A Tick Bite Leading to a Red Meat Allergy

Case Report

Hannah Schradick, MD and Chris Cleveland, MD

Background

- Alpha-gal syndrome is an IgE mediated allergic reaction to galactose-1,3-galactose found in mammalian (red) meat particularly beef, pork and lamb after exposure to tick bites.
- Typical symptoms of alpha-gal syndrome include angioedema, urticaria, gastrointestinal symptoms, and anaphylaxis that occur 3-5 hours after ingestion of mammalian meat, which is unusual for anaphylaxis.
- Despite the delay, the anaphylactic reaction can still be life threatening making SP. The alpha-gal syndrome significant importance for clinicians to recognize alpha-gal syndrome and educate patients of the importance of avoiding mammalian meat and carrying an Epipen for possible exposures.
- Clinicians should also be aware of the cross reactions that can occur with various medications in those with alpha-gal syndrome.

Case Presentation

- A 51-year-old male from Northwest Minnesota with no known co-morbidities presented to the Allergy clinic for evaluation of the following symptoms: truncal hives, diaphoresis, itchy palms, and diarrhea a few hours after the ingestion of pork sausage. No others in the household experienced similar symptoms.
- A few days later, he ingested ribeye steak with recurrence of the same symptoms within two hours.
- He avoided beef and pork products for a few weeks with no symptoms during that time. He proceeded to try elk with immediate onset of tongue numbness, itchy mouth, vomiting, hives, and itchy palms that improved with diphenhydramine.
- He was evaluated at his local clinic and was prescribed an EpiPen. He and his family has researched his symptoms and the possible association with ingestion of mammalian meat leading to suspicion of alpha gal syndrome as he recalled a wood tick bite about six weeks prior to the onset of his first episode of symptoms.
- He had not had any recent travel.
- He presented to the Allergy clinic with desire to be evaluated for alpha-gal syndrome.
- Vital signs and physical exam were unremarkable.
- Blood work in Table 1 indicate positive IgE levels for galactose-alpha-1,3-galactose and beef, equivocal IgE levels for pork, and negative IgE levels of mild milk and skin prick testing of beef, milk, and pork was positive.

Table 1: IgE level results

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Galactose-1,3-galactose IgE</td>
<td>18.2 KU/L</td>
<td>&lt;0.70 KU/L</td>
</tr>
<tr>
<td>Beef IgE</td>
<td>3.07 KU/L</td>
<td>0.70-3.49 KU/L</td>
</tr>
<tr>
<td>Pork IgE</td>
<td>0.47 KU/L</td>
<td>0.35-0.69 KU/L</td>
</tr>
<tr>
<td>Milk IgE</td>
<td>&lt;0.35 KU/L</td>
<td>&lt;0.35 KU/L</td>
</tr>
</tbody>
</table>

Conclusions

- The purpose of this case report is to emphasize the significance of recognizing the symptoms of alpha-gal syndrome particularly the classic symptom of delayed onset anaphylaxis. Not only does management include avoidance of red meat but also certain medications.

References


Disclosures

- The authors have no disclosures.

Figure 1: Tick species distribution map

https://www.chucknoonan.com/tick-tips.ptnl

Figure 2: From left to right: American dog tick, Brown dog tick, and Lone star tick

https://www.cirrusimage.com

https://www.drchucknoonan.com/tick/tick-tips.pml

Discussion

The patient was diagnosed with alpha gal syndrome and provided the recommendations to avoid all red meat and carry an EpiPen. Gelatin can also cause allergic reaction and should be avoided. Despite positive prick test, milk IgE was negative and he continued to tolerate without any reactions.
- Not only should red meat be avoided, a variety of medications have been identified to cause anaphylaxis in those with alpha-gal syndrome. Cetuximab, used to treat colorectal cancer, also contains the oligosaccharide galactose-alpha-1,3-galactose. Wen et. al. presented a case report of a fatality after administration resulting in IgE-mediated anaphylaxis. Heparin posses a risk of reaction as it is porcine-derived. This has serious implications in cardiac surgeries as Hawkins et. al. reports upwards of 50% risk of reaction to heparin during cardiopulmonary bypass surgery. In addition, it has been reported that individuals with biopsychotic valves and alpha-gal syndrome have hastened break down of the valve.
- Endemic to the Southeast USA, the Lone star tick (Amblyomma americanum) was originally thought to be the primary vector for the disease, however, as noted in this case report and recent literature, other tick species are capable of transmission. The distribution of tick species in the United States is shown in Figure 1. The patient had not traveled to any areas endemic to the lone star tick and likely source was from either the American dog tick (Rhipicephalus sanguineus) or Brown dog tick (Rhipicephalus sanguineus). The tick species American dog tick, Brown dog tick, and Lone star tick are shown in Figure 2.
- The mechanism of transmission is hypothesized to occur via tick saliva containing alpha-gal antigen transferred to host leading to sensitization.
- It is possible for the alpha-gal IgE titers to diminish with time if no additional tick bites occur. Further research is necessary to determine acceptable timing and IgE levels to reintroduce red meat.
Introduction

Foreign body aspiration occurs in all age groups. Aspiration of an organic foreign body such as iron sulfate can cause significant bronchial destruction via oxidizing necrosis. When iron comes in close contact with the bronchial mucosa, it gets oxidized from ferrous ions into a ferric form which is highly toxic to the mucosa causing severe inflammation, mucosal damage, and fibrosis. We here report a case of iron pill aspiration resulting in mucosal necrosis within 48 hours of presentation.

Case Presentation

A 69-year-old with a history of COPD on oxygen, alcohol dependence, liver cirrhosis presented with progressive shortness of breath and productive cough with pink/yellow sputum production to the emergency room. A CT chest was obtained, which showed a radio dense foreign body in the distal end of the bronchus intermedius. The patient was hospitalized and started on antibiotics and systemic steroids. Pulmonary service was consulted after 48 hours, and he underwent bronchoscopy. The airway exam did not reveal the foreign body seen on the CT scan. Instead, it showed significant inflammation, granulation tissue, and necrosis of the bronchus intermedius consistent with foreign body reaction. He was continued on systemic steroids, and antibiotics and a repeat endoscopy was performed. The exam was remarkable for significant granulation tissue with moderate to a large amount of thick secretions causing partial obstruction of the right lower lobe. Cryoprobe was used to remove the secretions and granulation tissue and was sent for pathology showing extensive iron-stained degenerated tissue and iron (confirmed by properly controlled Prussian blue stain for iron), confirming the diagnosis of iron pill aspiration.

Discussion

Unlike most foreign bodies, which remain intact in the tracheobronchial tree, the iron pill disintegrates in the airway and cannot be detected on bronchoscopy. Iron sulfate causes caustic necrosis by local production of cytotoxic oxidants and free radicals. It causes necrosis leading to severe and fatal bleeding, and late complications include bronchial necrosis and stenosis. In our patient, the pill was seen on the CT scan of the chest that was later not seen on the bronchoscopy due to rapid dissolution of the iron pill resulting in necrosis and granulation tissue.

Conclusions

Significant inflammation and necrosis are common in the aspiration of organic foreign bodies such as iron pills due to rapid dissolution and oxidative injury. Prompt diagnosis and timely management should be initiated to prevent significant airway damage.

References

- Bronchial stenosis following Ferrous sulfate aspiration : Case report and literature review. Venci, NM, Watson, TJ
Introduction

Type V hyperlipoproteinemia (T5H) or polygenic chylomicronemia is a rare form of hyperlipoproteinemia that occurs in an estimated 0.018% of cases. T5H is characterized by very high serum triglycerides, high VLDL, and presence of chylomicrons due to mixed genetic and secondary factors. Past studies have shown that patients with T5H typically have predisposing genetic factors in addition to other causes such as diabetes mellitus, hypothyroidism, alcohol use, triglyceride-inducing drugs, hormone therapy, pregnancy, and other underlying disorders (i.e., SLE, etc.). We present a case of severe hypertriglyceridemia and chylomicronemia associated with severe alcohol use consistent with the diagnosis of secondary T5H treated with statin therapy and discontinuation of alcohol.

Case Description

A 49-year-old male presented initially with nausea, vomiting, and mild abdominal pain in the setting of heavy alcohol use. Patient endorsed drinking 12-15 alcoholic drinks (168-210 grams) per day for the last 15 months. He was diaphoretic, ill-appearing, and had mild tremors consistent with alcohol withdrawal. He had a personal history of hypertension and alcohol use disorder, but not type 2 diabetes. He denied any chest pain, shortness of breath, seizures, hallucinations, abnormal gait, vision changes, or new skin rashes or lesions. On admission, he was found to have hypertensive urgency of 177/118 with a pulse of 57. Physical exam was negative for scleral icterus, jaundice, abdominal tenderness, or back pain.

He was initially worked up for alcohol withdrawal and acute pancreatitis and was found to have lipemic blood during venuupuncture, which required several attempts at blood draws. Once an analyzable blood sample was obtained, lab work was significant for hyponatremia, anion gap metabolic acidosis. Lipase was within normal limits. Lipid panel showed severely elevated triglycerides of 4205 mg/dL, total cholesterol level of 581 mg/dL, and elevated LFTs. He was started on IV normal saline.

Additional studies were ordered to further assess his lipoprotein status. Lipoprotein studies were positive for significant elevations in chylomicron cholesterol 89 mg/dL, chylomicron triglycerides 1718 mg/dL, VLDL cholesterol 383 mg/dL, and VLDL triglycerides 1518 mg/dL consistent with the diagnosis of secondary T5H due to alcohol use. It was decided that even with slightly elevated liver function tests to start patient on low-dose atorvastatin 20 mg and fenofibrate 180 mg.

Clinical Course

During the course of his hospital stay, the patient’s clinical picture was not consistent with acute pancreatitis, and this was ruled out with normal lipase. Triglyceridermia improved to 2,240 mg/dL with discontinuation of alcohol use and statin therapy. Upon discharge the patient was referred to chemical dependence, nutrition, and endocrinology for outpatient follow-up. He was discharged on atorvastatin 20 mg and fenofibrate 160 mg once daily. He declined chemical dependency referral but acknowledged understanding of importance of refraining from alcohol use. He did not follow-through with the endocrinology follow-up and repeat lipid studies were not completed after hospital discharge. Patient did not have symptoms of acute coronary syndrome of cardiovascular disease, though may need close follow-up in the future with his history of severe hypertriglyceridemia.

Discussion

T5H is characterized by an increase in triglycerides (TG) of greater than 1000-2000 mg/dL, chylomicron particles, chylomicron remnants, VLDL, and VLVD remnants; and decrease in HDL. It is often associated with clinical features of abdominal pain, nausea, vomiting, pancreatitis, and rarely xanthonomas and lipemia retinalis. T5H is a polygenic condition due to genetic and secondary cause including diabetes mellitus, alcohol use, and hormone therapy.

Alcohol is the second most common factor related to severe hypertriglyceridemia and chylomicronemia. Alcohol consumption is linearly associated with increase in TG levels in patients drinking more than 5 standard drinks per day—equivalent to 70g of ethanol daily. Alcohol stimulates VLDL secretion through enhanced assembly of VLDL combined with elevated hepatic delivery of free fatty acids as a result of enhanced adipose tissue lipolysis.

Symptoms of T5H can typically be controlled with dietary restriction of fats, simple sugars and alcohol intake or removal of offending agent. Historically fibrates, niacin, and statins are only minimally effective at treating very high hypertriglyceridemia. Lipoprotein lipase gene therapy is the most specific for an underlying gene disorder, but is still being studied for effectiveness and safety. In this case, the patient likely would not benefit from gene therapy since he responded well to the removal of offending agent, alcohol. In addition, a low dose statin and fenofibrate was used as an adjuvant therapy to lower lipids successfully even though the patient had moderate LFT elevation.

In patients with TG of 885 mg/dL or greater there is increased pancreatitis risk. In this case, the patient had nausea, vomiting, and mild abdominal pain with known alcohol use and TG over 4,000 mg/dL but pancreatitis was ruled out with serum lipase. Acute pancreatitis secondary to hypertriglyceridemia must not be missed and should be followed if patient continues to be symptomatic. Elevated TG contribute to increased cardiovascular disease (CVD) risk both directly and due to associated risk factors of obesity, metabolic syndrome, pro-inflammatory, and pro-thrombotic biomarkers, and diabetes. Therefore, it is also important to consider CVD risk assessment with high TG.

Lab Values

<table>
<thead>
<tr>
<th>Lipoprotein Studies</th>
<th>Value (mg/dL)</th>
<th>Ref Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol (total)</td>
<td>508 (H)</td>
<td>100-200</td>
</tr>
<tr>
<td>HDL</td>
<td>8 (L)</td>
<td>40-80</td>
</tr>
<tr>
<td>LDL</td>
<td>94 (H)</td>
<td>&lt;50</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>3431 (H)</td>
<td>50-150</td>
</tr>
<tr>
<td>Apolipoprotein</td>
<td>123 (H)</td>
<td>&lt;90 Desirable</td>
</tr>
<tr>
<td>VLDL cholesterol</td>
<td>383 (H)</td>
<td>&lt;30</td>
</tr>
<tr>
<td>VLDL triglycerides</td>
<td>1518 (H)</td>
<td>&lt;120</td>
</tr>
<tr>
<td>Beta VLDL Cholesterol</td>
<td>Not detected</td>
<td>&lt;15</td>
</tr>
<tr>
<td>Chylomicron cholesterol</td>
<td>89 (H)</td>
<td>Undetectable</td>
</tr>
<tr>
<td>Chylomicron triglycerides</td>
<td>1781 (H)</td>
<td>Undetectable</td>
</tr>
</tbody>
</table>

Table 1: Serum lipoprotein studies on admission

References

Case Description
A 51-year-old male presented to the emergency department (ED) with complaints of fever, chills, malaise, headache, seven-pound weight loss, and painful oropharyngeal ulcers of 10 days duration. He had previously received outpatient treatment for these symptoms with antibiotics. However, due to non-resolving symptoms, he returned to the ED with abdominal pain, nausea, vomiting, and diarrhea during the intervening period. Initial lab work including blood culture, stool multiplex polymerase chain reaction (PCR) assay, Cytomegalomavirus and Epstein Barr virus, West Nile virus, Lyme, and Q fever serologies, as well as Babesia and Anaplasma PCR were all negative. Imaging of the brain did not reveal any abscess or meningeal enhancement. A decision was made to perform cerebrospinal fluid (CSF) analysis which revealed findings consistent with a diagnosis of aseptic meningitis (Figure 1). He had significant outdoor exposure but did not recall any specific tick or mosquito bites. Powassan virus IgM specific antibody testing was ordered on the CSF, and it subsequently returned positive. Interestingly, his West Nile serology on CSF was also positive. Further testing with plaque reduction neutralization testing (PRNT) could not be performed due to insufficient CSF quantity. The patient was treated symptomatically and improved with supportive care. At his clinic follow up visit one-week later patient did not have any neurological sequelae.

<table>
<thead>
<tr>
<th>Laboratory Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clarity</td>
<td>Clear</td>
</tr>
<tr>
<td>Red Blood Cells (RBCs)</td>
<td>11 uL (normal &lt;0 uL)</td>
</tr>
<tr>
<td>Nucleated Cells</td>
<td>71 uL, lymphocyte predominance (normal 0-5 uL)</td>
</tr>
<tr>
<td>Glucose</td>
<td>53 mg/dL (normal 50-80 mg/dL)</td>
</tr>
<tr>
<td>Protein</td>
<td>60 mg/dL (normal 15-45 mg/dL)</td>
</tr>
</tbody>
</table>

Figure 1: The patient’s CSF results showing evidence of aseptic meningitis.

Discussion
Powassan virus is an emerging cause of tickborne encephalitis that should be considered in patients with febrile neurological illness in our region (Figure 2). *Ixodes cookei* and *scapularis* species serve as the primary vector. The incidence of Powassan virus has increased by 671% in the last 18 years thought in part to be due to the increasing geographic range of the *Ixodes scapularis* tick (Figure 3). Typically, patients have an initial prodrome 1-4 weeks after tick bite. Following that, some cases can have rapidly progressive neurological symptoms such as seizures, flaccid paralysis, nystagmus, and hemiplegia. Mortality can occur in up to 10% of cases, and long-term neurological sequelae occur in up to 50% of cases.

Diagnosis should be suspected in patients with CSF studies showing evidence of aseptic meningitis particularly in a patient with history of travel to endemic areas and hunting prairie dogs, who can be carriers of the virus. MRI imaging is generally nonspecific but can show features of encephalitis. A false positive result may be seen due to antigen cross reactivity with other flaviviruses, such as West Nile Virus and Saint Louise Encephalitis Virus. Confirmation of diagnosis is performed using plaque reduction neutralization testing (PRNT). Treatment is generally supportive. Due to the increasing incidence of Powassan virus in recent years, it is an important diagnosis to consider in cases of aseptic meningitis with negative results on multiplex assay of common pathogens that cause meningitis and encephalitis.

Conclusion
- Powassan virus is a rare yet emerging cause of tickborne encephalitis endemic to the Great Lakes Region of the US and Canada
- It is an important diagnosis to consider given its high mortality rate and propensity for long-term neurological sequelae
- CSF IgM antibody testing with PRNT testing should be performed if Powassan virus is suspected.

References
1. CDC. Powassan virus for healthcare providers. https://www.cdc.gov/powassan/healthcareproviders.html
Extracranial Manifestations of Giant Cell Arteritis: An Underreported Entity

Katrina Lybeck MD, Michael Seaman MD, Alessandra Spagnolia – University of North Dakota School of Medicine & Health Sciences

Introduction
- Giant cell arteritis (GCA) is a common large vessel vasculitis with affinity for the aortic arch and cranial branches
  - Classically affects the temporal artery causing jaw claudication, vision changes, and headache
  - Mesenteric ischemia is an increasingly recognized manifestation – mortality approaches 50-70%
- Persistent elevation in ESR (>90 mm/h) is a hallmark feature
- Mesenteric involvement can present as chronic vague abdominal pain or with acute bowel ischemia
- Limb claudication is a common presentation in GCA

Physical examination: significantly tender abdomen with rigidity
- Lactic acid: 6.9 – WBC 48.9 – Creatinine 2.14 – ALT 384 – AST 2.8
- Troponin 6.74 – STAT TTE: LVEF 25% with global hypokinesis
- Emergent OR (HD #1): Ischemic right colon, liver, and stomach
- Subsequently developed ATN and ischemic hepatitis
- Initiated stress dose steroids on HD #3 – Rheumatology consult
- Elected to pursue comfort care on HD #17 due to respiratory decompensation after extubation

Case Description
- 69-year-old male with a history of MGUS, tobacco use, and diabetes mellitus type 2 presented with acute onset abdominal pain – initially diagnosed with ACS at an outside facility
  - Treatment: heparin gtt, nitroglycerin, clopidogrel, aspirin

Discussion
- Due to extensive collaterals, pain often does not develop in mesenteric ischemia until involvement of >50% of 2/3 arteries
- Intraoperative findings typically show patchy necrosis within the distributed vessel territory +/- microperforations
- Tissue examination shows transmural necrosis with giant cell aggregations, granulomatous changes, and disruption of the internal elastic lamina
- Treatment consists of high dose corticosteroids and early surgical consultation

Conclusions
- Alternative etiologies for acute mesenteric ischemia should be considered in patients who lack traditional risk factors or fail to respond to initial treatment
- Mesenteric duplex ultrasonography, CTA abdomen/pelvis, or MRA abdomen/pelvis can be utilized to diagnosis vasculitis-associated mesenteric ischemia
- Early involvement of an interdisciplinary team can aid in diagnosis and management

References
**Background**

- Dermatomyositis is one of the autoimmune inflammatory myopathies that classically presents with characteristic rash and muscle weakness and affects the lung, skin, and skeletal muscles.
- Clinically amyopathic dermatomyositis (CADM) is a rare, often misdiagnosed, subset as it lacks the typical weakness.
- At least 5 myositis-specific autoantibodies (MSAs) have been identified in association with CADM – each with a distinct phenotype, especially regarding pattern and severity of pulmonary involvement.
- The anti-MDA-5+ subtype is associated with development of rapidly progressive interstitial lung disease (RP-ILD) that is aggressive and fatal – with a 1-year mortality rate up to 40%
- Testing for specific MSAs can take several weeks which can delay diagnosis and initiation of proper treatment leading to a search for alternative biomarkers and methods of diagnosis.

**Case Description**

- 55-year-old Spanish speaking female presented with 1 month of worsening rash and muscle aches.
- Physical examination: aphthous ulcers, papules of bilateral upper worsening rash and muscle.
- 5/5 strength in bilateral upper and lower extremities
- 3,402 AST (U/L), 1,029 ALT (U/L)
- Ferritin (ng/mL)

**Discussion**

- Positive ANA - empiric prednisone (40 mg BID) started on day #3
- Rheumatology clinic: rapid prednisone taper to 20 mg daily
- In 3 weeks, MSA testing confirmed anti-MDA-5+ CADM
- 6 days later: presented in acute hypoxic respiratory failure
- Started on IV methylprednisolone, IVIG, and intubated
- Rituximab was added due to refractory respiratory failure
- Continued deterioration - died within 8 weeks of symptom onset

**Conclusion**

- Anti-MDA-5 positivity is highly associated with RP-ILD & mortality
- Biomarkers (ferritin and/or anti-MDA-5 levels) should be obtained and used to monitor response to treatment
- Appropriate treatment includes high dose corticosteroids plus an immunosuppressant – exact regimen not yet identified
- Rituximab and/or IVIG can be used in refractory cases
- Successful prevention of RP-ILD is vital to reducing mortality

**References**


Kathrina Lybeck, MD – University of North Dakota School of Medicine and Health Sciences
Management of Inflammatory Myositis in a Patient with Massive Creatine Kinase Elevation
Andrew Horting, MD, MPH, PGY1
Vinita Vaidya, MBBS, PGY3

**Objective**
- Creatine kinase (CK) is an enzyme involved in energy storage and generation. It is present in great concentrations in the myofibrils and mitochondria of skeletal muscle cells.
- Elevated levels of CK in serum therefore typically represent damage to muscle.
- Severe elevations in CK can be associated with life-threatening acute kidney injury (AKI), electrolyte imbalances, and occasionally coagulopathies, and therefore require rapid intervention.
- Aggressive fluid administration and treatment of underlying causes are cornerstones of management.
- Bicarbonate is often administered to prevent renal failure, though its use is controversial.
- Hemodialysis does not play a role in prevention of kidney injury in this setting.
- AKI or electrolyte abnormalities are treated according to standard medical management.

**Introduction**

- 67-year-old woman who presented June 2020 with severe, sudden onset bilateral lower extremity weakness.
  - Also endorsed melena.
  - No fever, chills, chest pain or shortness of breath.
  - Experienced a 10-pound unintentional weight loss in one year.
- Previous diagnoses: Meningioma status post resection, COPD, atrial fibrillation, stroke following procedure, coronary artery disease, dyslipidemia on statin, peripheral artery disease.
- No current alcohol use. Former smoker.

**Initial Presentation**

- 6/5: CK 82,739 U/L (normal 30-170)
  - ALT: 140 U/L (0-55); AST: 114 U/L (0-35)
- Normal creatinine.
- Normal urine output
- Arterial blood gas: Compensated metabolic acidosis
- Urinalysis: consistent with myoglobinuria.
- Ultrasound of abdomen, chest x-ray, CT of chest with contrast did not reveal cause of elevated CK.
- Right ankle-brachial index was normal. Left showed severe arterial disease.
- MRI of upper legs: bilateral edema of musculature, consistent with polymyositis (Fig. 1)

**Clinical Course**

- Treated with aggressive fluid resuscitation.
- Given her risk of kidney failure, this patient was offered bicarbonate treatment but declined as it would require blood draws every three hours.
- Muscle biopsy revealed active myopathy with scattered necrotic fibers, consistent with immune-mediated necrotizing myopathy.
  - Autoimmune panel: only weakly-positive Anti-Ku and anti-SSA, consistent with polymyositis or dermatomyositis.
  - Started on prednisone.
- Found to be fluid overloaded. Given alternating fluids and furosemide.
  - After 13 days, CK improved to 4,000. Transaminases were nearly normalized. Never developed AKI.
- Following discharge, experienced near resolution of symptoms. Remains on low-dose steroid one year later.

**Bicarb for CK Elevation**

- Bicarbonate is frequently administered to patients with rhabdomyolysis and severe CK elevation to prevent AKI.
- Renal injury is caused by the heme protein myoglobin (not CK itself) through multiple mechanisms, including direct toxic effect on tubules and precipitation causing tubular obstruction.
- Bicarbonate is theorized to provide benefit by alkalinizing urine, therefore preventing precipitation of heme proteins.
- Administered if patient has normal calcium and is not alkalotic.
  - These must be frequently monitored
  - Titrated for urine pH of greater than 6.5.
  - Evidence for efficacy of bicarbonate to prevent AKI in this setting is limited and poor quality.
- CK elevation has been used as a predictor of AKI in patients with rhabdomyolysis, though it is not very specific.
  - Likelihood of AKI is also dependent on the underlying cause of muscle breakdown.

**Citations**

Idiopathic Hemophagocytic Lymphohistiocytosis with CNS Involvement in an Adult Male  
Anya de Leeuw, MD, PGY-1; Hallie Thompson, MD, PGY-1; and Vinita Vaidya, MD, PGY-3
University of North Dakota School of Medicine and Health Sciences and Sanford Health-Fargo

Introduction

- Hemophagocytic lymphohistiocytosis (HLH) is a relatively rare condition.
- Systemic inflammation, hypercytokinemia and multi organ failure
- HLH is most commonly diagnosed in it’s primary, or familial form, presenting in children within the first year of life.
- Secondary or acquired HLH is associated in patients with predisposing factors for activation such as malignancy, autoimmune disease, or infection.
- Criteria for diagnosis is taken from the Histiocyte Society HLH- 2004 diagnostic criteria

Case

- 51-year-old male
- No significant past medical history
- Several weeks of fever, night sweats, dyspnea, anorexia and >30lb weight loss
- One year previously the patient presented with similar symptoms which spontaneously resolved

Findings

- Physical exam: no abnormal findings
- During admission the patient was febrile, pancytopenic, with elevated creatinine, ferritin, INR, CRP, triglycerides and LDH (Figure 1)
- The ferritin continued rising throughout the admission, however the ESR remained normal
- Negative CMV, EBV, Toxoplasmosis & West Nile sputm, CSF and urine
- Abdominal ultrasound noted hepatosplenomegaly. The brain MRI showed abnormal signals in the frontal lobes bilaterally (Figure 2)
- Biopsy of the brain was negative for malignancy and infection. Liver biopsy confirmed hemophagocytosis. Bone marrow aspirate revealed hemophagocytic features with no overt signs of malignancy
- Soluble Interleukin-2 was elevated at 9700 U/mL. Genetic HLH screen was normal

Lab Results

<table>
<thead>
<tr>
<th>Laboratory Study</th>
<th>Patient’s Value</th>
<th>Normal Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>White blood cell count (WBC)</td>
<td>3.8 K/uL</td>
<td>4.0-11.0 K/uL</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>7.4 g/dL</td>
<td>13.5-17.5 g/dL</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.03 mg/dL</td>
<td>0.80-1.30 mg/dL</td>
</tr>
<tr>
<td>Ferritin</td>
<td>1,394 ng/mL</td>
<td>21-275 ng/mL</td>
</tr>
<tr>
<td>INR</td>
<td>1.6</td>
<td>2.0-3.5</td>
</tr>
<tr>
<td>CRP</td>
<td>100.4 mg/L</td>
<td>0.0-8.0 mg/L</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>156 mg/dL</td>
<td>50-150 mg/dL</td>
</tr>
<tr>
<td>LDH</td>
<td>1,085 U/L</td>
<td>125-145 U/L</td>
</tr>
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</table>

Figure 1: Laboratory studies on admission.

Figure 2: T2 FLAIR MRI brain showing right frontal lobe hyperintensity.

Diagnosis

Per HLH- 2004, five out of eight diagnostic criteria for HLH were met, hemophagocytosis, splenomegaly, elevated ferritin, triglycerides, and IL2. Consequently, a diagnosis of HLH of unknown etiology was confirmed.

Treatment & Outcome

The patient was treated with high dose dexamethasone and etoposide with an appropriate clinical response. Creatinine returned to baseline, and no significant organ dysfunction was observed. Due to improvement on MRI at one month IT methotrexate was not indicated.

Conclusions

- HLH is a rare condition causing overactivation of macrophages and T cells leading to life threatening inflammation and cytokine storm
- Diagnosis of HLH is confirmed with molecular diagnosis and/or at least five of eight criteria listed in the HLH 2004 Diagnostic Criteria
- Prompt treatment of HLH with dexamethasone and etoposide has been shown to reduce the mortality rate of the disease

References