CLINICAL VIGNETTE

A Tick-borne Relapsing Fever Treated with Empiric Doxycycline

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Case

A 32-year-old male with no significant medical history presented to his primary care physician for a return to work note after a week-long illness with fevers (Tmax of 103°F), chills and rigors, headaches, nausea, vomiting and night sweats. His symptoms had largely resolved but did report bilateral leg cramps with exertion. His husband had similar symptoms. A few days before symptoms onset a week ago he completed a 3000 ft elevation mountain climb in Las Vegas, NV. His exam was unremarkable and an extensive panel of labs were ordered. His coccidioides IgG/IgM antibodies were negative along with negative creatine kinase (CK), Epstein-Barr virus (EBV) IgM/IgG and cytomegalovirus (CMV) IgM/IgG. His inflammatory markers Ferritin, Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP) were elevated with a normal leukocyte count. Monocytes and granulocytes were elevated on his differentials. Other positive labs included Chlamydia Pneumoniae IgG with negative Chlamydia Pneumoniae IgM. His symptoms were mild enough that the patient was comfortable traveling to New Jersey.

Five days later he presented to urgent care with fevers, chills, rigors as well as new bilateral hip pain. He became acutely anxious with diffuse, non-exertional chest pain that resolved without intervention. At urgent care chest tightness and elevated Heart rate to 140 beats per minute were noted. The urgent care physician advised the patient to proceed to the emergency department for Systemic Inflammatory Response Syndrome (SIRS) requiring a Sepsis workup. In the emergency department patient labs were significantly abnormal. Leukocytosis of 20.54 cells/mm^3, erythrocyte sedimentations rate (ESR) 75 (N<15 mm/hr), C-reactive protein (CRP) 35.4 (N>0.3 mg/dL), and Procacitonin of 4.21 (N 0.1-0.49 mg/mL). He was admitted to medicine service. On further questioning the patient reported his husband had similar symptoms which improved with doxycycline. While in the emergency department he received two liters of Normal saline and empirical intravenous (IV) cefepime. On Hospital Day 2 antibiotics changed to doxycycline given high suspicion for atypical infection. Additional testing included a computed tomography (CT) chest which was normal. CT abdomen and pelvis noted a mildly enlarged spleen. Extensive infectious and autoimmune testing returned nonrevealing. Labs notable for mild hemolytic anemia and thrombocytopenia, both likely due to infection and improved over the hospitalization. Initially there was moderate suspicion for babesiosis given hemolytic anemia and travel history, however parasite smear was negative. Beta-natriuretic peptide (BNP) was mildly elevated to 300s (N=100 pg/mL), but no signs or symptoms of heart failure and unremarkable transthoracic echocardiogram (TTE). His Chlamydia trachomatis IgM returned positive. Infectious disease specialist noted this was likely a false positive as he tested negative (twice) in the two weeks prior and he had negative PCR testing for chlamydia. The patient's serologies for histoplasma, parvovirus, Q fever serologies, rickettsia serologies, strongyloides, trichinella, soluble IL2 receptor were all negative.

The patient improved during the hospital admission and was discharged home on a two-week course of doxycycline. The Infectious Disease specialist saw the patient two weeks post hospital discharge and clarified that the definitive diagnosis would have required a sendout PCR for relapsing fever pathogens at the time of illness. The Lyme IgM positive from his hospitalization suggested that whatever borrelia species that caused his relapsing fever may have induced antibodies that cross-reacted with the B.burgdorferi assay. Serum samples were tested with a two-tier approach using the qualitative Borrella hermsi whole cell antigen test. Confirmatory results returned 2 months after presentation. The first tier is an antibody (total lg) enzyme linked immunosorbent assay (EIA) which was positive. The serum was further tested with the second-tier, IgM and IgG Western immunoblots (WB) which were also positive.

Discussion

Relapsing Fever presents with recurrent fever episodes post spirochete infection from either tick-borne (TBRF) or louse-borne relapsing fever. Tick-borne relapsing fever can be transmitted to humans through 2 types of spirochete bacteria Borrelia hermsii and Borrelia turicatae. Borrelia hermsii is located in the Mountainous West and Borrelia turicatae often found in the Southwest and South Central region. Louse-borne relapsing fever is found in the spirochete Borrelia recurrentis prevalent in the developing world. Borrelia recurrentis is spread person to person by the body louse.[2]

Relapsing fever will present with an acute onset fever but with intervals of being afebrile and recurring fevers.[3] The incubation between exposure to borrelia and the fever can often be three to twelve days.[3] Our patient presented with fever for 7 days post potential Borrelia species exposure but then was afebrile for 5 days prior to his fever recurring. Other vague symptoms of relapsing fever could be headaches, joint pain, and rigors. The generalized symptoms can present with the onset of fever but can also present with recurrent fever. It's been determined the number of spirochetes present contributes to the severity of generalized symptoms.[4]

There can also be systemic organ complications including pulmonary, hematologic, neurologic and cardiologic manifestations. In Relapsing Fever patients can present with dizziness and delirium. More specifically Tick-Borne Related Fever can contribute to neurologic complications such as facial palsy, myelitis and meningitis due to spirochete invasion. The neurologic complication will often not be present with the first onset fever. The cardiologic complications can often be fatal, contributing to myocarditis. In TBRF the pulmonary complication can be fatal contributing to acute respiratory distress syndrome found in patients in the states of California, Nevada and Washington.[5] Hematologic issues often arise with Relapsing Fever include thrombocytopenia more commonly in Louse-Borne Relapsing Fever than in Tick-borne Relapsing fever. Our patient platelets dropped to 64 x10E3/uL and recovered upon treatment.

On physical examination patients with Relapsing Fever may have an enlarged spleen which our patient did have confirmed on CT radiography. Patients can also have abdominal pain, left shoulder pain and an enlarged liver. A gallop can often be auscultated when patients present with myocarditis. When neurologic complications are present patients can be noted to have unilateral or bilateral Bell's Palsy. This is due to infiltration of spirochetes in the 7th cranial nerve. Patients can also present with deafness due to infiltration of the 8th cranial nerve by the Borrelia species.

The laboratory findings are vague, and include anemia, leukocytosis and a very high erythrocyte sedimentation rate. There can also be elevated liver enzymes along with low albumin.[6]

To confirm a diagnosis the best test is thick and thin smears of blood to see if the potential Borrelia species can be identified. If the organism cannot be identified by smear the recommendation is a polymerase chain reaction (PCR) testing should be performed. Serology testing is often used after a patient has already been treated. Our patient had already completed treatment when the serology testing was added on to the blood work by the infectious disease specialist.

When a patient presents with TBRF it can be quite challenging to differentiate between other similar infections like Dengue, Babesiosis, Malaria, Ehrlichiosis, Rickettsioses, and Brucellosis. The epidemiologic background during history can help differentiate it from other infections. Initiating antibiotics immediately will hopefully prevent any severe or fatal complication of TBRF. When patients have no neurologic complications and are not severely ill they can safely be treated with oral doxycycline. Patients with severe symptoms requiring hospitalization can start intravenous (IV) beta-lactam therapy and transition to oral therapy when clinically stable. Our patient received intravenous Cefepime while admitted and then transitioned to oral doxycycline. When neurologic symptoms or complications are present, patients will need 14 days of intravenous (IV) therapy with penicillin or ceftriaxone. In pregnant women, in whom tetracyclines are contraindicated are recommended to take Intravenous therapy with penicillin or another beta-lactam antibiotics for 14 days regardless of severity or if neurologic complications are present.

Preventing exposure can hopefully reduce risk of being exposed to ticks transmitting TBRF. Houses should be designed ideally with concrete walls and completely sealed. This is obviously impractical. Rural cabins in North America prove challenging to avoid exposure since rodents which can carry the ticks nest in roofs or live beneath porches.[7] Our patient had stayed in a cabin in Las Vegas.

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