CLINICAL VIGNETTE

An Unusual Cause of Headache: CMV Viremia in an Immunocompetent Patient

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Clinical Case

A 35-year-old man in otherwise good health presents with headache. The headache started about two weeks ago, described as sharp and pounding, discomfort, localized mainly to the frontal area. The headache abates for a few hours after taking ibuprofen but then returns. He has no prior history of headaches. The headache seems to get worse when bending over and he has also noticed feeling much more fatigued since his headache started, missing work for a few days. He developed a fever 3 days ago, up to 102º F, temporarily alleviated with acetaminophen or ibuprofen. He also reports night sweats for the past few nights. He is a physician and denies any needle sticks or recent travel. He has no pertinent family history. He is married and has a 6-month old child and a healthy dog at home. He denies any tobacco or illicit drug use and drinks alcohol occasionally. His review of systems is negative aside from a mild cough with nasal congestion and rhinorrhea for the past week. He denies any neck stiffness or other neurologic symptoms other than headache.

The patient's exam include normal temperature of 37ºC, pulse 103, blood pressure 129/71, respiratory rate 17 and oxygen saturation of 97% on room air. He was well-nourished in no acute distress, with pupils equal, round and reactive to light. His oropharynx, was normal with mildly erythematous nasal mucosa, and neck with normal range of motion. The remainder of his exam was normal, including skin, cardiac, abdominal lymphatics, and normal neurologic exam.

Laboratory evaluation revealed a normal chemistry panel, normal complete blood count and urinalysis. HIV 1 and 2 Ag/Ab screen was negative. HCV antibody screen was negative. LDH level was slightly elevated at 379 U/L. Brain CT scan was normal and lumbar puncture was notable for 4 WBCs with 2% segmented neutrophils, 66% lymphocytes and 32% monocytes. CSF glucose was normal at 60 mg/dL and protein was mildly elevated at 62 mg/dL. Gram stain showed moderate WBCs, no bacteria and CSF bacterial culture was negative. HSV PCR and enterovirus PCR of CSF were negative. Coxsackie B 1-6 antibodies from CSF were not elevated. Serum heterophile antibody was negative. Serum CMV IgG and IgM antibodies were positive. Serum CMV DNA quantitative PCR was also positive at 159 IU/mL.

Patient's acute presentation with new headache, fever, night sweats and excessive fatigue was most likely due to acute CMV infection. Over the next few weeks, his symptoms gradually improved, initially with resolution of his fevers, followed by resolution of his night sweats and headache. Repeat serum CMV DNA quantitative PCR was recommended but was not done.

Discussion

Cytomegalovirus (CMV) is a member of the herpesvirus family and, can cause an acute (primary) infection followed by a latent infection. The severity of the CMV infection often depends on the immunity of the host. Infection in immunocompromised patients can be significant, leading to increased morbidity and mortality. Infection in immunocompetent patients is usually asymptomatic but can lead to a mononucleosis syndrome. Rarely, primary CMV infection in immunocompetent patients can lead to severe organ-specific complications with increased morbidity and mortality.[1] Primary CMV infection leads to the production of immediate-early, early and late viral proteins, with synthesis of viral DNA, which is often found in monocytes, megakaryocytes, myeloid progenitor cells and dendritic cells. Secondary CMV infection is caused by either reactivation of latent CMV or reinfection with a new exogenous strain. Reactivation of CMV can happen at any time, with higher risk during systemic immunosuppression, such as glucocorticoid use or HIV infection.[2] The prevalence of CMV antibody increases as one gets older. In the United States, CMV seroprevalence was estimated at 36 percent for children as opposed to 91 percent in patients over 80 years old.[3]

CMV transmission occurs through the exchange of bodily fluids, including breast milk. The virus is known to be sexually transmitted and can be detected in the genital tract.[4] Close contact is a known risk factor for transmission, as the virus is shed and passed through upper respiratory tract secretions and urine. Seroconversion is more common among family members and children in daycare centers. Healthcare workers and workers in daycare centers are also more susceptible to seroconversion given their potential work exposures.[5] CMV is also commonly transmitted blood products and transplantation of organs from seropositive donors.[6]

The most common presentation of symptomatic cytomegalovirus infection in immunocompetent adults is a syndrome resembling infectious mononucleosis. The most common cause of infectious mononucleosis is Epstein-Barr virus (EBV) which is diagnosed by the presence of heterophile antibody. When the test for heterophile antibody is negative in a patient with symptoms of classic infectious mononucleosis, the cause is usually CMV infection.[7] However, there are distinctions in the mononucleosis syndrome caused by CMV versus EBV. Whereas EBV infections tend to cause enlarged cervical lymph nodes, tonsillitis and splenomegaly, CMV infection are less so, as systemic symptoms such as fevers and myalgias are more prominant. Also, the average age of patients with CMV mononucleosis tends to be older than those with EBV infection.[8]

Laboratory evaluation for mononucleosis syndromes reveals two classic hematologic abnormalities: the presence of atypical lymphocytes on peripheral blood smear and an absolute lymphocytosis with greater than 50 percent mononuclear cells. Interestingly, some patients with active CMV infection do not have atypical cells at the time of presentation. Other hematologic findings of mononucleosis include mild anemia, reduced haptoglobin levels, cold agglutinins, thrombocytopenia, positive antinuclear antibodies, elevated levels of rheumatoid factor and subclinical transaminitis.[9]

The vast majority of immunocompetent patients affected by primary cytomegalovirus infection have minimal or no symptoms. Patients with symptomatic CMV infection, particularly those with mononucleosis syndrome, recover over a period of days to weeks. Antiviral therapy is usually not indicated.[1,2]

Conclusion

Our patient presented with a new daily persistent headache, fever, night sweats and excessive fatigue most likely due to acute CMV infection causing a mononucleosis syndrome. He may have been more at risk to CMV infection given his occupation as a physician. He was evaluated by an infectious diseases specialist who agreed with the diagnosis and was provided reassurance and advice on supportive care measures. Over the next few weeks, his symptoms gradually resolved.

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