Anaplasmosis: A Colostrum of Vague Symptoms Often Leading to a Delayed Diagnosis

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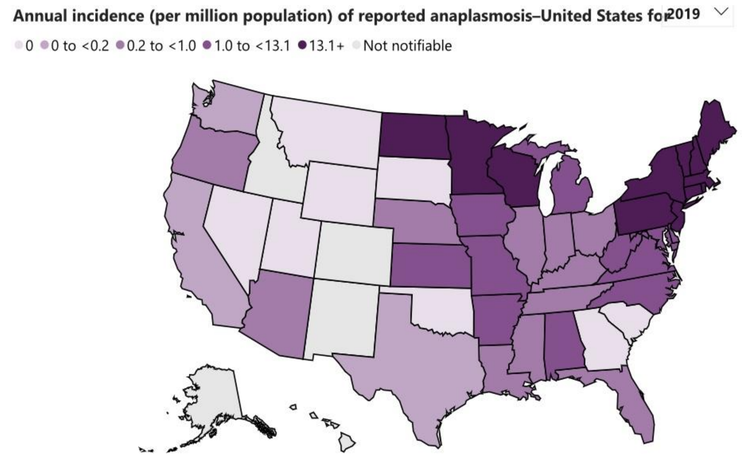
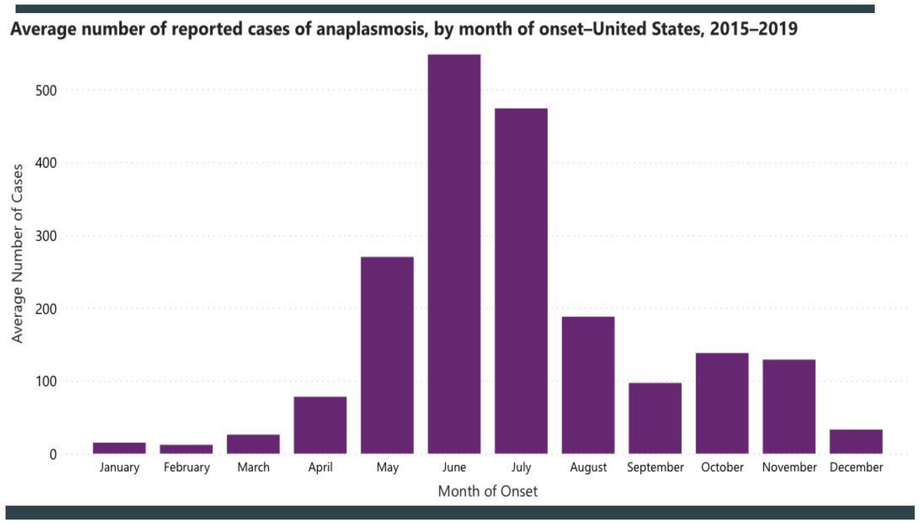
Introduction

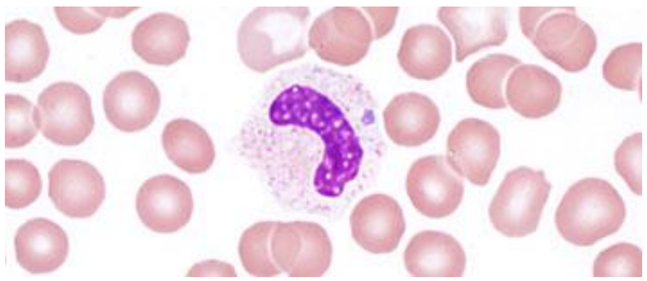
- Anaplasmosis is a tickborne disease caused by the bacterium *Anaplasma phagocytophilum.*
- In the United States, the bacteria is carried by the blacklegged tick (Ixodes scapularis) in the Northeast and Midwestern United States
- In rare cases, *A. phagocytophilum* has been spread by blood transfusion.
- CDC data shows that tick borne illness peaks in summer months of June and July and is reported most frequently in the upper midwestern and northeastern states.





Case Description

- 58-year-old male presents to the ER with 1-week history of diarrhea, shortness of breath, weakness and subconjunctival hemorrhages.
- Patient had fever, tachycardia, hypotension and hence sepsis protocol was started.
- Acute hypercapnic hypoxic respiratory failure
- Labs- platelets 30, WBC 3.5, Hb 9.6, AST 224, ALT 121, procalcitonin 28, LDH 652. creatinine 4.81, BUN 65.
- Patient was started on ceftriaxone, IV fluids, BiPAP, DuoNeb's and blood cultures were obtained.
- Respiratory status improved and he informed that he pulled ticks off in late June when he was harvesting hay
- Raised suspicion about tick-borne diseases and samples were sent for Babesiosis, Anaplasmosis and Borrelia. All serologies came back positive.
- Prompt antibiotic therapy was initiated with doxycycline, azithromycin, and atovaquone
- The patient was discharged following clinical stability and completed a 10-day course of antibiotics.



Morulae detected in a granulocyte on a peripheral blood smear, associated with *A. phagocytophilum* infection. Photo/Bobbi S. Pritt, Mayo Clinic

Discussion

- Signs and symptoms of anaplasmosis and Babesiosis begin within 2-4 weeks after the bite of an infected tick.
- Early symptoms include fever, chills, headaches, muscle aches, and loss of appetite.
- Late Illness can cause respiratory failure, bleeding problems and death.
- General lab findings include anemia, thrombocytopenia, leukopenia and elevations in hepatic transaminases.
- Detection of Anaplasmosis is done by DNA PCR, Blood smear microscopy and serology.
- CO-TESTING is very important
- Anaplasmosis is treated with doxycycline 100 mg BID. Babesiosis is treated with a combination of azithromycin 500 mg OD and atovaquone 750 mg BID.
- Post-tick bite antibiotic prophylaxis is not recommended to prevent anaplasmosis.

Conclusion

- The diagnosis of anaplasmosis often is made based on clinical signs and symptoms. Treatment should not be delayed pending the receipt of laboratory test results.
- Always take a thorough patient history, including recent tick bite, exposure to areas where ticks are commonly found and travel history
- Educate your patients - Prevention is better than cure.

Clinical Operational Tolerance in Liver Transplant: Are We Making Any Progress?

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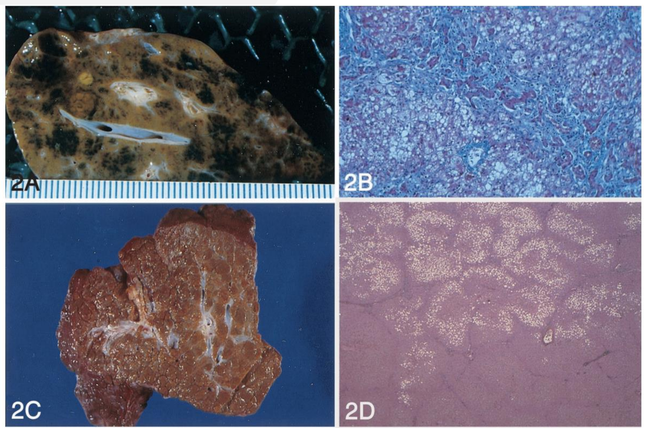
Introduction

- Hereditary tyrosinemia type 1, is the most severe disorder of tyrosine metabolism. HT1 occurs in 1 in 12,000 to 1 in 100,000 individuals of Northern European descent.
- Life-long immunosuppression is key in managing liver graft protection from recipient rejection. However, it is associated with increased morbidity and mortality
- Clinical operational tolerance is defined as successful immunosuppressive drug cessation maintained for at least 12 months with stable graft function and no histopathologic evidence of rejection
- Up to 20% of selected patients undergoing liver transplantation could safely withdraw immunosuppression.

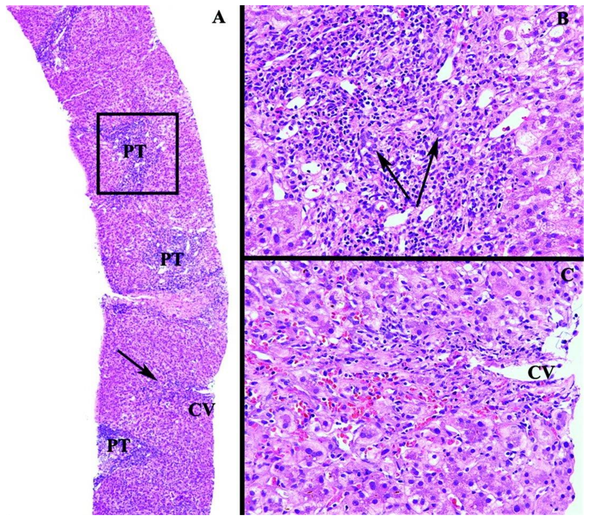
Case Presentation

- A 31-year-old male with biopsy confirmed renal glomerulosclerosis on peritoneal dialysis was evaluated for advanced fibrosis/cirrhosis of his hepatic graft.
- At the age of 1 he was diagnosed with HT-I- and underwent cadaveric liver transplant in 1992 at the University of Wisconsin at 16 months of age.
- His post-transplant course was complicated by size mismatch between the donor and recipient with narrowing at the biliary anastomosis for which he underwent sphincterotomy with placement of a self-expanding metal stent.
- He was on cyclosporine monotherapy for immunosuppression for nearly two decades. He subsequently decided to self-discontinue the cyclosporine and was lost to follow-up for 10 years.
- During his initial evaluation in the hepatology clinic labs were significant for alkaline phosphatase of 277 U/L, ALT 104 U/L and AST 58 U/L.
- Viral, metabolic and autoimmune hepatitis serologies were negative.
- Ultrasound with doppler revealed coarsened echotexture with mild ascites.
- FibroScan consistent with <11% of the liver with fatty change and stage 3/4 fibrosis.
- Liver biopsy showed mixed portal and lobular hepatitis consistent with moderate T-cell mediated rejection RAI equals 5 of 9 and periportal fibrosis with areas of bridging fibrosis stage 3 of 4.

Biopsy



Autopsy liver from a 3-month-old infant with tyrosinemia type I (or hepatorenal tyrosinemia, HT1) who died in fulminant liver failure. Source: Tyrosinemia: A Review. 4. 212-21. 10.1007/s100240010146.



Liver biopsy interpretation for causes of late liver allograft dysfunction. Source: Hepatology, Volume: 44, Issue: 2, DOI: (10.1002/hep.21280)

Discussion

- This case is unique in two aspects: The relatively young age of the recipient and duration of graft survival off immunosuppression.
- Mechanism of tolerance involves passenger leukocytes, inflammatory response and Tef deletion vs Treg proliferation.
- Serum biomarkers are ideal, due to being non-invasiveness and include increase in CD4 + CD25 + T-cell, increase subset of Treg and decreased NKs and exhausted CD8+Tef.
- Invasive biomarkers are more reliable predictors of operational tolerance (OT). Biopsy forms the gold standard.
- NCT00647283 and LIFT trial can show promising results.
- Different strategies like using CNI or mTOR-I inhibitors can facilitate a safe IS withdrawal

Conclusion

- While elucidating more sensitive and specific diagnostic tools is an important research priority, the overriding research agenda should aim to ensure allograft health in the complete absence of IS
- Tolerance is the only pathway that fully aligns the best long-term interests of both the patient and the allograft—the only way to achieve 1 graft for 1 (long) life

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Venlafaxine-Induced Liver Injury

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Introduction

Venlafaxine, a widely used serotonin and norepinephrine reuptake inhibitor first marketed in 1993 for the treatment of major depressive disorder and generalized anxiety disorder is generally safe and has a low side effect profile. [1,2] Though rare, a few cases of liver injury due to venlafaxine use have been identified in literature.[1,2,3] We present a case of venlafaxine-induced liver injury.

Learning Objectives

- Hepatotoxicity is a serious side effect of venlafaxine
- Close monitoring of serum hepatic markers, including bilirubin, is important when initiating SNRIs such as venlafaxine
- Steroids may be used to treat liver inflammation once offending agent is stopped

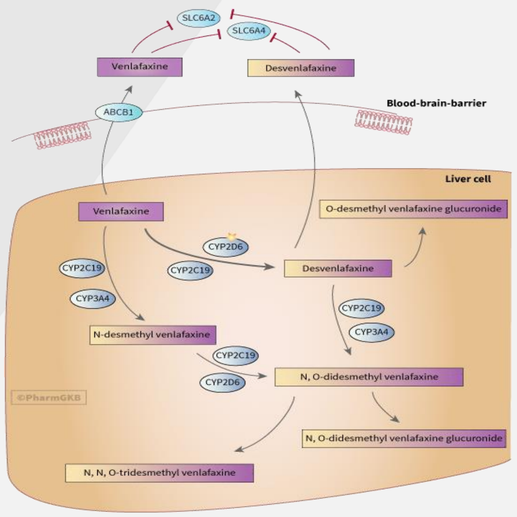

Figure 1: Metabolism of Venlafaxine.[7]

Case Description

The patient was a 76-year-old female s/p cholecystectomy several years prior brought to the emergency department with nausea, vomiting, abdominal pain, and generalized weakness for three weeks. On presentation lab work showed hepatic function values consistent with cholestatic hepatitis. Right upper quadrant ultrasound showed echogenic liver parenchyma consistent with fatty liver. MCRP showed mildly prominent common bile duct without stones or obstruction. Infectious hepatitis panel was nonreactive. Acetaminophen level was zero.

Without identifiable cause of the hepatitis, the patient was started on prednisone to cover for presumed autoimmune hepatitis. Serum autoimmune hepatitis markers were negative. A liver biopsy was pursued due to lack of identifiable cause for hepatic inflammation.

Parameter	Value	Normal Range
Alkaline Phosphatase	1,457	40-150 U/L
ALT	124	0-55U/L
AST	501	5-45 U/L
Total Bilirubin	2.1	0.2-1.2 mg/dL
Indirect Bilirubin	0.6	0.0-0.8 mg/dL
Direct Bilirubin	1.3	0.0-0.5mg/dL
GGTP	3,464	0-40 U/L
CRP	136.9	<5.0 mg/dL

Table 1: Serum lab studies on admission

Clinical Course

The patient was treated for depression with fluoxetine but was switched two months prior to venlafaxine. She denied ever starting venlafaxine, which was later found to be false. Liver function tests (LFTs) improved during her inpatient admission since the medication was held. She was discharged home on prednisone and ursodiol, but the prednisone was not continued at home. She was admitted again with previous symptoms and her LFTs rose again. Patient was discharged home a second time with close gastroenterology follow-up outpatient. After discharge the patient's primary care provider verified that patient had been taking venlafaxine per home health nursing report prior to initial admission.

Liver biopsy showed periportal fibrosis and bridging ductular reaction concerning for drug induced injury without inflammation aligned with autoimmune hepatitis. After venlafaxine was discontinued, patient was placed on a prednisone. The ursodiol was stopped. The hepatitis slowly improved.

Discussion

Acute liver injury is a rare adverse effect of venlafaxine. Risk factors for drug-induced liver injury (DILI) include age and polypharmacy.[4] DILI can lead to more serious acute liver failure, so it imperative that clinicians routinely monitor LFTs while using therapeutic doses of SNRIs. According to a study in France, no difference was found between SNRIs and SSRIs and risk of serious liver injury, however it is likely that pa tients with higher risk of liver injury were not placed on SNRIs.[5] When antidepressant medications are mixed with anti-psychotic or anticonvulsant drugs the risk of DILI is higher.[6] The primary treatment for DILI is stopping the medication and starting short term steroids for liver inflammation.

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Rare Breast Pathology with Cylindroma of Breast on Surgical Resection

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Background

Common breast pathologies include invasive ductal carcinoma, invasive lobular carcinoma, ductal carcinoma in situ, and lobular carcinoma in situ.

Cylindromas are usually associated with head or neck locations. Although they may appear to malignant, these solitary growths are typically benign.

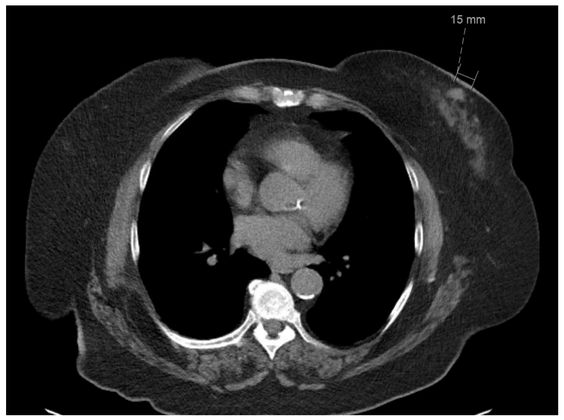
This poster aims to educate on the cause, presentation, pathology, and management of this little-known side pathology.

Presentation

Patient is a 79-year-old female with past medical history notable for obesity, obstructive sleep apnea, hypertension and previous basal cell carcinoma of the face who presented to emergency department for a fall.

Patient fell while walking up stairs and sustained injury to chest.

Work up at that time showed concern for area of calcifications in left breast on trauma CT scan.



Diagnostic Course

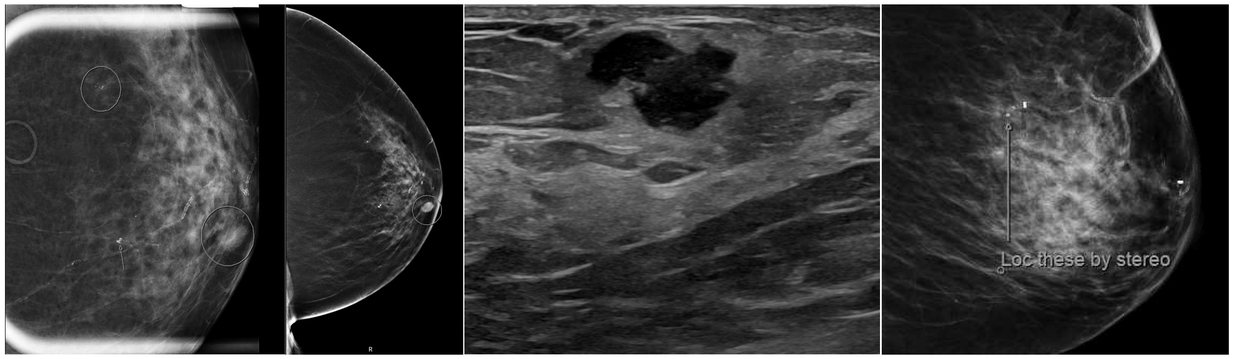
Breast imaging work up with Breast Clinic started three days after initial CT scan including diagnostic mammogram and breast ultrasound.

- Two areas of pleomorphic calcifications in left breast (5 mm and 10 mm)
- ACR BI-RADS 4C

With suspicious findings patient able to bee seen by breast clinic for follow up two weeks after. Stereotactic ultrasound-guided biopsy completed at that time with localization.

- Invasive ductal carcinoma with basaloid features (10 mm site)
  - Properly controlled estrogen receptor is low positive (1%), progesterone receptor is negative, and HER2 oncoprotein immunohistochemical stain is negative for overexpression (score 0)
- Indeterminate calcifications at 5 mm site

Patient was then scheduled for partial mastectomy x2 with sentinel lymph node biopsy the following month.

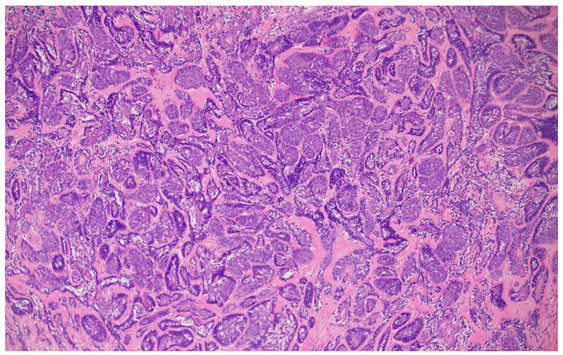


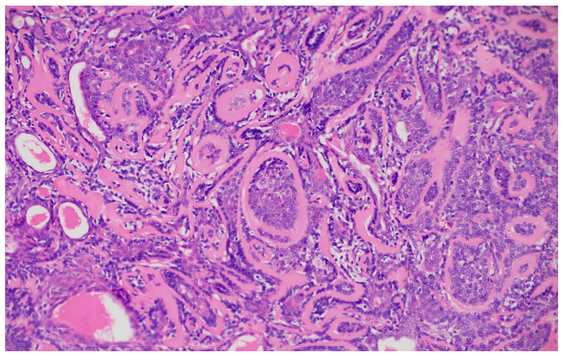
Pathology

Patient pathology reviewed in-house as well as inter-departmental consultation from Mayo Clinic. For the 5 mm small mass, incidental atypical ductal hyperplasia (ADH) in a background of fibrocystic changes found. Sentinel lymph node biopsy x2 completed and negative for tumor.

10 mm mass on imaging that previously showed invasive ductal carcinoma resulted with Cylindroma, 24 mm in greatest dimension.

Pathology slides found to have epithelial proliferation. Histomorphologic features and immunohistochemical staining patterns are those of a cylindroma. The core biopsy slides are challenging, with this very rare entity of breast cylindroma showing overlapping features and marker positivity with other entities such as adenoid cystic carcinoma and basaloid invasive ductal carcinoma.





Management

No current data available for cylindroma of the breast, though dermatologic cylindromas are typically treated with surgical resection only.

Patient underwent partial mastectomy with great recovery of surgical incisions at follow up.

Medical oncology with no indication for chemotherapies. Radiation oncology does not feel need for radiation of breast.

Take Home Points

Cylindromas are rare dermatologic benign tumors that typically occur in the head and neck region. This case adds to two other documented cases of breast cylindroma in the literature.

Cylindromas present similarly to other breast lesions and must be worked up fully to avoid diagnostic error.

Current management recommendations are for surgical resection without the need for chemoradiation.

Current Screenings

- Women age >25 should undergo formal risk assessment for breast cancer
- Women with an average risk of breast cancer should initiate yearly screening mammography at age 40
- Women with a higher-than-average risk of breast cancer should undergo yearly screening mammography and be offered yearly supplemental imaging; this screening should be initiated at a risk-based age
- Screening mammography should cease when life expectancy is <10 years

The American Society of Breast Surgeons

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