CLINICAL VIGNETTE

Fever of Unknown Origin as a Manifestation of Acute Ebstein-Barr Infection: A Case Report

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Introduction

Infectious Mononucleosis is a disease that we think of primarily as a disease of adolescence typically characterized by sore throat, cervical lymph node enlargement, fatigue, splenomegaly and fever most often lasting several weeks. However, it can also be a disease that can present in a myriad of ways in older adults including an acute symptomatic hepatitis and fever of unknown origin.[1]

Case Report

A 54-year-old woman presented to urgent care with 11 days of fever, chills and body aches of her neck, arms and legs. She denied cough, congestion, sore throat, rash, vomiting, diarrhea, lymph node swelling, or abdominal pain. The patient's subjective fever was present mainly at night and would come and go during the day. She did not check her temperature at home. She also had associated night sweats. She denied any recent travel, sick contacts or animal exposures. At the first presentation, it was thought that the patient might have an infection, a new rheumatologic disease, or a new malignancy. Her vitals upon presentation to urgent care showed a pulse of 110 and a temperature of 38.3. Initial labs at urgent care were only significant for a negative monospot, an AST of 67, an ALT of 81, a CRP of 4.5, a platelet count of 127, a white blood cell count of 3,600, procalcitonin of 0.3, negative blood cultures, and a negative acute hepatitis panel. An abdominal ultrasound showed a mildly enlarged liver with fatty change and mild splenomegaly. Chest x-ray was normal. Several days later upon follow up with her primary care doctor, the patient had a worsening AST of 427 and ALT of 501 and leukopenia and was referred to the emergency room for further evaluation.

The patient was admitted to the hospitalist service and infectious disease and hematology were consulted. Abdominal and chest CT which showed prominent lymph nodes enlarged in the upper abdomen likely reactive in nature. Bone marrow biopsy demonstrated no lymphocytic aggregate and no evidence of infiltrative lymphoma. She subsequently underwent excisional biopsy of her enlarged subcarinal lymph node via mediastinoscopy which showed prominent reactive interfollicular hyperplasia, consistent with acute EBV-related lymphadenopathy. Her EBV DNA PCR returned at 426, along with a positive heterophile antibody test (Monospot) and EBV-VCA IgM positive/IgG negative test, all consistent with acute EBV infection.

Over the course of her hospitalization, her leukopenia resolved, AST/ALT trended down and her fevers defervesced and she was discharged home on hospital day 3.

Discussion

Infectious Mononucleosis is not a disease that is classically thought of as causing fever of unknown origin. It usually presents in adolescence with the classic symptoms of pharyngitis, cervical lymph node enlargement, fever, and fatigue.[2] Lymph node involvement typically involves the posterior cervical nodes rather than the anterior cervical nodes.[2] However, older adults often do not develop the classical clinical syndrome.[3] It can particularly be a challenge to diagnose in patients older than 35 years. Our patient never developed pharyngitis or peripheral lymphadenopathy, and our patient's only presenting symptom was fever. Almost all older patient have fevers that persist beyond 2 weeks. Studies have also shown higher rates of hepatitis, cholestasis, and hepatomegaly.[3] Older patients also have decreased splenomegaly, lymphadenopathy, and pharyngitis when compared with young patients with infectious mononucleosis.[4] In addition, patients may undergo unnecessary tests.[3] For example, our patient had both a bone marrow biopsy and an excisional lymph node biopsy due to concern for leukemia and lymphoma. Finally, older patients have fewer atypical lymphocytes and less lymphocytosis than younger patients.[3]

Although our patient eventually had a positive heterophile antibody test while in the hospital, these antibodies were not present when she was first tested at urgent care. Heterophile antibodies usually appear within 1 week after infectious mononucleosis begins and peak at about 2 to 5 weeks. If the Monospot is negative, it is possible to test for EBV-specific antibodies to specific antigens for a serologic diagnosis. These antigens include VCA and EA which are expressed during the lytic phase, and EBNA which is expressed in B cells. Detection of VCA IgM confirms acute EBV infection. Current recommendations suggest combining IgG and IgM VCA assays with tests for EBNA antibodies.[3]

The treatment of infectious mononucleosis is still supportive, as the infection is primarily self-limited in most immunocompetent individuals. Patients with splenomegaly should avoid heavy lifting and contact sports for 2 to 3 weeks. Acyclovir has

been shown to decrease oropharyngeal shedding of the virus, but does not affect duration or severity of the illness.[5]

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Submitted March 16, 2018