure as the initial manifestation of thyrotoxicosis during pregnancy.

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Abstract

Changes in cardiovascular physiology during pregnancy include systemic vasodilation, increased plasma volume, and increased cardiac output. These changes create an increase in preload and decrease in afterload resulting in a hyperdynamic state. Similar changes are found in hyperthyroidism. Cardiac reserve is tested when the hyperdynamic states of pregnancy and hyperthyroidism are combined, but most healthy patients are able to compensate. It usually takes a third event to push these patients into clinical heart failure. We present a case of a patient who was not able to compensate and presents with biventricular heart failure secondary to Graves disease during pregnancy.

Introduction

The cardiovascular system undergoes many physiological changes during pregnancy to accommodate the increasing demands of the mother and growing fetus. Increased levels of estrogen and progesterone lead to systemic vasodilation and decreased systemic vascular resistance. There is also significant activation of the Renin-Angiotensin-Aldosterone System (RAAS) resulting in increased plasma volume. In total, these changes lead to increased cardiac preload and decreased cardiac afterload resulting in a hyperdynamic state characterized by increased cardiac output. Some studies have reported the increase in cardiac output can be up to 80-85% higher than the pre-pregnancy state. Healthy mothers are usually able to adapt to these hemodynamic changes with little to no symptomatology. However, another insult that introduces similar hemodynamic changes can overwhelm cardiac reserve and lead to heart failure. We present a case in which this scenario occurs.
Case Description

Our patient is a 31-year-old gravida 5 para 1 female at 22 weeks gestation that presented to an outside facility with complaints of gradual and progressive dyspnea on exertion over the last month. Evaluation at the outside facility included a chest radiograph, electrocardiogram, and transthoracic echocardiogram that were significant for sinus tachycardia, biatrial enlargement, bibasilar pulmonary congestion, and a right ventricular systolic pressure (RVSP) of 30 mmHg. She was started on intravenous diuretics, beta-blockers, and transferred to our hospital for higher level of care. Physical exam upon arrival at our facility was notable for 2+ pitting lower extremity edema, exophthalmos, tachycardia, and bibasilar rales on pulmonary auscultation. Right heart catheterization showed elevated wedge pressure of 28 mmHg. Thyroid studies were significant for thyroid stimulating hormone (TSH) <0.005 μU/mL, free T4 (FT4) 6.23 ng/dL, anti-thyroid peroxidase level (anti-TPO) >1300 IU/mL, and thyroid stimulating immunoglobulin (TSI) of 447% suggesting heart failure from thyrotoxicosis. She was started on propylthiouracil, propranolol, and diuretics with good response and discharged home. She stopped taking her anti-thyroid medication after 2 weeks for an unclear reason, and returned to the hospital after 3 weeks with pre-term labor and decompensated heart failure. During this admission she had an emergent cesarean section at 26 weeks gestation due to fetal distress. She resumed treatment for hyperthyroidism postpartum with resolution of heart failure while her baby was observed in the neonatal intensive care unit.

Discussion

Hyperthyroidism has a prevalence of 1.3% in the United States with women affected more than men. The most common form of hyperthyroidism is Graves disease, which is an autoimmune disorder where autoantibodies stimulate the TSH-receptor on thyroid
follicular cells causing upregulation of thyroid hormone.\textsuperscript{7} The annual incidence of Graves disease is around 20-30 cases per 100,000 individuals.\textsuperscript{8}

Thyroid hormone plays a crucial role in the regulation of cardiovascular function. Excess thyroid hormone causes an increased resting heart rate, stroke volume, blood volume, cardiac output, and decreased systemic vascular resistance through direct and indirect effects.\textsuperscript{10} These changes lead to many of the cardiovascular manifestations of Graves disease, including tachycardia, widened pulse pressure, and dyspnea. Other signs and symptoms of Graves disease include proptosis, eye-lid lag, and goiter. Heart failure due to hyperthyroidism only occurred in 5.6 per 100,000 individuals in a study by Siu \textit{et al.}

In a study by Sheffield \textit{et al.}, Graves disease affected 1 out of 1700 deliveries over a 28-year period. The manifestations of Graves disease tend to regress during pregnancy due to the relative immunosuppressed state caused by pregnancy.\textsuperscript{6} When present, uncontrolled Graves disease can lead to miscarriage, pre-term delivery, pregnancy-induced hypertension, low-birth weight, pre-eclampsia, and maternal heart failure. As described above, pregnancy and hyperthyroidism lead to an increase in cardiac preload and a decrease in cardiac afterload. Healthy mothers are able to compensate for the hemodynamic changes of pregnancy and do not present with heart failure. The hyperdynamic state is stretched even further when pregnancy is combined with overt hyperthyroidism, however the majority of these patients are still able to compensate. A third hyperdynamic event, such as hemorrhage, sepsis, or pre-eclampsia/eclampsia, is required to cause heart failure in a majority of patients.\textsuperscript{4}

The phenomenon of pregnancy, hyperthyroidism, and a third hyperdynamic event has been demonstrated in multiple case reports. Sheffield \textit{et al.} described 13 patients who presented with heart failure secondary to thyrotoxicosis in the setting of pregnancy. Eleven of the 13 patients had an obstetric complication that added a third insult to their cardiac
reserve. The 2 patients who did not have an obstetric related complication were described as having mild anemia, which was also true in our case. A drop in serum hemoglobin is to be expected during pregnancy however, with a nadir near 10.5 g/dL. Our patient’s hemoglobin at the time of admission was 9.8 g/dL, which is unlikely to introduce a significant stressor to the cardiovascular system.

Conclusion

Heart failure due to hyperthyroidism during pregnancy is a relatively rare event that typically requires a third hyperdynamic insult to have any clinical significance. As our case demonstrates, a third event is not always necessary. Clinicians should have a low threshold to evaluate thyroid function in a pregnant patient presenting with heart failure. Early recognition and treatment can prevent severe maternal and fetal morbidity and mortality.

References


A Rare Case of Macrophage Activating Syndrome

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Introduction

Macrophage Activating Syndrome (MAS) is a rare and possibly fatal systemic inflammatory disorder that results when macrophage activation leads to hemophagocytosis causing a depression of cell lines, liver dysfunction and coagulopathy. Because of the high mortality profile early diagnosis is key. The non-specificity of symptoms are associated with a broad differential of disease processes. However with a closer review, literature search, and pathology follow-up, we diagnosed the patient correctly and initiated life-saving treatment.

Case presentation

A 21-year-old female with no known past medical history other than dental extraction of four wisdom teeth one month prior presented to an outside hospital with complaints of fever, fatigue, night sweats and an unintentional weight loss of 20 pounds. Patient is married with two children and currently in part time school. She lives with her husband and school aged children. She had no history of sick contacts or recent travel. She denied tobacco and illicit drug use, but reported occasional alcohol use. She was unemployed and had no family history of autoimmune disease or illness.

Patient reported going to an outside clinic a week prior to admission where she was prescribed antibiotics. She completed her course with no alleviation of her symptoms. On admission to outside hospital, patient was found to be hypotensive, febrile and pancytopenic (hemoglobin = 5.7 g/dL, WBC = 3.6 K/uL, platelet = 9 K/uL, retic count = 0.8%). She was also noted to have renal failure. She was admitted to the intensive care unit for work-up and started on broad spectrum antibiotics. The patient continued to
decompensate requiring intubation and initiation of vasopressor support. She was transferred for higher level of care. On arrival to our facility, she was noted to be tachycardic at a rate to 160-190 beats per minute with a mean arterial pressure of 55-60 mmHg. She was requiring norepinephrine at 50 mcg/min. Vasopressin and neosynephrine were eventually added to wean norepinephrine down to 30 mcg/min since she was requiring a very high dose. The patient subsequently arrested with pulseless electrical activity requiring chest compressions. Return of spontaneous circulation was achieved after 5 minutes of chest compressions with administration of epinephrine once. At that time, the patient was in a state of severe lactic acidosis of 11.5 mmol/L with a pH of 6.9 and SVO2 of 90%. She was given 2 ampules of sodium bicarbonate and continuous renal replacement therapy (CRRT) was initiated. Her heart rate remained at 180 beats per minute with a narrow QRS complex pattern presumed to be SVT. Echocardiogram was ordered and revealed biventricular heart failure. The patient was transitioned to epinephrine, vasopressin and dobutamine in the setting of heart failure. A chest x-ray was ordered and showed diffuse bilateral alveolar opacities consistent with ARDS or diffuse alveolar hemorrhage. Brain natriuretic peptide and cardiac enzymes were markedly elevated. Patient also had transaminitis and an elevated creatinine kinase enzyme level. Ferritin was noted to be 5,568 mcg/L. At the outside hospital it was found to be over 18,000 mcg/L. Autoimmune work-up was initiated and revealed an ANA titer of 1:640 with speckled pattern. HIV, EBV, CMV were negative, many other infectious processes were ruled out. Preliminary blood cultures were negative, although outside blood cultures reported growing gram negative rods. Speciation revealed the organism to be Neisseria Sicca. Patient was continued on broad spectrum antibiotics. Plasma exchange was offered as a last resort for gram-negative sepsis in the setting of multi-organ failure. The patient remained in a very guarded condition. There was uncertainty as to what precipitated this
rapid decline and multiorgan failure in a previously healthy woman suspected of having an autoimmune disease.

Investigation

Bone marrow aspiration performed on admission revealed a preliminary result of hemophagocytosis (HLH). Patient was presumed to have HLH by meeting 5/8 of criteria. According to the HLH 2004 Diagnostic criteria, diagnosis can be established if patient meet more than five of the eight criteria including: fever, splenomegally, cytopenia in more than 2 cell lineages, hypertrigliceridemia and hypofibrinogenemia (triglycerides greater than 265 mg/dL or fibrinogen less than 1.5 g/L), hemophagocytosis, low or absent NK-cell activity, ferritin greater than 500 mcg/L, and/or the presence of soluble CD25 greater than 2400U/mL (6). It was thought to be likely secondary to autoimmune disease given positive anti-nuclear antibody and anti-double stranded DNA. However, it was hard to confirm the diagnosis in this acute setting.

Treatment

High-dose dexamethasone therapy was chosen over eptoposide given the patient’s recent liver failure and severe infection. The patient was treated with high-dose solumederol with no additional immunosuppressive agents. She continued to improve based on the parameters of ferritin, LDH and blood lines. The patient was eventually weaned off ventilation and circulatory support and transferred to step-down unit for physical rehab and recovery.

Final outcome

Final bone marrow analysis revealed a hypo-cellular bone marrow replaced with sheets of macrophages and evidence of hemophagocytosis consistent with macrophage activation syndrome. The patient was continued on maintenance prednisone therapy and was referred to hematologic specialty clinic for continued follow-up.
Discussion

Macrophage Activation Syndrome is a rare form of HLH. It is a fatal systemic inflammatory disease resulting from uncontrolled proliferation of T cell and excessive activation of macrophages (1,2). It is thought that a deficiency of perforin, a protein expressed on lymphocytes and macrophages, leads to persistent lymphocyte activation. It also causes excessive production of interferon gamma and GMSF leading to activation of macrophages (1). Perforin is a protein that the cytolytic cell utilizes to induce apoptosis of target cells including tumor cells and those infected by viruses. With the inability to kill target cells, there is uncontrolled proliferation of T cells and macrophages leading to decreased natural killer cells and cytotoxic cell function (7). Sustained macrophage activation causes the release of TNF-alpha, IL1, IL6 associated with the clinical symptoms and tissues damage associated with MAS (1, 5). It has also been hypothesized that the lack of NK cells and cytotoxic T-cells needed to terminate an immune response leads to sustained macrophage activity, which may play a role in secondary HLH (3). Accumulation of intracellular ferritin needed for the maturation of macrophages can be seen as a marker of histiocyte proliferation and active phagocytosis by macrophages. MAS, on the spectrum of HLH, presents acutely with non-remitting high fever, lymphadenopathy, hepatosplenomegally, pancytopenia, liver dysfunction, hypertriglyceridemia and hyperferritinemia. It is also possible to note low erythrocyte sedimentation rate (ESR), decreased fibrinogen levels, and coagulopathy (1,4). Numerous well differentiated macrophages actively phagocytosing haematopoetic elements on examination of the bone marrow is the pathognomonic feature in MAS (4). It is important to recognize MAS early because treatment is essential. The hyperinflammatory response can be fatal if left untreated (2). High dose corticosteroids are the cornerstone of therapy and should be initiated early. Steroids that cross the blood brain barrier should be preferred. Even in the
setting of a highly febrile pancytopenic patient with suspected infection, immunosuppression is required to control the hyperinflammation syndrome and avoid multiorgan failure (2,4). Cyclosporin A, plasma exchange, IVIg and cyclophosphamide have also been proposed as therapies but no supporting studies have proven efficacy. Once treatment is initiated ferritin levels have been proven to be a reliable parameter for response to therapy (1).

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Multidermatomal extension of Ramsay Hunt should raise suspicion for HIV/AIDS.

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Introduction

Herpes Zoster is commonly associated with HIV infected patients. It is frequently the first manifestation of HIV. Thus, a patient who presents with herpes zoster infection should always be tested for HIV infection.

Case description

A previously healthy 32-year old homosexual man initially presented to his primary care physician with concern for a burn on his neck after using heating pads for neck discomfort. Subsequently, he developed pain and rash around the ipsilateral ear with complete paralysis of the left side of the face. An extensive rash (Figure 1) with lower motor neuron palsy of the left facial nerve was noted at presentation in the emergency room.

The patient was initially treated with broad spectrum antibiotics along with ofloxacin and dexamethasone ear drops for the ear canal inflammation. A wick was placed to prevent stenosis. Polymerase chain reaction and cultures from unroofed vesicles were positive for herpes zoster. The patient was found to be positive for HIV-1 with a CD4 count of 283/µL, and viral load of 16,900 copies/mL. Patient showed improvement with intravenous acyclovir and high dose oral prednisone. At one year follow-up he had mild residual facial nerve palsy, but was able to close his eyes. His CD4 count recovered to normal levels with HAART.

Discussion

Ramsay Hunt syndrome (RHS) is a peripheral facial nerve palsy along with erythematous vesicular rash over the ear caused by VZV reactivation in the geniculate
ganglion of the facial nerve.\(^1\) Decreased cell mediated immunity has been implicated in Ramsay Hunt syndrome.\(^2\) The immunocompromised status in our patient likely contributed to the multidermatomal presentation. Although acyclovir has been shown to reduce incidence of herpes zoster in HIV infected patients, routine prophylaxis is not recommended.\(^3\) It is critically important to consider HIV/AIDS in a patient presenting with RHS of herpes zoster extending over multiple dermatomes. Early initiation of antiviral therapy is crucial to have optimal long term outcomes and reduce the chances of complications. Steroids may be considered on an individual basis.

Conclusion

Testing patients for HIV should be part of the initial management of herpes zoster infections. Early detection and treatment of HIV can bring favorable outcomes with long term survival and better quality of life. It is important that physicians can recognize skin infections that are commonly associated with HIV.

References


Elevated Lipase levels in Small Bowel Obstruction

Fathima Zahra Kamil Faiz, MD

Abstract

This is a case of a 69 year old man with prior abdominal surgeries who presented with nausea, vomiting and abdominal pain. Laboratory values showed an elevated lipase and liver function tests, suggestive of acute biliary pancreatitis. When further history revealed that he had not had a bowel movement in a week, there was high suspicion for small bowel obstruction. A stat CT scan of his abdomen and pelvis showed high grade small bowel obstruction and a contained perforated sigmoid abscess. The patient was taken to the OR emergently and confirmed to have small bowel obstruction with an incarcerated ventral hernia. This case demonstrated the association between elevated pancreatic enzymes and small bowel obstruction. This correlation has been previously described in bariatric surgery case reports but not in patients with other surgeries as in this case. Small bowel obstruction can be fatal if not recognized early and it is beneficial to obtain abdominal imaging to rule out obstruction in patients who have an elevated lipase.

Introduction

Small bowel obstruction (SBO) occurs when there is an interruption in the passage of intestinal contents through the gut lumen. If this diagnosis is missed, SBO can lead to gut necrosis and sepsis. Consequently, the mortality of an untreated SBO is close to 80%\(^1\). While some patients can present with typical symptoms of bilious vomiting, abdominal pain and obstipation, others may have a more nonspecific presentation. Here we present the case of a patient initially admitted with a picture of acute pancreatitis but was found to have complicated small bowel obstruction.
Case Discussion

A 69-year-old man with known incisional and hiatal hernias presented to the emergency room with a 10-day history of abdominal discomfort, nausea and vomiting. Initial labs showed a Lipase >1000 and AST and ALT twice the upper limit of normal. The patient was admitted to the medicine floor with a diagnosis of acute pancreatitis. On physical exam, patient had decreased bowel sounds and a large non-reducible ventral hernia with no focal tenderness. Based on further history from the family, it was discovered that the patient had not had a bowel movement for the past seven days. Given the combination of emesis and constipation with a hernia and history of abdominal surgeries, there was concern for small bowel obstruction. A CT scan of his abdomen and pelvis showed high grade small bowel obstruction and a contained perforated sigmoid abscess (See Figure 1 and Figure 2). Of note, his pancreas appeared normal.

The patient was taken to the OR emergently and confirmed to have small bowel obstruction with an incarcerated ventral hernia that contained about four feet of bowel. Additionally, he was found to have a perforated sigmoid mass associated with a pelvic abscess. Given that the mass appeared malignant, the patient underwent recto-sigmoid resection with a colostomy and Hartman pouch procedure. The patient did well post-operatively and was discharged with close oncology follow up. Pathology showed invasive adenocarcinoma of the colon
Figure 1: CT Abdomen showing markedly dilated loops of bowel noted in coronal view.

Figure 2: CT Abdomen showing incarcerated hernia leading to small bowel obstruction, noted in sagittal view.
Discussion

According to the ACG, acute pancreatitis can be diagnosed if they meet two out of the three following criteria:\(^2\):

- Abdominal pain, nausea, vomiting
- Serum lipase/amylase thrice the upper limit of normal
- Typical findings on abdominal imaging

However, abdominal imaging should only be considered if there is significant doubt about the diagnosis or if the patient fails to respond to treatment\(^2\). In this case, the only objective finding was an elevated lipase and seemed to confound the actual diagnosis of SBO.

The surgical literature has several case reports\(^3,4,5\) where patients with a gastric bypass or Roux-en Y gastrojejunostomy (RYGB) presented with abdominal pain and elevated pancreatic enzymes and were admitted as pancreatitis but failed to improve. Subsequent imaging would always show complex SBO. A 2015 retrospective study\(^4\) of 99 cases of SBO in RYGB patients concluded that there was an association between SBO and elevated pancreatic enzymes. A 2009 case report\(^5\) of a similar clinical presentation concluded that any RYGB patient with abdominal pain and elevated lipase should have an abdominal CT.

The mechanism of how small bowel obstruction leads to an elevated lipase is thought to be from increased intraluminal back pressure caused by the obstruction. This leads to a reflux of intestinal content into pancreatic ducts that subsequently activates pancreatic zymogens. This concept is referred to as reflux pancreatitis and was noted in bariatric surgery literature and is mostly associated with SBO. However, the reflux pancreatitis was never necrotic or life-threatening. Similarly, liver enzymes are simultaneously elevated by the same mechanism, and the patient is often falsely diagnosed with gallstone pancreatitis. In conclusion, when evaluating any patient with a history of abdominal surgeries, who
presents with abdominal complaints and elevated pancreatic and liver enzymes, abdominal imaging should be considered to rule out SBO. Additionally, small bowel obstruction must be included in the differential diagnosis of elevated pancreatic enzymes.

References


Spontaneous Tumor Lysis Syndrome in Metastatic Breast Cancer

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Abstract

Acute tumor lysis syndrome (ATLS) is an oncologic emergency caused by rapid lysis of malignant cells. Spontaneous tumor lysis syndrome (STLS), in the absence of cytotoxic therapy, frequently occurs in hematologic malignancies. Rarely, STLS occurs in solid non-hematologic malignancies. We report a case of STLS in a patient with metastatic breast cancer.

Introduction

ATLS represents an oncologic emergency and left untreated can be fatal. ATLS most frequently occurs in hematologic malignancies after initiation of cytotoxic therapy but can occur spontaneously in hematologic malignancies with large burden of disease and high proliferative rate. Cases of STLS are well known and documented in lymphoma and leukemia. Only few case reports describe STLS in solid non-hematologic tumors. We present the second known case of STLS in a patient with metastatic breast cancer.

Case Presentation

A 29-year-old African American woman presented to the hospital with a rapidly enlarging left breast mass and dyspnea. Less than one month prior to admission, she was diagnosed with Stage IV invasive ductal carcinoma of the left breast (estrogen receptor weakly positive, progesterone receptor negative, HER2 negative). Proliferative rate of the tumor as measured by the cellular marker Ki67 was 95%. CT imaging prior to admission showed a massive necrotic mass involving the entire left breast measuring 10.8cm x 8.4cm x 11.1cm; several bilateral pulmonary nodules; diaphragmatic pleural metastatic implants;
moderate loculated left pleural effusion; and innumerable necrotic liver metastasis with replacement of the entire left hepatic lobe (Figure 1a and 1b).

Figure 1a. CT chest showing a large, necrotic, left breast mass.

Figure 1b. CT abdomen showing multiple necrotic liver metastases.
The patient was admitted for induction of palliative chemotherapy with doxorubicin and cyclophosphamide. On physical exam, she was normotensive but tachycardic. The entire left breast was firm with a large, fungating lesion superior to the areola with serosanguinous discharge. There was a palpable 4cm left axillary node. Breath sounds were decreased at the left lung base. The liver was palpable several fingerbreadths below the right costal margin.

Laboratory findings on admission (Table 1) revealed renal insufficiency, elevated potassium, elevated uric acid, and elevated LDH. This was concerning for STLS, so chemotherapy was delayed. She was started on intravenous normal saline and received one dose of rasburicase. Daily therapy with allopurinol was also started. Her laboratory data improved after treatment (Table 1), and she then received doxorubicin and cyclophosphamide. Unfortunately, her clinical course was complicated by a rapidly accumulating pleural effusion, which led to hypoxia and cardiac arrest resulting in her death on hospital admission day six.

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<td>7.9</td>
<td>49</td>
<td>1.6</td>
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</tbody>
</table>
Discussion

ATLS is the result of rapid tumor necrosis with the release of cellular contents into the blood stream leading to metabolic derangements such as hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia. Hyperuricemia increases the risk of uric acid crystallization in renal tubules and can lead to renal failure. The release of potassium increases the risk of hyperkalemia—the most dreaded complication of which is cardiac arrhythmias and death. The release of phosphate can result in hyperphosphatemia. Phosphate precipitation with calcium can worsen pre-existing renal failure and result in hypocalcemia.

ATLS most frequently occurs after cytotoxic therapy in hematologic malignancies, however, it can occur spontaneously and is well described in literature. STLS is rarely described in solid non-hematologic malignancies. Upon literature search, we found the following case reports of STLS in solid non-hematologic tumors as shown in Table 2. There is only one published case report of STLS in metastatic breast cancer ¹.

<table>
<thead>
<tr>
<th>Table 2. Published case reports of STLS in solid non-hematologic tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Germ cell tumors</td>
</tr>
<tr>
<td>Colon cancer</td>
</tr>
<tr>
<td>Pheochromocytoma</td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
</tr>
<tr>
<td>Lung adenocarcinoma</td>
</tr>
<tr>
<td>Squamous cell carcinoma of lung</td>
</tr>
<tr>
<td>Gastric adenocarcinoma</td>
</tr>
<tr>
<td>Metastatic adenocarcinoma of unknown primary</td>
</tr>
<tr>
<td>Prostate cancer</td>
</tr>
<tr>
<td>Squamous cell carcinoma of maxillary sinus</td>
</tr>
</tbody>
</table>

Risk factors for ATLS include rapidly proliferating or chemosensitive malignancies, pre-existing renal insufficiency, elevated uric acid at baseline, and extensive tumor burden.
as quantified by bulky disease >10cm, elevated LDH greater than two times the upper limit of normal, or elevated white blood cell count above 25,000/μl.

In this case report, we believe that our patient showed evidence of STLS. Prior to receiving any chemotherapy, she presented with renal insufficiency, hyperkalemia, and hyperuricemia. She had multiple risk factors including extensive tumor burden with massive necrosis seen on CT imaging, highly proliferative tumor, and elevated LDH. We excluded other causes of AKI such as parenchymal kidney disease and post-renal obstruction by CT imaging. Additionally, with the administration of fluids and rasburicase, her renal function improved and laboratory data normalized. Her death was attributed to rapidly accumulating pleural effusion resulting in hypoxia and cardiac arrest.

STLS can be life threatening, therefore awareness and early recognition is important. Although, solid non-hematologic tumors are classified as low or intermediate risk of TLS based on expert guidelines, it is important to maintain an elevated index of suspicion in patients with risk factors and weigh the benefit of prophylaxis.

References


Positional ST Segment Elevation Caused by a Ventricular Pseudoaneurysm

De Cicco IA MD, Velasquez AH MD, McBride CL MD, Au J MD, Aisenberg GM MD, Postalian A MD, Quintana-Quezada RA MD, Llanos Chea F MD, Ocazionez Trujillo D MD, Dhoble A MD, Arain S MD, The University of Texas at Houston Health Science Center

Introduction

Ventricular pseudo-aneurysms (VPAs) are a rare but severe complication of myocardial infarction (MI), first described by William Harvey in 1649 [1]. The relationship between coronary artery disease (CAD) and cardiac rupture was established by Joseph Hodgron in 1850 when he noted that scar tissue originating within infarcted myocardium was susceptible to rupture [2,3]. When blood passing from the ventricle through the area of rupture is surrounded by adjacent structures such as pericardium or fibrous tissue, a VPA is formed [4]. VPAs can also form as a complication of cardiac surgery, tumor invasion or trauma [5].

We report the case of a patient with a ventricular wall rupture that was contained within the pericardium, presumably due to fibrosis formed as a consequence of prior coronary artery bypass grafting (CABG). The patient was also noted to have intermittent positional ST segment elevation on electrocardiogram (ECG), possibly caused by intermittent coronary artery compression by the VPA.

Case Presentation

An 84-year-old woman presented to our hospital complaining of pressure-like chest pain that radiated to her back and left mandible. She had a history of CAD treated with CABG 18 years earlier. Approximately 2 months prior to presentation, she underwent percutaneous coronary intervention with stent placement to the right coronary artery, the coronary angiogram was done due to recurrent angina pectoris and a recent abnormal treadmill stress test. On physical examination, she was diaphoretic and appeared
uncomfortable. Auscultation revealed a 3/6 systolic murmur best heard overlying the left sternal border. Bilateral lower extremity 1+ pitting edema was present. Serial ECGs revealed intermittent ST elevation in leads I and aVL. Interestingly, the ST elevation occurred while the patient was seated or standing and resolved when she was supine. These episodes were also associated with hypotension. Pertinent laboratory examination findings included a troponin I of 9.48 ng/ml and troponin T of 1.160 ng/ml. The patient underwent emergent coronary angiography but no culprit lesion was identified. During the procedure, she developed cardiogenic shock requiring intra-aortic balloon pump insertion and vasopressor therapy. Once she was transferred to the coronary care unit, a transthoracic echocardiogram was done and revealed a large echolucent mass anterior to the right ventricle which compressed the right ventricular outflow tract. Subsequently, a computed tomography (CT) of the chest with intravenous iodinated contrast was obtained to better characterize the mass. It showed a focal defect in the anterior wall of the left ventricle with linear extravasation of contrast and a contained hematoma within the pericardium. In anticipation of possible surgical intervention, a cardiac magnetic resonance image (MRI) was done, which showed a pericardial hematoma of 3.2 cm x 6.1 cm x 5.5 cm (Figure 1), secondary to left ventricular rupture. Upon further review of the imaging, left ventricular wall thinning and hypokinesis of the anteroseptal segments were noted, presumed to be secondary to a chronic infarct of the left anterior descending artery territory. Right heart catheterization and left ventriculography were performed, confirming free wall rupture with a contained pseudo-aneurysm (Figure 2). After discussing the case with the patient’s family, a decision was made to pursue conservative management. The patient recovered successfully and remained hemodynamically stable after discontinuation of mechanical and pharmacologic support.
Figure 1. MRI showing ventricular pseudoaneurysm. Panel A showing the pseudoaneurysm in the sagittal plane. Panel B showing the pseudoaneurysm in the coronal plane.

Figure 2. Extravasation of contrast through the Left Ventricular wall (Arrow).
Discussion

Prior literature suggests that approximately 55% of VPAs are secondary to MI, 33% related to cardiac surgery, 18% to trauma and 5% to infection. Only 20% of these cases present with ST segment elevation [5], which may complicate the diagnostic process. The mortality of ventricular rupture without emergent surgical repair has been reported to be as high as 90% [6].

Echocardiogram is a widely available and sensitive diagnostic tool which can identify pericardial effusion, the most common finding in patients with left ventricular wall rupture [7,8]. CT, MRI and ventriculography are other useful tools to diagnose VPAs and measure left ventricular volumes [9,10]. In the acute setting, it is imperative to diagnose VPAs promptly due to the extremely high mortality that can result when no intervention takes place [2].

Our patient presented with ST elevation and elevated cardiac enzymes. Coronary angiography did not reveal coronary artery occlusion. After careful review of the echocardiogram, and considering the patient was having ST elevation on ECG that was reproducibly related to posture, we hypothesize that there was intermittent external compression of the left anterior descending artery (LAD). When the patient was sitting or standing, the pseudoaneurysm compressed the LAD resulting in anginal symptoms and ST segment elevation in leads I and aVL. This coronary artery compression was not observed in the CT or MRI owing to the fact the patient was supine during image acquisition.

Regarding the cause of the ventricular rupture, we postulate that wire perforation may have occurred during the left ventriculogram done 2 months prior to presentation. However, we believe our patient’s pseudoaneurysm developed as a consequence of a subclinical transmural myocardial infarction that occurred sometime between the last percutaneous coronary intervention and this presentation. If the VPA had been a
consequence of the prior ventriculogram, it would have formed much earlier. We also hypothesize that the patient survived without surgical intervention because the VPA occurred in the setting of a poorly-compliant scarred pericardium as a consequence of prior sternotomy during her CABG, resulting in a small to moderate hematoma that prevented further blood loss.

References

Call for awareness of West Nile virus infection.

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Abstract

Background: West Nile virus is endemic in the United States of America causing West Nile fever and West Nile Neuroinvasive disease (WNND) including meningitis, encephalitis or acute asymmetric flaccid paralysis during the months of July and September. Based on the initial non specific symptoms it can be difficult to distinguish West Nile Neuroinvasive disease from bacterial meningitis.

Methods: We present a short case series of 3 cases which presented at the Lyndon B Johnson and Memorial Herman Hospital and were diagnosed with West Nile infection. Patient’s medical records were reviewed to obtain hospital course, laboratory and imaging data.

Results: Three patients presented to 2 different hospitals in Houston, Texas from July to September in 2014 with fever and confusion. Meningitis was suspected as initial diagnosis in these patients. CSF stain/culture, HSV PCR, VDRL, Enterovirus and blood cultures were negative. All 3 patients received empiric broad spectrum antibiotics including Vancomycin, Ceftriaxone, and Ampicillin for presumed bacterial meningitis. In all cases CSF serologies subsequently were positive for West Nile virus.

Conclusion: Antibiotics do not play any role in management of WNND and should only be administered with suspected bacterial meningitis (eg, positive Gram stain, WBC >1000/microL, glucose <40 mg/dL). Patient with viral meningitis need supportive care and reassurance. Adverse events are only seen in patients who are immunosuppressed with neurological deficits.
Introduction

West Nile virus is a member of Japanese encephalitis viral antigen complex. It was discovered in New York City in 1999 and since then it has become endemic in USA and Canada especially in the months of July to September. Most infections are caused by transmission of virus after mosquito bites but can also be transmitted via blood product transfusions and organ transplants.

About 20% patients with WNV infections develop a fever with other symptoms such as headache, body aches, joint pains, vomiting, diarrhea, or rash. Most people with this type of West Nile virus disease recover completely, but fatigue and weakness can last for weeks or months. Less than 1% of people who are infected with WNND syndrome with a serious neurologic illness such as encephalitis or meningitis, and acute flaccid paralysis (CDC).

Clinical presentation of WNND is different from bacterial cerebrospinal fluid infections but sometimes it can be challenging to distinguish between them. We present a short case series of patients with West Nile infection which were mistreated as bacterial meningitis.

The primary objective of this study is to increase awareness of West Nile infection amongst primary care physicians especially in patients presenting with fever and confusion in the months of June to September.

Case Series

Case 1

A 63 year old man with no past medical history presented with confusion and subjective fever. Fifteen days prior to admission, he experienced worsening fatigue, nausea, and bilateral frontal headaches. He denied any photophobia, phonophobia, cough, urinary symptoms, sore throat, or pain. Due to a 103.2 °F fever, leukocytosis of 12 k/uL, and disorientation, he underwent a lumbar puncture. Cerebral spinal fluid (CSF) analysis demonstrated opening pressure of 16 cm H2O, glucose 66 mg/dL, protein 41.6 mg/dL, 7
WBC/uL with 60% neutrophils, 28% lymphocytes and 12% monocytes. The patient was started on Vancomycin, Ceftriaxone, and Ampicillin for presumed bacterial meningitis. CSF stain/culture, HSV PCR and VDRL were negative. CXR showed no acute abnormalities. Blood cultures did not grow any organisms. The primary team decided to hold antibiotic treatment on admission to the medical floor and monitor the patient carefully. The patient clinically improved while remaining afebrile. He was discharged after 3 days of observation. Five days post discharge CSF serologies were positive for west nile virus. Patient was diagnosed with West Nile viral meningoencephalitis.

Case 2

A 42 year old man with history of migraines presented with severe headache, myalgias, fatigue and fever since 5 days prior to admission. At the onset of symptoms he went to a local clinic and was prescribed amoxicillin. He took it for 5 doses but his symptoms did not improve and he decided to come to the emergency department (ED) for further evaluation. The patient was afebrile on arrival. He denied any history of recent travel or sick contacts. On physical exam, the patient was alert and oriented times three. Initial CBC and CMP were normal. In the ED, lumbar puncture was performed which showed 70 WBC (63% neutrophil, 30% lymphocytes), 77 glucose, and 57 protein. He was empirically started on acyclovir, ceftriaxone, and vancomycin for meningitis. Acyclovir was discontinued by the primary team due to a low suspicion of Herpes infection however other antibiotics were given intravenously for 7 days. His symptoms continued to improve over the next 7 days. At the time of discharge, he had no fever, headaches, or meningeal signs and was back to his usual state of health. Final blood culture, CSF bacteria stain/culture and HSV PCR and enterovirus PCR came back negative. Two days after discharge CSF serologies came back positive for West Nile Virus. The patient was diagnosed with West Nile meningitis.
Case 3

A 56 year old man with past medical history of hypertension, dyslipidemia, and coronary artery disease presented after being found unresponsive. On exam, he was febrile with a temperature of 104 °F and non-responsive to verbal stimuli. He was paralyzed on his right arm and bilateral lower extremities. Additionally, his left arm had decreased muscle strength. Laboratory studies were notable for 17.7 k/uL leukocytosis. CSF analysis revealed 13 RBC/uL, 28 WBC/uL with 45% neutrophils and 41% lymphocytes, 70 mg/dL glucose, and 76 mg/dL protein. Gram stain, culture, and syphilis testing of CSF were negative. Viral studies of CSF were not ordered. The patient was started on vancomycin, cefepime, ampicillin, and acyclovir for presumed bacterial meningitis. His hospital course was complicated by sepsis due to hospital acquired Acinetobacter pneumonia and bacteremia with chronic respiratory failure, kidney injury requiring renal replacement therapy, sacral decubitus ulcers and right gluteal abscess complicated with osteomyelitis. Due to worsening of the patient’s clinical condition with little improvement in mental status, repeat lumbar puncture was performed. Serology for west nile virus was positive 28 days after initial presentation. The patient was eventually stabilized after being treated for pneumonia, bacteremia, and osteomyelitis. Patient was initiated on hemodialysis and is awaiting placement for a long term acute care facility.

Discussion

West Nile neuroinvasive disease is an endemic disease in United States with over 16000 cases reported since 1999. Clinical presentation is different from bacterial cerebrospinal fluid infections but sometimes can be challenging to distinguish between them. Most people (70-80%) who become infected with West Nile virus do not develop any symptoms. Cases are more frequently seen in the months of July to September with an incubation period of 2 weeks. In acute presentations patients tend to have abrupt onset of
low grade fever, fatigue, headaches with varying severities of mental status changes ranging from mild headaches to severe coma. One study has shown that clinical outcome depends at age, gender and specific neurological deficits at onset [2].

The diagnosis is made by detection of IgM antibody in serum or CSF using enzyme linked immunosorbent assay or in some cases with detection of viral RNA by nucleic acid amplification tests such as polymerase chain reaction (PCR). A Canadian study with 276 symptomatic cases of West Nile virus showed the yield of the diagnostic testing was low. Of 191 were tested by both serology and PCR, 86 (45.0%), 111 (58.1%), and 180 (94.2%) were detected by PCR, serology, and combined PCR and serology, respectively [3]. CSF studies can show picture of early bacterial infection with normal or low glucose, elevated protein and moderate pleocytosis (<500 cells/microliter) with lymphocytic predominance. In case of WNND CSF WBC counts are usually around or less than 230 cells/mm3 as seen in all 3 of our cases. However, neutrophilic predominance as high as 50% of cell count can be seen in these cases at the time of early presentation in 35-40% of patients [4]. In all the three cases presented in this series there was neutrophil predominance which might be the reason the patients were treated with antibiotics for suspected bacterial meningitis.

Due to low yield of the CSF and serum testing repeat lumbar should be performed if there is high suspicion or lack of clinical improvement in the patient after 10 days. This was evident in the case 3 of our series. On imaging, which is seldom required for diagnosis, CT scan of the brain is often normal acutely and MRI brain shows diffusion weighted or T2 weighted imaging in the regions of basal ganglia, thalami, caudate nuclei, brainstem, and spinal cord [5]. In the case series presented above the diagnosis was made without imaging. It is important to obtain a good travel and exposure history in all the patients to exclude other viral illness like dengue, herpes simplex, varicella zoster, St Louis encephalitis and
enterovirus. Bacterial meningitis and tick borne illnesses such as lyme disease and rocky mountain spotted fever are also included in the differential diagnosis.

There is no proven treatment for WNND. Supportive care including intravenous fluids, pain medications and nursing care are mainstay for treatment. Antibiotics do not play any role in management of WNND and should only be administered with suspected bacterial meningitis (eg, positive Gram stain, WBC count >1000/μL, glucose concentration <40 mg/dL [2.2 mmol/L]). Role of Interferon, Ribavarin and IVIG are unclear and there is no evidence by randomized control trial. In our cases patients were mistriaged on admission and given unnecessary antibiotics for a clinical picture of bacterial meningitis. While treating these patients one should know that serious adverse outcomes are only seen in immunosuppressed patients who develop WNND with severe muscle weakness or deterioration in the level of consciousness. Thus if bacterial meningitis is ruled out based on initial CSF testing then empiric treatment with broad spectrum antibiotics should be avoided.

Conclusion

Despite a very different clinical presentation physicians often treat viral encephalitis with multiple broad spectrum antibiotics. Several viruses including West Nile virus, St. Louis encephalitis virus, Eastern equine encephalitis virus, California encephalitis virus, and Western equine encephalitis virus may present with similar symptoms. The use of unnecessary antibiotics often leads to increased cost, anxiety and possible toxic effects. All of the above mentioned patients needed supportive care and reassurance at presentation rather than prompt antimicrobials. It is important to recognize that West Nile virus presents in a different way than bacterial meningitis. Obtaining a thorough history, assessment of exposures, time of presentation (July to September) and CSF WBC count are important factors which can be used to distinguish the cases from bacterial meningitis.
References

1. Centers for Disease Control and Prevention West Nile virus. 


Increasing Safety of NSAID Prescribing to Osteoarthritis Patients.

Sarah Kazzaz MD, Anju Mohan MD, Manoj Thangam MD, Jamise Crooms MD, Nidal Ganim MD, Jonas Gunawan MD, Pooja Gidwani MD, Raynumdo A Quintana Quezada MD, Madelyn Rosenthal MD, Yi Chun Yeh MD.

Abstract

Osteoarthritis is commonly encountered in the primary care setting. Nonsteroidal anti-inflammatory drugs (NSAIDs) are frequently used for pain control but patients are usually unaware of the adverse effects of these medications. The study team conducted a retrospective analysis for a baseline data, followed by intervention phase aimed to increase counseling for patients on NSAIDs about the medication side effects in primary care clinics. During baseline period 54% (6/11) patient with OA were taking NSAIDs, of these 17% (1/6) had a contraindication and 17% (1/6) received counseling. During the pilot period, 95% (20/21) patients with OA were on NSAIDs. From these, 35% (7/20) had a contraindication, and 57% (4/7) of those with contraindication received counseling.

Introduction

The average annual prevalence of osteoarthritis (OA) in the ambulatory health care system in the United States is estimated to be 3.8%, which amounts to 7.7 million patients with OA.\(^1\)\(^2\) According to the American college of Rheumatology guidelines, the initial pharmacologic for OA includes NSAIDS, acetaminophen, tramadol, and intraarticular steroids.\(^1\)\(^3\)

Non-steroidal anti-inflammatory drugs (NSAIDs) are frequently used due to ease of availability over-the-counter, perceived safety profile, and relatively low cost. When properly prescribed, NSAIDs can provide an effective and safe treatment for OA. However, they must be used with caution as they are associated with numerous adverse effects and are contraindicated in certain patient populations (See Table 1).
Table 1: Potential adverse effects.\textsuperscript{2,3,4}

<table>
<thead>
<tr>
<th>Organ System</th>
<th>Adverse Effects</th>
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<tr>
<td>Gastrointestinal (GI)</td>
<td>GI bleed, Dyspepsia, Peptic Ulcer Disease</td>
</tr>
<tr>
<td>Renal</td>
<td>Acute Renal Failure, Uncontrolled Hypertension</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Increased Risk of Myocardial Infarction</td>
</tr>
<tr>
<td>Hematological</td>
<td>Antiplatelet Effects</td>
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</tbody>
</table>

The American College of Rheumatology (ACR) recommendations state that health care providers should not use oral NSAIDS in patients with contraindications to these agents and should be aware of the warnings and precautions associated with the use of these agents.\textsuperscript{3} Recommendations for specific populations can be found in Table 2.

Table 2: Recommendations for osteoarthritis therapy in specific patient populations.\textsuperscript{5}

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Recommended Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Person’s older than 75 yrs of age</td>
<td>Topical NSAIDs instead of oral NSAIDs</td>
</tr>
<tr>
<td>GI ulcer with no GI bleed in over 1 year</td>
<td>COX-2 selective NSAID or NSAID + PPI</td>
</tr>
<tr>
<td>GI ulcer with GI bleed within 1 year</td>
<td>COX-2 selective NSAID + PPI</td>
</tr>
<tr>
<td>Chronic kidney disease stage IV or V</td>
<td>Strongly suggest NSAID avoidance</td>
</tr>
</tbody>
</table>

Ensuring appropriate NSAID prescribing practices is an important aspect of maintaining the health of patients with OA. Therefore, we developed a quality improvement initiative to evaluate current prescribing tendencies of NSAIDs for OA associated pain in one of our ambulatory clinics.
Objectives

• To decrease inappropriate use of NSAIDs in OA patients with relative contraindications.

• To increase counseling and documentation regarding NSAIDs through the use of a text template in clinic progress note.

Methodology

This quality improvement study was undertaken by internal medicine residents from the University of Texas in Houston working in 2 outpatient clinics. Patients with a history of OA were identified by residents and faculty during ambulatory clinic. Information regarding NSAID use and the coexistence of relative contraindications was gathered between November 2015 to January 2016. We defined relative contraindications to include myocardial infarction, percutaneous intervention, coronary artery bypass grafting, congestive heart failure, peripheral artery disease, hypertension, history of upper GI bleeding, chronic kidney disease with a glomerular filtration rate of less than 60 for at least 12 months, and use of anticoagulation therapy. We also noted whether patients were taking NSAIDs appropriately: correct dosing, ingestion with meals, and not concurrent with proton pump inhibitors. Lastly, residents determined whether appropriate counseling for NSAID use was provided and documented.

We developed an intervention, which aimed to increase counseling concerning contraindications to NSAID use via text template in the clinic progress note (See Box 1).
Box 1: Clinic template for counseling regarding NSAID use in OA.

“I certify that I have counseled the patient on the risks of their NSAID medication usage based on the pertinent positive statements regarding the patient’s past medical history, as above. These adverse risks include progression of HTN as well as increased risk of coronary artery disease, MI, development and progression of CKD as well as increased risk of peptic ulcer disease and GI bleeding.”

In the post intervention phase, we reviewed records from February to April 2016 to document compliance with the use of our text template. We noted if residents have reevaluated NSAID use in patients diagnosed OA and provided counseling concerning contraindications. Assessment of counseling and reevaluation of NSAID prescriptions was based on documentation in patient charts.

Results
During the baseline period (November 2015), 54% (6/11) of patients with OA seen were taking NSAIDs. A total of 17% (1/6) of patients had a contraindication to NSAID use but had received counseling. Another 17% (1/6) of patients had a contraindication but had not received counseling.

During the intervention phase, 95% (20/21) patients with OA were taking an NSAID. Of these, 35% (7/20) had a contraindication, and 57% of those with a contraindication (4/7) received counseling which was documented using our text template. Of note, all of the patients that received counseling decided to continue NSAID use.

Discussion

Participation in this project raised awareness among residents to counsel patients regarding NSAID contraindications. During the pilot study, we counseled more than half of patients using NSAIDs despite any relative contraindication (4/7). However, our limited baseline data makes it difficult to determine if our intervention actually increased counseling in our clinics. Since we only had 2 patients in the baseline group with a relative contraindication to NSAIDs, potential pre-intervention and post-intervention percentages may not be representative of any improvement. The limited study size makes useful comparisons difficult.

Future projects ought to have a longer study period to improve patient size. Additionally, our template was utilized inconsistently. The etiology for reduced template utilization was likely the extra time and effort required to upload and populate the template. In the future, electronic automatization of template loading and populating may help improve template use.

It is interesting to note that all patients in our study who received counseling decided to continue NSAID therapy. These individuals desired to understand potential
complications associated with NSAID use but ultimately determined pain control to be more important.

References


Iron Deficiency Anemia and Thrombocytosis: The Search For A Link.

Nathaniel P. Avila MD, Emma L. Dishner MD, Gabriel M. Aisenberg MD.

Abstract

Background: The association of iron deficiency anemia (IDA) and reactive thrombocytosis (RT) is frequently described, but the causation between IDA and RT is still unclear.

Aims: To identify a causative link between RT and IDA.

Methods: We retrospectively reviewed the charts of patients with IDA and tabulated their demographic, clinical, and laboratory data between March 2011 and March 2012. Patients with RT and without RT were compared.

RESULTS: Among 194 patients with IDA 70 had RT (group T) and 124 did not have RT (group NT). Thrombocytosis was more common in women than in men. Patients in group T had significantly higher total leukocyte and lymphocyte counts than those in group NT, but those values were within normal values. In our series iron, ferritin or transferrin levels, creatinine, hemoglobin, reticulocytes, mean corpuscular value, and hemoglobin A1c were similar in both groups. There was no difference in the relative prevalence of chronic inflammatory disease.

Conclusion: The link between IDA and RT remains elusive. Given the complexity involved in the development of both IDA and RT, it seems plausible that the mechanism that links one to the other will be discovered through laboratory-based rather than clinical data.

Key words: iron deficiency anemia, thrombocytosis, reactive thrombocytosis, ferritin, anemia.
Introduction

Thrombocytosis is defined as an elevated platelet count above the upper normal limit of 400,000/μl. It can result from a clonal bone marrow proliferation (defined then as primary), or can be reactive (secondary thrombocytosis). Iron deficiency anemia (IDA) is frequently listed as a cause of reactive thrombocytosis (RT). Though the gold standard for diagnosis of iron deficiency anemia (IDA) is the absence of iron stores in a bone marrow examination, the associated cost and invasiveness makes the test less desirable than surrogate examinations. Among available tests, the levels of transferrin and its iron saturation lose sensitivity when anemia is mild, and are of low specificity owing to its diurnal variation and level changes in inflammatory states. On the contrary, low levels of ferritin have no other explanation than iron deficiency, making it a reliable marker of such condition. Previous research has found useful markers to discriminate between clonal versus reactive thrombocytosis, but the underlying mechanisms leading to RT in IDA remain elusive. Our study aims to find a link between these conditions.

Methods

The study was undertaken at Lyndon B. Johnson Hospital (LBJH), a tertiary care center in Houston, Texas, after obtaining Institutional Review Board approval; patient consent requirements were waived. Our hospital admits about 14,000 patients per year.

From March 2011 to March 2012, we collected information from the electronic records of patients older than 18 years with ferritin levels lower than normal (10-291 ng/ml). We defined as current episode the one in which the patient had a low serum ferritin level.

We used a standardized questionnaire to retrieve information from the medical records. This included demographic data (age and sex), clinical data (known history of rheumatic disease or active cancer), and laboratory data (serum iron, transferrin,
creatinine, hemoglobin, mean corpuscular volume, platelet count, serum creatinine, white blood cell count and its differential, reticulocyte count, sedimentation rate). The cause of IDA was also extracted from the medical records: we classified these data in broad categories first (example: genital bleed, upper gastrointestinal bleed), and then in more specific ones (example: fibroids, or gastric ulcer).

We investigated the number of previous episodes of thrombocytosis while the patient had microcytic anemia, as well as thrombocytosis prior to the recorded anemia, and calculated the duration of both the anemia and thrombocytosis.

Statistics

Categorical variables were analyzed using the Fisher exact test, and discrete variables were analyzed using the Student t test for unpaired samples. A two-sided P < 0.05 was considered indicative of statistical significance. We calculated a correlation coefficient (r) between the highest platelet level measured during the episode in which the ferritin level was measured, and that serum ferritin level.

Results

One hundred and ninety four patients met inclusion criteria. Table 1 describes their baseline characteristics (See Table 1). Their median ± standard deviation age was 45±13 years old. The female/male ratio was 4.24/1 (157 women and 37 men). One hundred and seventeen (60%) patients were seen in the ED/Hospital, and seventy-seven (40%) patients were seen in the outpatient clinics.

The cause of the IDA was unknown or undisclosed for the majority of patients (84, 43%), and was attributed to genital bleed in 55 (28%) patients, lower gastrointestinal bleed in 25 (13%) patients, and upper gastrointestinal bleed in 23 (12%) patients. Seven patients (4%) had miscellaneous causes. Overall the most frequent specific cause in our
patient population was bleeding fibroids (17.9% patients). No specific cause was associated statistically with a higher probability of thrombocytosis.

Forty-eight patients had thrombocytosis on the same day (±2 days) of the ferritin result. When counting from the origin of recorded microcytic anemia, 66 patients had thrombocytosis recorded in 348 occasions (5 times/patient). Many of the 194 patients had microcytic anemia for an average of 1073 ± 1147 days prior to the current episode. Counting previous and current episodes, we found thrombocytosis in 78 patients. Of these, 8 were excluded since they had thrombocytosis before having anemia. Then, we selected 70 patients with thrombocytosis (36% of patients with low ferritin) (GROUP T) and 124 patients without thrombocytosis (GROUP NT).

Table 1-Baseline characteristics (n=194)

<table>
<thead>
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<th>Characteristics</th>
<th>Value</th>
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<tr>
<td>Age</td>
<td>45±13</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>37/157</td>
</tr>
<tr>
<td>Ferritin</td>
<td>4.7±1.96  range 0.5-7.9 ng/ml</td>
</tr>
<tr>
<td>Iron</td>
<td>25±25 μg/dl</td>
</tr>
<tr>
<td>TIBC</td>
<td>449±104 μg/dl</td>
</tr>
<tr>
<td>Hgb</td>
<td>8.3±2 g/dL</td>
</tr>
<tr>
<td>MCV</td>
<td>70.7±10 fl</td>
</tr>
<tr>
<td>Platelets</td>
<td>312,000 ± per μl</td>
</tr>
<tr>
<td></td>
<td>135,000</td>
</tr>
<tr>
<td>WBC</td>
<td>7,110 ± 2,570 per μl</td>
</tr>
<tr>
<td>ANC</td>
<td>5,090 ± 6,610 per μl</td>
</tr>
<tr>
<td>ALC</td>
<td>2,100 ± 2,000 per μl</td>
</tr>
<tr>
<td>AMC</td>
<td>500 ± 200 per μl</td>
</tr>
<tr>
<td>AEoC</td>
<td>190 ± 240 per μl</td>
</tr>
<tr>
<td>ABC</td>
<td>56 ± 76 per μl</td>
</tr>
<tr>
<td>Retic count †</td>
<td>2.1 ± 1 per μl</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.9 ± 0.8 mg/dL</td>
</tr>
<tr>
<td>Chronic inflam. disease ‡</td>
<td>30</td>
</tr>
</tbody>
</table>

ANC= absolute neutrophil count; ALC: absolute lymphocyte count; AMC: absolute monocyte count; AEoC: absolute eosinophil count; ABC: absolute basophil count.

NOTES:
†: Reticulocyte count: 96 entries
‡: Chronic inflammatory disease: active cancer or rheumatic disease
Table 2 compares those with and without thrombocytosis. Thrombocytosis was more common in women than in men (See Table 2). The total number of leukocytes or the number of lymphocytes was significantly higher in the GROUP T, but in both cases the values were within normal range. Within the GROUP T there were 4 patients (6%) who had thrombocytopenia at the moment of inclusion (2 of those 4 had pancytopenia), whereas within the GROUP NT there were 20 patients (16%) with thrombocytopenia on inclusion (10 of those 20 had pancytopenia) ($P=0.04$). Only 4 patients in GROUP T had the sedimentation rate measured (always elevated), while 11 had it measured in GROUP NT (elevated in 9 of them). These few patients are insufficient to draw conclusions upon a potential association. Iron, transferrin or ferritin levels were not different between groups.

<table>
<thead>
<tr>
<th></th>
<th>With thrombocytosis (n=70)</th>
<th>Without thrombocytosis (n=124)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>44 ± 12</td>
<td>46 ± 14</td>
<td>0.65</td>
</tr>
<tr>
<td>Sex (Male)</td>
<td>7 (10%)</td>
<td>30 (24%)</td>
<td><strong>0.02</strong></td>
</tr>
<tr>
<td>Platelet (median/range)</td>
<td>416,000 (76,000-872,000)</td>
<td>259,000 (16,000-396,000)</td>
<td></td>
</tr>
<tr>
<td>Ferritin</td>
<td>4.40 ± 2</td>
<td>4.86 ± 1.9</td>
<td>0.12</td>
</tr>
<tr>
<td>Iron</td>
<td>26 ± 31</td>
<td>24 ± 22</td>
<td>0.51</td>
</tr>
<tr>
<td>TIBC</td>
<td>451 ± 100</td>
<td>447 ± 106</td>
<td>0.80</td>
</tr>
<tr>
<td>Transferrin saturation</td>
<td>6 ± 0.07%</td>
<td>5 ± 0.05%</td>
<td>0.59</td>
</tr>
<tr>
<td>Hgb</td>
<td>8.0 ± 2.2</td>
<td>8.4 ± 2.2</td>
<td>0.48</td>
</tr>
<tr>
<td>MCV</td>
<td>69 ± 11</td>
<td>71 ± 10</td>
<td>0.20</td>
</tr>
<tr>
<td>WBC</td>
<td>8,000 ± 2,820</td>
<td>6,600 ± 2,300</td>
<td><strong>&lt;0.001</strong></td>
</tr>
<tr>
<td>ANC</td>
<td>6,100 ± 8,300</td>
<td>4,500 ± 5,400</td>
<td>0.10</td>
</tr>
<tr>
<td>ALC</td>
<td>2,100 ± 800</td>
<td>2,000 ± 2,400</td>
<td><strong>0.04</strong></td>
</tr>
<tr>
<td>AMC</td>
<td>520 ± 240</td>
<td>450 ± 230</td>
<td>0.07</td>
</tr>
<tr>
<td>AEoC</td>
<td>210 ± 250</td>
<td>170 ± 240</td>
<td>0.21</td>
</tr>
<tr>
<td>ABC</td>
<td>70 ± 10</td>
<td>50 ± 50</td>
<td>0.07</td>
</tr>
<tr>
<td>Retic count</td>
<td>2.25 ± 1.3</td>
<td>2.06 ± 0.8</td>
<td>0.41</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.00 ± 1.2</td>
<td>0.85 ± 0.4</td>
<td>0.19</td>
</tr>
<tr>
<td>Chronic inflammatory</td>
<td>10 (14%)</td>
<td>20 (16%)</td>
<td>0.84</td>
</tr>
</tbody>
</table>

disease
ANC= absolute neutrophil count;
ALC: absolute lymphocyte count;
AMC: absolute monocyte count;
AEoC: absolute eosinophil count;
ABC: absolute basophil count
Discussion

In this retrospective study we found no significant difference between patients with and without thrombocytosis, other than the fact that thrombocytosis was more common in women than in men. The difference in the number of leukocytes, or lymphocytes is significant, yet within normal values.

Several elements participate in the regulation of iron cycle: transferrin and its receptor in the bone marrow red cell precursors, erythropoietin, ferritin, ferroportin, hepcidin, C-reactive protein (CRP) and interleukin 6 (IL-6), the last two being non-specific serum markers of inflammation \(^{15}\). Interleukin 6 promotes the hepatic release of hepcidin, which prevents adequate delivery of iron to the bone marrow erythroblasts. Several studies have assigned IL-6 a role in the development of thrombocytosis mediated by synthesis and release of thrombopoietin (TPO) in inflammatory \(^{16}\) and postoperative states \(^{17}\). Moreover, a study showed temporal correlation between the peak of IL-6, CRP and TPO levels and a peak in platelet count in a series of pediatric patients with proven infection, though that study did not examine the concomitant presence of IDA \(^{18}\). Finding proof for the presence of an inflammatory state is a difficult task in absence of clinical markers of inflammation. Laboratory markers of inflammation lack both sensitivity and specificity. Furthermore, elevation of such markers is not necessarily associated with anemia, or with thrombocytosis \(^{19}\). Whether the platelet elevation reflects the response to IL-6 soluble receptors, as described in patients with essential thrombocytemia \(^{20}\), or polymorphism of the IL-6 gene \(^{21}\) rather than to the actual IL-6 levels requires further study. The retrospective nature of our study prevents us from clearly assessing the coexistence of inflammatory conditions; also, sedimentation rate, a non-specific inflammatory marker was requested in the minority of our patients.
The role of erythropoietin on the development of thrombocytosis remains debatable. Mortality was higher among patients on hemodialysis, who while being on erythropoietin without iron supplementation, had iron depletion leading to thrombocytosis. However, mortality was not observed more often among patients who had erythropoietin treatment for reasons different than advanced renal disease.

The mechanism by which IDA causes RT has also been studied in animal models. An iron deficiency diet caused thrombocytosis, with larger platelets and increased aggregation, not mediated by TPO or IL-6. Meanwhile, older reviews discard a direct role of iron deficiency upon the development of thrombocytosis simply because patients with IDA can present with RT, but also with normal or low platelet levels. Two studies found that women with low iron, low transferrin saturation and low ferritin had more commonly thrombocytosis, but we could not replicate these findings.

Regarding the response to iron therapy, a study showed that pediatric patients treated with oral iron and whose platelets were in average above 400,000/µl evolved with decreasing platelets level, whereas those treated with intramuscular iron and whose baseline platelet levels were normal at baseline evolved with reactive thrombocytosis within a week of treatment, creating even more confusion. Other researchers found a more consistent dose-response correction of RT in IDA.

The retrospective nature of this work limits the ability to find a causal link. A prospective approach may more accurately capture data on inflammatory or infectious conditions, rapidity of anemia development, and the etiology of IDA, once the latter is diagnosed.

In conclusion, the link between IDA and RT remains elusive. Some inflammatory markers are mostly, but not always increased in IDA making their pathogenic role less clear. Given the complexity and multiplicity of the determinants involved in the
development of both IDA and RT, it seems plausible that the mechanism that links one to
the other will be discovered through laboratory-based rather than clinical data, provided
that most variables can be controlled in that setting.

References

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