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Cytomegalovirus-Induced Hepatitis in an Immunocompetent Patient

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Conflict of interest: None declared

Patient: Female, 20
Final Diagnosis: Cytomegalovirus-induced hepatitis
Symptoms: Chills • cough dry • decreased appetite • fever
Medication: —
Clinical Procedure: —
Specialty: Gastroenterology and Hepatology

Objective: Rare disease

Background: Hepatitis is a descriptive term given for any inflammation of the liver. It can be characterized as inflammatory cells infiltrating normal hepatic parenchyma, which destroys their ability to perform normal physiologic functions. Hepatitis is a common disorder in immunocompetent populations, mainly attributed to viruses, alcohol, drugs, or autoimmune causes.

Case Report: Cytomegalovirus is a virus mostly affecting immunocompromised patients, resulting in infectious mononucleosis-like symptoms as well as hepatitis in liver transplant patients, but is generally benign in immunocompetent hosts. This report presents an unusual case of hepatitis caused by Cytomegalovirus in an immunocompetent patient with previous Herpes Simplex virus infection. A 20-year-old African-American woman presenting with intermittent subjective fevers and chills, sore throat, non-productive cough, and decreased appetite 1 month ago was diagnosed with a case of Cytomegalovirus-induced hepatitis.

Conclusions: This report clearly emphasizes the need for investigation of other disease entities such as Cytomegalovirus as a potential cause of hepatitis in an immunocompetent patient after more common causes of hepatitis have been ruled out.

MeSH Keywords: Cytomegalovirus Infections • Fever • Hepatitis, Viral, Human

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/890945

Background

Cytomegalovirus (CMV) is a dsDNA virus belonging to the family of *Herpesviridae* and subfamily *Betaherpesviridae*. It is also known as HSV-V, in line with the more popular HSV-I and HSV-II nomenclature, as they belong to the same family. CMV-associated diseases and their subsequent presentations depend mostly on the age at infection and the immunity status of the patient. With respect to neonates, it is a member of the TORCH group of organisms, which results in hydrops fetalis and various fetal malformations; however, after the neonatal period, CMV results in asymptomatic infection in almost 90% of reported cases. The illness that develops in adults usually mimics that of infectious mononucleosis, but is heterophile-negative, which distinguishes it from the heterophile-positive Epstein-Barr virus (EBV). CMV, in most cases, remains latent in the body, similar to its Herpesvirus counterparts, and is benign in immunocompetent hosts. However, if the immune status of an individual declines, the virus can reactivate and can cause dysfunction in multiple organs, including but not limited to: pneumonia and pulmonary embolism, myocarditis, encephalitis, retinitis, hemolytic anemia, and portal vein thrombosis. The most common manifestations of CMV are gastrointestinal in nature and present as esophagitis and colitis [1–5]. Some sporadic cases of fatal fulminant hepatitis and cholestatic jaundice have also been reported [5,6]. This report describes a case of hepatitis due to CMV in an otherwise immunocompetent host, which is an often undiagnosed and unrecognized causative agent of hepatitis.

Case Report

A 20-year-old African American woman presented to the Emergency Department with a chief complaint of subjective fevers for 1 month. Fevers were described as being intermittent, occurring mostly at night, and accompanied by a nonproductive cough, chills, and decreased appetite. She reports never having measured her temperature at home but after feeling feverish, frequently took Ibuprofen and Paracetamol for symptomatic relief. The symptoms progressively worsened over a 1-month period, which ultimately prompted her to seek treatment. She reports feeling well 1 month ago until she suddenly developed a sore throat prior to having the fevers. She denied any recent sick contacts, travel, or TB exposure. Her only significant past medical history included migraines. Her only significant past surgical history was ankle surgery in 2010 secondary to a motor vehicle accident. Her sexual history was significant for having 1 partner for the past 3 years. She reported having had a total of 7 male partners in her lifetime. She recently was started on and has been using daily oral contraceptive pills (OCPs), which were initiated a month and a half ago. She used barrier protection prior to this. She intermittently used condoms with her current partner.

On admission, the patient was febrile, with a temperature of 102°F. Her vital signs were significant for mild tachycardia with a pulse rate of 104 beats per minute and tachypnea with a respiratory rate of 22 breaths per minute. Her blood pressure was within normal limits at 114/71 mm of Hg and she was saturating at 100% oxygen on room air. She was anicteric, without jaundice, and had normal liver and spleen size. The rest of her physical examinations, including the abdomen, was grossly unremarkable and within normal limits. Laboratory data revealed a slightly increased WBC count of 10 900 cells/ml of blood with 10% bands, and 22% atypical lymphocytes with 4% Basophils. She had a negative Rapid Strep Test, negative monospot, and a non-reactive rapid HIV test. Her chest X-ray result was normal and abdominal ultrasound revealed mildly increased echogenicity of her portal triad. The gallbladder size and biliary system were otherwise normal in size. CT scan of the abdomen and pelvis revealed mild hepatic steatosis but was otherwise unremarkable.

Complete metabolic profile revealed an elevation in alanine aminotransferase (ALT) at 614 U/l, aspartate aminotransferase (AST) at 594 U/l, and an alkaline phosphatase of 107 U/l. The ALT to AST ratio, often a useful diagnostic marker for hepatic dysfunction, was not significant, as the ratio was 1.03. A total bilirubin level was well within normal range. The symptoms of the patient and the mild steatosis, with increase in both ALT and AST, clearly suggested hepatitis. Further work up with pan cultures of her blood and urine were ordered on admission. The patient was started on the Systemic Inflammatory Response Syndrome (SIRS) criteria protocol and was given a 500 cc bolus of normal saline followed by maintenance fluid at 150 cc/hour. She was placed on venous thromboembolism (VTE) and gastrointestinal prophylaxis.

Throughout her inpatient stay, the patient remained stable with the exception of continuous spikes in temperature causing fevers as high as 103°F in the evenings and onset of diarrhea. Urine cultures as well as blood cultures drawn twice did not show any source of infection. A workup of the diarrhea was initiated with cultures of her stool, which was also sent for ova and parasite testing; both were normal, as well as a Fecal Occult Blood Test (FOBT). With the backdrop of strong suspicion for hepatitis, a hepatitis panel for A, B, and C, as well as an ANA profile to rule out autoimmune causes, were done and both were negative. A CBC was performed with peripheral smear and flow cytometry, revealing atypical lymphocytosis with no evidence of clonality. Serology was positive for CMV IgM at 1.6, HSV IgM at 1.43, HSV IgG at 49.6, and EBV IgG at 8.0. Quantitative PCR is the criterion standard for the early detection and management of CMV infections. The presence of specific [1000 to 100 000 copies/ml] CMV DNA in a clinical specimen may suggest active infection, reactivated infection, or latent infection without disease. However, due to unavoidable

circumstances, CMV PCR could not be done in this patient. Given the acute nature of hepatitis and all causes of hepatitis being excluded, it can be inferred that the patient had an acute CMV infection due to a positive IgM and negative IgG for CMV, resulting in elevation of her liver function tests and subsequent hepatitis, despite the lack of CMV QPCR results.

Discussion

Hepatitis is a common disease entity caused by a multitude of processes. Drugs and other environmental factors such as acetaminophen overdose or other chemical exposure, autoimmune phenomenon such as hemochromatosis, Wilson's disease, or primary biliary cirrhosis, idiopathic physiologic occurrence such as in non-alcoholic steatotic hepatitis (NASH), or most commonly as a manifestation of chronic viral illness with Hepatitis B and C, are all possible factors inducing hepatitis. However, reports of Cytomegalovirus-induced hepatitis are rare, especially in immunocompetent individuals. Much of medical literature implicating CMV as the causative agent for hepatitis involves either immunocompromised hosts or previous orthotopic liver transplant recipients. In these cases, the incidence of CMV hepatitis runs from as low as 2–17% to as high as 34%. The viral burden is compounded by a series of factors, including immunosuppressive regimens, the serological status of a positive donor, and a high viral load in peripheral blood.

Acute fulminant hepatitis due to CMV requiring emergency liver transplant in an immunocompetent patient has been described, but these too are rare occurrences [12–14]. More commonly seen, though still infrequent, are the sporadic cases of CMV-induced hepatitis not resulting in fulminant liver failure. The first such case of CMV-related hepatitis was reported by Lamb and Stern [6–13,15]. Like most of the reported cases, the disease presents with abnormal liver function tests, including a slight increase in serum total bilirubin and serum alkaline phosphatase, as well as a concurrent transaminitis of ALT and AST not exceeding 5 times the normal value. Again, the disease process in immunocompetent patients is usually self-limiting in nature. In our case, the patient presented with a high fever and few other symptoms. Without serology for CMV it would have been impossible to determine the cause, indicating its importance in the differential diagnosis after all other likely causes have been ruled out.

Conclusions

We present a case of hepatitis caused by CMV in a young and immunocompetent female patient. Although there are a few cases of fatal fulminant hepatitis caused by CMV, this is one of the few cases of CMV-induced hepatitis in an immunocompetent patient that followed an otherwise subclinical course. This report emphasizes the need to investigate CMV as a causative agent irrespective of immune status in a patient with hepatitis when clinical signs and history warrant such testing.

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