A Tick Bite Leading to a Red Meat Allergy

Case Report

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Background

- Alpha-gal syndrome is an IgE mediated allergic reaction to galactose- alpha-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, uticaria, 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 the diagnosis of alpha gal syndrome of 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.
- Symptoms improved with Bismuth subsalicylate and diphenhydramine.
- 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 had 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
- Skin prick testing of beef, milk, and pork was positive.

Lab test	Result	Reference Range
Galactose-alpha-1,3-galactose IgE	18.2 kU/L	<0.70 kU/L
Beef IgE	3.07 kU/L	0.70-3.49 kU/L
Pork IgE	0.47 kU/L	0.35-0.69 kU/L
Milk IgE	<0.35 kU/L	<0.35 kU/L

Table 1: IgE level results

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

https://www.cirrusimage.com/Arachnid_American_dog_tick.htm
https://www.walthamservices.com/blog/tick-control/brown-dog-ticks/
https://entnemdept.ufl.edu/creatures/urban/medical/lone_star_tick.htm

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.

Figure 1: Tick species distribution map

https://www.drchucknoonan.com/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 skin 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 possess 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 bioprosthetic 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 (*Dermacentor variabilis*) 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

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Disclosures

- The authors have no disclosures.

A Case of Missing Pill-Iron Pill Aspiration

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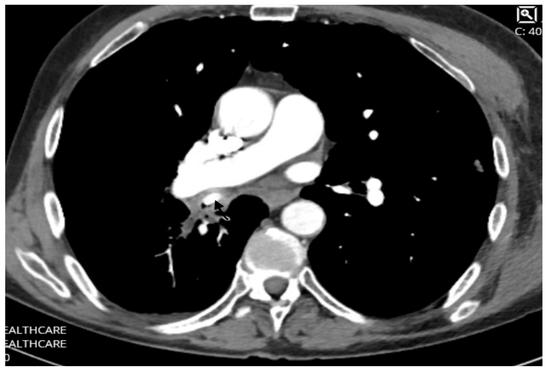
Introduction

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.

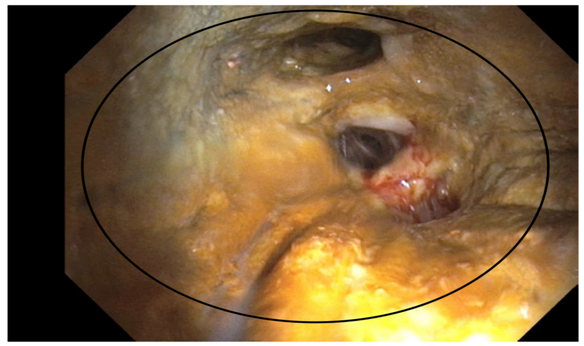
Case Presentation

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 mucosa 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 amounts 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.

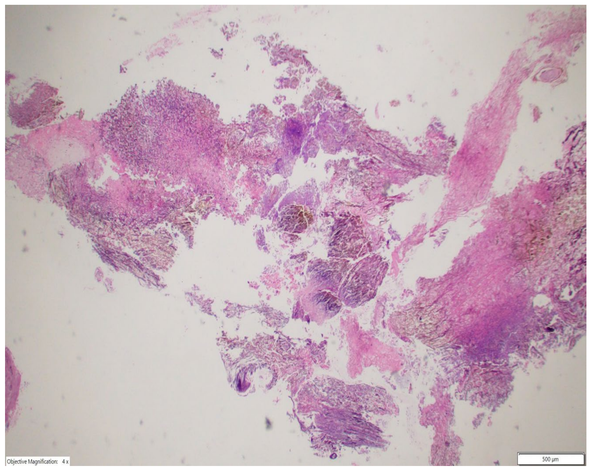
Images and slides



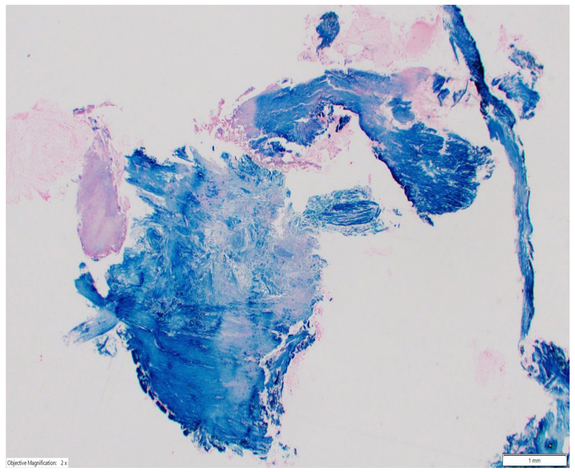
CT image showing the aspirated Iron pill



Bronchoscopy showing extensive inflammation, granulation tissue, and necrosis of the bronchus intermedius but not the Iron pill seen on CT



Endobronchial biopsy showing respiratory mucosa with extensive iron-stained degenerated tissue



Prussian blue-stain showed extensive staining for Iron

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.

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A Case of Alcohol-Induced Type V Hyperlipoproteinemia

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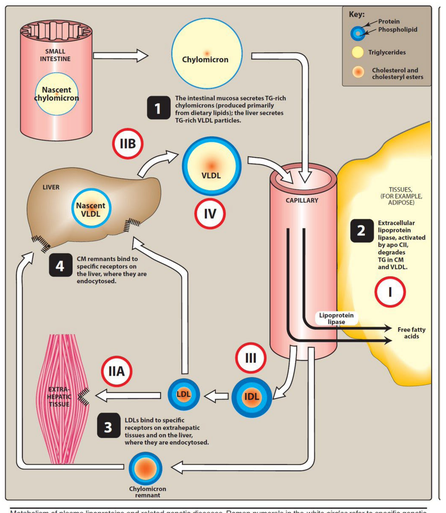
Introduction

Type V hyperlipoproteinemia (T5H) or polygenic chylomicronemia is a rare form of hyperlipoproteinemia that occurs in an estimated 0.018% of cases.[1,2] T5H is characterized by very high serum triglycerides, high VLDL, and presence of chylomicrons due to mixed genetic and secondary factors.[1] 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.).[1] 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.

Learning Objectives

- Discontinuation or treatment of offending factor(s)
- Use of fenofibrates and statins to reduce triglycerides and chylomicronemia
- Consider CVD risk assessment with the significant elevation of triglycerides



Metabolism of plasma lipoproteins and related genetic diseases. Roman numerals in the *white circles* refer to specific genetic types of hyperlipidemias summarized on the facing page. CM = chylomicron; TG = triglyceride; VLDL = very–low-density lipoprotein; LDL = low-density lipoprotein; IDL = intermediate-density lipoprotein; apo CII = apolipoprotein CII found in chylomicrons and VLDL.

Source : Lippincott Illustrated Reviews, Pharmacology - Whalen, Karen

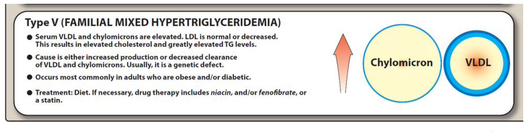


Figure 1: Lipid and lipoprotein metabolism; Type V hyperlipoproteinemia.[3]

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 venipuncture, which required several attempts at blood draws. Once an analyzable blood sample was obtained, lab work was significant for hyponatremia, severe hyperkalemia, and an 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 VDLD 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.

Lab Values

Lipoprotein Studies	Value	Ref Range
Cholesterol (total)	508 (H)	100-200 mg/dL
HDL	8 (L)	40-80 mg/dL
LDL Triglycerides	94 (H	<50 mg/dL
Triglycerides	3431 (H)	50-150 mg/dL
Apolipoprotein	123 (H)	<90 Desirable > 140 Very high
VLDL Triglycerides	383 (H)	<30 mg/dL
VDLD Triglycerides	1518 (H)	<120 mg/dL
Beta VLD Cholesterol	Not detected	<15 mg/L
Beta VLVD Triglycerides	Not detected	<15 mg/L
Chylomicron cholesterol	89 (H)	Undetectable
Chylomicron triglycerides	1781 (H)	Undetectable

Table 1: Serum lipoprotein studies on admission

Lipids	Value	Ref Range
Cholesterol	581 (H)	100-200 mg/dL
HDL	15 (L)	40-80 mg/dL
LDL	Indeterminate due to elevated TGs	
Triglycerides	4205 (H)	50-150 mg/dL
CMP		
Glucose	107	70-100 mg/dL
Na	129 (L)	135-145 meq/L
Potassium	8.9 (H)	3.5-5.3 meq/L
CO2	12 (LL)	20-29 meq/L
Anion Gap with K	28 (H)	6-20 meq/L
BUN	13	2-22 meq/L
Creatinine	1.18	0.80-1.3 mg/dL
Mg	2.0	18-2.4 mg/dL
Bilirubin (total)	1.2	0.2-1.2 mg/dL
Alkaline Phos	87	30-150 U/L
ALT	260 (H)	0-55 U/L
AST	475 (H)	0-35 U/L
CK	128	30-200 U/L
Total Protein	9.6 (H)	6.0-8.2 g/dL
Albumin	3.8	3.5-5.0 g/dL
Lipase	40	5-80 U/L
eGFR	66	>= 60 mL/min/1.73m^2

Table 2: Comprehensive metabolic panel and lipid panel on admission.

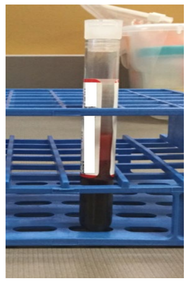


Figure 2: Photo of patient's lipemic blood sample.

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. Triglyceridemia improved to 2,240 mg/dL with discontinuation of alcohol use, and statin and fibrate therapy. Upon discharge the patient was referred to chemical dependance, 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 hyperlipoproteinemia.

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.[1] It is often associated with clinical features of abdominal pain, nausea, vomiting, pancreatitis, and rarely xanthomas and lipemia retinalis.[2] T5H is a polygenic condition due to genetic and secondary cause including diabetes mellitus, alcohol use, and hormone therapy.[1,4,5,6]

Alcohol is the second most common factor related to severe hypertriglyceridemia and chylomicronemia.[5] 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.[5] 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.[5]

Symptoms of T5H can typically be controlled with dietary restriction of fats, simple sugars and alcohol intake or removal of offending agent.[6] Historically fibrates, niacin, and statins are only minimally effective at treating very high hypertriglyceridemia.[1] Lipoprotein lipase gene therapy is the most specific for an underlying gene disorder, but is still being studied for effectiveness and safety.[1] 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 fenofibrates were 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.[5] In this case, the patient had nausea, vomiting, and mild abdominal pain with known alcohol use and TG over 4,000mg/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.[1] 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.[5] Therefore, it is also important to consider CVD risk assessment with high TG.[7]

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Powassan Virus: A Rare Yet Emerging Cause of Tickborne Encephalitis

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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, Cytomegalomirus 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.

Laboratory Test	Value
Clarity	Clear
Red Blood Cells (RBCs)	11 uL (normal <0 uL)
Nucleated Cells	71 uL, lymphocyte predominance (normal 0-5 uL)
Glucose	53 mg/dL (normal 50-80 mg/dL)
Protein	60 mg/dL (normal 15-45 mg/dL)

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

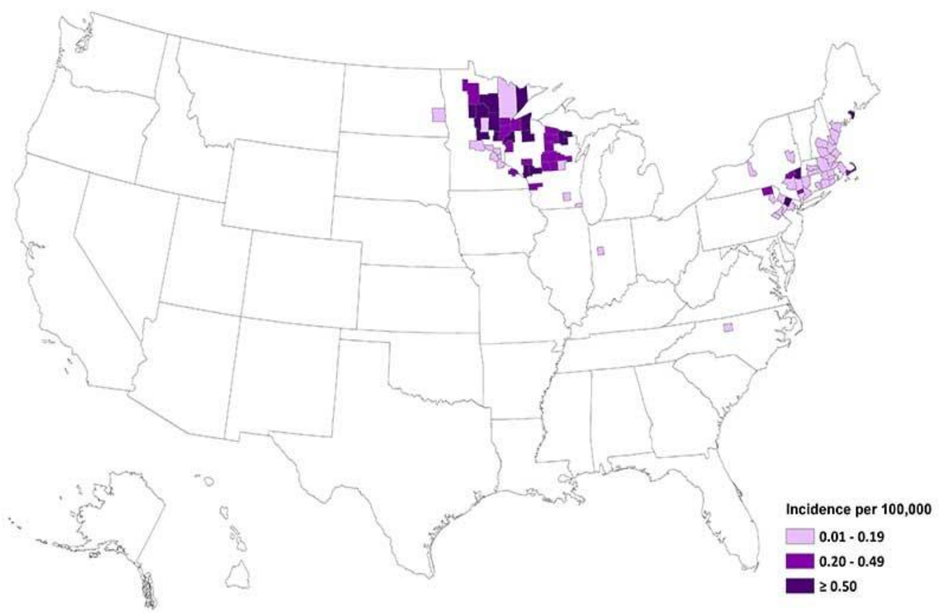

Figure 2: Powassan virus average annual incidence by county of residence, 2010-2019. Source: ArboNET, Arboviral Diseases Branch, CDC.

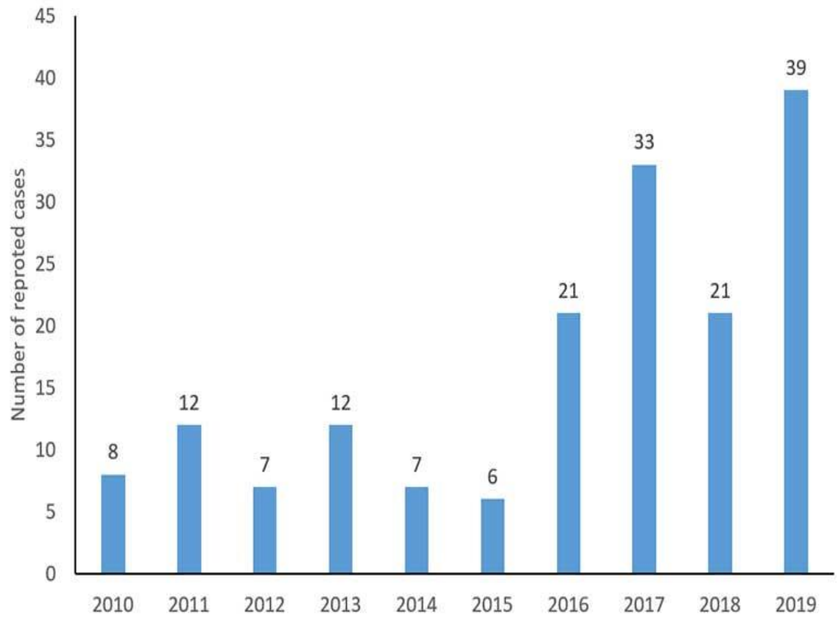

Figure 3: Powassan virus cases reported by year, 2010-2019. Source: ArboNET, Arboviral Diseases Branch, CDC.

Discussion

Powassan virus is an emerging cause of tickborne encephalitis that should be considered in patients with febrile neurological illness in our region [1] (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 [2] (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.[3]

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.[4] 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.**

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Extracranial Manifestations of Giant Cell Arteritis: An Underreported Entity

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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

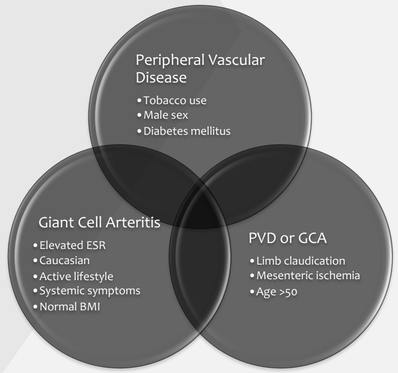

Figure 1: PVD and GCA were the leading differential diagnoses for the underlying etiology of mesenteric ischemia in this case. Risk factors and symptoms are shown for the patient.

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
- Physical examination: significantly tender abdomen with rigidity
- Lactic acid: 13.5 – WBC 48.9 – Creatinine 2.14 – ALT 384 – AST 280
- 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

<u>Review of Prior Evaluation from Mayo Clinic</u>

- ESR persistently elevated in the 90s – minimally elevated CRP
- A1C: 6.9 – LDL: 55 – ANA and ANCA negative
- PET-CT: diffuse scattered uptake in the large and small bowel; mild uptake in the bilateral distal SFA and popliteal arteries
- Temporal artery doppler US: no abnormalities
- MRA: heterogenous mural enhancement of the bilateral femoral arteries

CT Abdomen/Pelvis

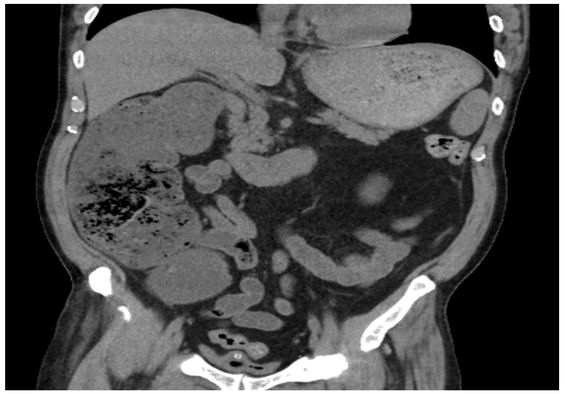

Image 1: CT abdomen/pelvis showing severe dilation of the right hemicolon and stomach with significant periportal stranding. No obvious pneumoperitoneum.

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

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Rapid Respiratory Failure in Dermatomyositis – A Rare Rheumatologic Emergency

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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

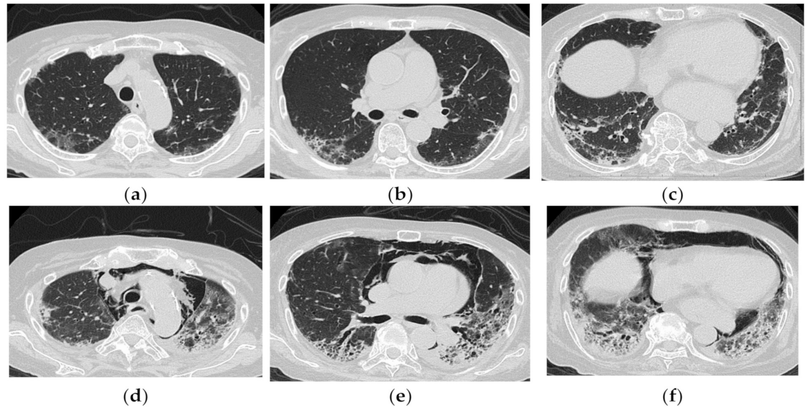
Case Description

- 55-year-old Spanish speaking female presented with 1 month of worsening rash and muscle aches
- Physical examination: aphthous ulcers, papules of bilateral upper extremity flexor surfaces, and erythematous rash of chest
  - 5/5 strength in bilateral upper and lower extremities

	Admission	Day 2	Day 3	Day 5	Day 6	Discharge
ALT (U/L)	1,029	1,092	1,063	892	1,237	684
AST (U/L)	1,611	1,855	1,806	1,285	1,842	543
Ferritin (ng/mL)	3,402		4,858	3,576	7,028	3,105

- R-factor: 17.3 suggesting a hepatocellular injury pattern
- GI consult: recommended liver biopsy
  - Pathology: non-specific infectious versus drug-induced inflammation
- 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

High-Resolution Chest CT in RP-ILD



Egashira R. High-Resolution CT Findings of Myositis-Related Interstitial Lung Disease. *Medicina*. 2021; 57(7):692. https://doi.org/10.3390/medicina57070692

Discussion

- The anti-MDA-5 positive subtype of CADM is highly associated with RP-ILD and fatality approaches 50% once RP-ILD is present
- Hallmark features of RP-ILD: ground-glass opacification (GGO), traction bronchiectasis, and bronchovascular thickening
  - Randomly distributed GGOs are a poor prognostic indicator
- Proposed biomarkers correlating with disease severity & RP-ILD:
  - Anti-MDA-5 levels: costly and time consuming to perform
  - Ferritin: widely available and routinely tested, but non-specific
- High-resolution chest CT (HRCT) can help determine the extent and severity of pulmonary involvement
  - Specific findings can predict anti-MDA-5 positivity
- Anti-MDA-5+ CADM, especially with high-risk features, requires treatment with high dose corticosteroids plus one (or more) immunosuppressant
  - Cyclosporine, cyclophosphamide, and tacrolimus all show promising results but require further investigation

Conclusion

- Anti-MDA-5 positivity is highly associated with RP-ILD & mortality
- HRCT should be obtained in all patients suspected of CADM at onset and repeated one month later
- 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 regimens not yet identified
- Rituximab and/or IVIG can be used in refractory cases
- Successful prevention of RP-ILD is vital to reducing mortality

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Management of Inflammatory Myositis in a Patient with Massive Creatine Kinase Elevation

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Introduction

- 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.

Initial Presentation

- 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.

Objective

- 6/5: CK **82,739** U/L (normal 30-170)
  - 6/4: CK 8,304 U/L
- Transaminases elevated
  - ALT 410 U/L (0-55); AST 2,114 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)

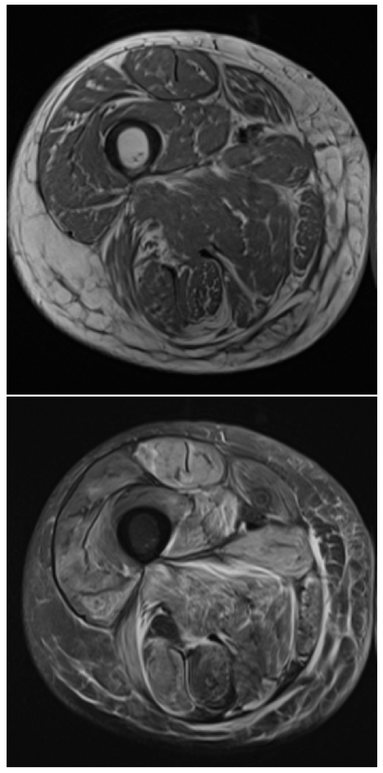

Fig. 1: *T1- (top) and T2-weighted axial MRIs of this patient's right upper leg, demonstrating diffuse edema of musculature*

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.

Learning points

- Dramatic elevations in CK are often associated with significant muscle breakdown, the byproducts of which can result in life-threatening complications. Familiarity with appropriate management is necessary to prevent loss of life.
- This case illustrates a successful outcome following treatment of inflammatory myositis with the administration of prednisone and aggressive fluid repletion.
- The use of bicarbonate for renal protection in CK elevation is an individualized choice requiring clinical judgement due to limited evidence demonstrating benefit.
  - Despite dramatic elevation in CK, this patient never developed AKI, even without the use of bicarbonate.

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Idiopathic Hemophagocytic Lymphohistiocytosis with CNS Involvement in an Adult Male

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Introduction

- Hemophagocytic lymphohistiocytosis (HLH) is a relatively rare condition[1]
- Systemic inflammation, hypercytokinemia and multi organ failure [1]
- HLH is most commonly diagnosed in it's primary, or familial form, presenting in children within the first year of life[2]
- Secondary or acquired HLH is associated in patients with predisposing factors for activation such as malignancy, autoimmune disease, or infection.[2]
- Criteria for diagnosis is taken from the Histiocyte Society HLH- 2004 diagnostic criteria[3]

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 sputum, 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 reveled hemophagocytic features with no overt signs of malignancy
- Soluble Interleukin-2 was elevated at 9700 U/mL. Genetic HLH screen was normal

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

Figure 1: Laboratory studies on admission.

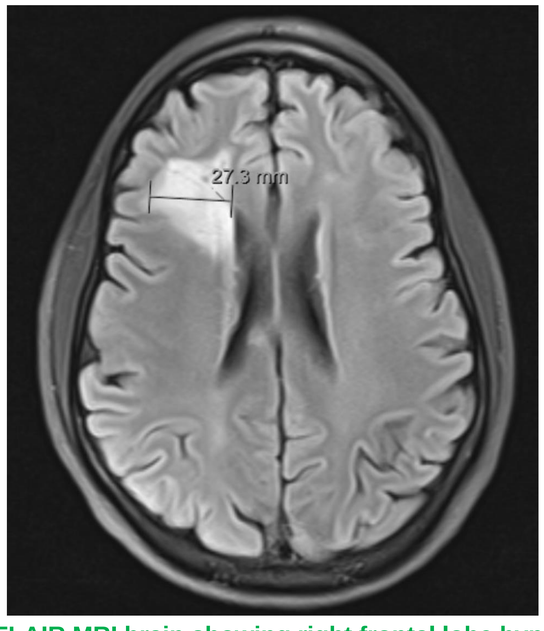

Figure 2: T2 FLAIR MRI brain showing right frontal lobe hyperintensity.

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.

HLH- 2004 Diagnostic Criteria[3]
1. A molecular diagnosis consistent with HLH mutation (PRF1, UNC13D, STX11, or STXBP2)
2. OR Five of Eight Criteria Below:
• Fever
• Splenomegaly
• Cytopenia (at least 2 of 3): Hemoglobin <9 g /dL, platelet count<100,000, and neutrophil count<1
• Hypertriglyceridemia (greater than or equal to 265 mg/dL) and/or hypofibrinogenemia (less than or equal to 150 mg/dL)
• Hemophagocytosis in bone marrow, spleen, or lymph nodes
• Low or absent NK cell activity
• Ferritin greater than or equal to 500 ng/mL
• Soluble IL-2 receptor level >2400 U/mL

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**

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