CLINICAL VIGNETTE

Strongyloidiasis – A Case Study

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Case Report

A 63-year-old female with past history significant for stage III breast cancer on maintenance Tamoxifen, along with prior alcohol abuse, was transferred with headaches, intermittent fevers, and altered mental status from an outside hospital. She lives primarily in Central America since retirement 3 years ago and frequently visits the United States.

She was hospitalized at UCLA two months prior for evaluation of intermittent fever and leukocytosis. CT body imaging was negative, along with negative infectious and rheumatologic workup. Past history was remarkable for heavy alcohol use for more than 25 years with recent sobriety. She also had hypertension and hypothyroidism.

She was initially evaluated for fever and headaches at an outside hospital and transferred to UCLA for a higher level of care. Upon arrival at UCLA, she was sedated and verbally non-responsive. Her exam included BP162/99, pulse 150, RR 72, and temperature 102.7^{o}F. She was on BiPAP with O_2 saturation of 99%. Head and neck exam was unremarkable without adenopathy. Her lungs had bibasilar crackles. Cardiac exam was only significant for tachycardia with regular rhythm and no murmurs.

Laboratory values on arrival included white blood cell count 15.13 x 10^3/uL, hemoglobin 9.7 g/dL, hematocrit 29.5%, platelet 78, neutrophil 67.7%. Sodium 131, potassium 3.8, chloride 105, CO_2 12, BUN 30, creatinine 1.5, glucose 87, troponin 20, BNP 3070, ESR > 100, and lactate 19.

Imaging

CT scans of the chest, abdomen, and pelvis upon arrival to UCLA were unremarkable other than signs of aspiration. CT scan of the brain showed no acute findings, and MRI brain imaging showed no acute abnormalities.

Course

Shortly after arrival at UCLA, she became hypotensive to 50/30 and unresponsive. She was intubated and started on levophed, phenylephrine, and Vasopressin. She was pan-cultured and started on Vancomycin and piperacillin/tazobactam. Troponin peaked at 20, and echocardiogram showed an ejection fraction of 15% consistent with acute myocardial infarction related to sepsis. Dialysis was also started for oliguric renal failure. In addition, spot EEG monitoring revealed seizure activity, and patient was loaded on levetiracetam.

Lumbar puncture revealed elevated protein of 944 and elevated white blood cell count of 873 with lymphocytic predominance. Infectious Disease advised empiric therapy for tuberculosis and fungal meningitis, as well as broadened bacterial coverage. Doxycycline was added for atypical vs. zoonotic infection. Multiple infectious serologies were sent (mycoplasma, hantavirus, rickettsia, Q fever, HIV, dengue fever, and malaria) and returned negative. All cultures (blood, urine, sputum, CSF, and stool) also returned negative.

Hematology/Oncology was also consulted after new bleeding from the endotracheal tube. This was eventually attributed to heparin therapy for deep vein thrombosis prophylaxis. Heparin was held, and after transfusion, all signs of hemorrhage stabilized.

At this point, the patient clinically improved, becoming more alert and was able to follow simple commands. The patient's overall hemodynamics also improved; she was taken off the pressors with improvement in urine output.

Unfortunately, the patient then developed new symmetric mottling of her feet that rapidly ascended up the extremities, consistent with livido reticularis. Dermatology was consulted for skin biopsy and added strongyloides infection as a possible cause for acute livido. Antibodies were sent and patient was empirically started on Ivermectin. Despite treatment, the patient soon decompensated with septic shock. The skin biopsy showed ectatic dermal and subcutaneous blood vessels focally containing erythrocytes with no vasculitis or malignancy. No definitive etiology was determined. After discussion with family, comfort care measures were initiated, and the patient died. After her death, the strongyloides antibodies returned positive.

Discussion

Strongyloidiasis is caused by 2 species of the intestinal nematode *Strongyloides.* The most common and of greater clinical importance is *Strongyloides stercoralis.* The main

mode of infection is through contact with soil that is contaminated with free-living larvae.[1] When the larvae come into contact with skin, they are able to penetrate and migrate through the body. They eventually find their way to the small intestine where they lay their eggs. Most of these larvae will be excreted in the stool.[1]

The majority of patients with strongyloidiasis have an uncomplicated medical course. As many as 50% of patients remain asymptomatic and can survive decades undiagnosed.[1] Symptoms typically involve gastrointestinal, pulmonary, and dermatologic systems. Severe symptoms may develop, and death is possible especially in immunocompromised individuals.

Gastrointestinal symptoms are often nonspecific, including epigastric abdominal cramping, nausea, vomiting, chronic diarrhea, constipation, pruritus ani, and, rarely, small bowel obstruction. Prolonged malabsorption of fat and protein can lead to a celiac-like syndrome, characterized by steatorrhea, hypoalbuminemia, and peripheral edema.[2]

Symptomatic pulmonary strongyloidiasis that results from migrating larvae is observed in 10% of patients. Initial infection may trigger an asthma-like condition. Symptoms include productive cough, occasionally with blood-streaked sputum, dyspnea, and fever. In severe (disseminated) disease, pneumonitis may cause hemoptysis and difficulty breathing. A respiratory distress syndrome (ARDS) may occur and require intubation.[2]

Skin penetration by larvae can also create pruritic papulovesicular lesions. Typically, skin penetration is on the feet but may be at any site that contacted infected soil (for example, around the anus). Larva currens (racing larvae), the pathognomonic rash of *Strongyloides* infection, is a pruritic linear or serpiginous urticarial rash that may consist of one or more such bands and creeps 5-15 cm/h up the body. The rash, thought to be an allergic response to the migrating larvae, often manifests as a pruritic wheal or linear urticaria. It can resemble livedo reticularis due to spasms of the blood vessels or an abnormality of the local circulation.[2]

Altered mental status, focal seizures, or nuchal rigidity may indicate central nervous system involvement. Symptoms of meningitis may include headache, nausea, vomiting, and, in extreme cases, coma. Bacterial meningitis that occurs concurrently with the strongyloides hyperinfection syndrome is usually caused by enteric gram-negative organisms.[2]

Strongyloidiasis is difficult to diagnose because the parasite load is low, and the larval output is irregular. A single stool examination using conventional techniques fail to detect larvae in up to 70% of cases. Several immunodiagnostic assays have been found ineffective in detecting disseminated infections and show extensive cross-reactivity with other parasitic disease such as hookworms, filariae, and schistosomes.[3]

Typically, a single dose of ivermectin at 200 µg /kg is the drug of choice for the treatment of uncomplicated strongyloidiasis. A follow-up stool examination is needed after therapy to confirm results. In chronic cases, ivermectin can be given every 3 months until stools are negative in at least three subsequent tests.[4] Thiabendazole or albendazole can also be used as an alternative. In a study of 88 patients with strongyloidiasis, 31 patients received thiabendazole 25 mg/kg/ every 12 hours for three consecutive days, 22 patients received ivermectin 200 mcg/kg as a single dose, and 35 patients received ivermectin for two consecutive days. The efficacy rates were 78, 77, and 100 percent in the thiabendazole, ivermectin single dose, and ivermectin two-dose regimens, respectively. Sixteen percent of patients taking thiabendazole experienced side effects in contrast with three percent in the combined ivermectin groups.[5] Hyperinfection carries a high risk of gram-negative septicemia and thus broad spectrum coverage is recommended.[6]

Conclusion

Strongyloides stercoralis infects an estimated 30-100 million people worldwide.[7] Infection usually results in asymptomatic chronic disease of the gut, which can remain undetected for decades. However, hyperinfection syndrome can also occur, which can affect virtually every organ system. Patients with hyperinfection syndrome and disseminated disease can have catastrophic clinical outcomes such as sepsis, disseminated intravascular coagulation (DIC), meningitis, renal failure, and respiratory failure. In this case, the cause of death was most likely related to neurologic disease, possibly due to meningitis in the setting of significant liver failure.

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Submitted December 5, 2014