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Case Report

Acute CMV Hepatitis and Pneumonia in A Young Immuno-Competent Male: A Case Report

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Abstract

Background: It is an opportunistic pathogen causing disease mainly in immunosuppressed patients. Immunocompetent hosts may contract CMV infection and mostly demonstrate a benign subclinical disease ranging from being asymptomatic to a self-limiting, febrile mononucleosis-like syndrome accompanied with lethargy, arthralgia and hepatitis. Hereby we report an extremely rare case of invasive CMV pneumonia and hepatitis in an immunocompetent young adult.

Case: This is the case of a 38-year-old previously healthy male patient presenting with a 5-day duration of a high-grade fever measuring 39 °C. Laboratory workup was consistent with liver abnormalities but negative for EBV, CMV, HAV, HBV, HCV, and brucellosis. CT scan of the abdomen and pelvis showed hepatosplenomegaly along with sub-centimetric mesenteric lymphadenopathy. During his hospital stay, he developed pancytopenia. A blood smear showed 4% atypical lymphocytes and thrombocytopenia. The viral workup was repeated after 1 week of hospitalization and showed active CMV infection. During his stay, he developed desaturation and a persistent fever. A CT scan of the chest showed patchy areas of ground glass opacities in both lower lobes and in the lingula, consolidation in the right lower lobe, and small bilateral pleural effusions. The patient was subsequently diagnosed with CMV pneumonia, for which he was given a ganciclovir course. Our patient was eventually diagnosed with severe CMV hepatitis along with CMV pneumonia which is rare in an immunocompetent young male.

Conclusion: Acute CMV hepatitis is not uncommon in immuno-competent patients. Therefore, physicians ought to be vigilant to make a diagnosis of CMV infection in case of non-specific prodromal symptoms associated with acute hepatitis of unknown etiology. When indicated, anti-viral therapy should be given for 2 to 3 weeks followed by a documentation of CMV viral load clearance from blood.

Keywords: Cytomegalovirus; Immunocompetent; Pneumonia; Hepatitis

Learning Points

- Familiarize readers with the concept of CMV infection in immuno-competent patients
- Understand that CMV infection can range from mild symptoms to severe invasive infection with end-organ damage in immuno-competent patients
- Evoke a rare case of acute CMV hepatitis complicated by pneumonia in a young immuno-competent male patient

Introduction

Human cytomegalovirus is the 5th member of the viral family known as herpesviruses. It is an opportunistic pathogen causing disease mainly after congenital infection or in immunosuppressed

patients. The prevalence of CMV seropositivity in human ranges from 50–95% depending on the population and underlying risk factors: women, older age groups, persons of lower socioeconomic status, and in developing countries [1].

In the literature, three subtypes of HCMV infection were recognized. Primary infection occurs in an individual who becomes infected for the first time without possessing previous immunity against this virus. Afterwards, the virus becomes latent from which it may reactivate (second type of infection). The third type of infection is called reinfection where superinfection occurs upon contact with an infectious individual in someone who has already been infected despite possession of natural immunity [2].

Immunocompetent hosts may contract CMV infection and mostly demonstrate a benign subclinical disease ranging from being asymptomatic to a self-limiting, febrile mononucleosis-like syndrome accompanied with lethargy, arthralgia and hepatitis. Rarely, a tissue invasive illness involving the ocular, respiratory, gastrointestinal, blood [including hemophagocytic lymphohistiocytosis (HLH)] or other organ-systems may complicate the course of infection [3]. On the other hand, in the immunocompromised patient, CMV infections can result in significant morbidity, increased risk of mortality, and end-organ failure [2].

It is essential to recognize the atypical manifestations of acute CMV infection in immunocompetent hosts in order to facilitate prompt diagnosis, optimize tests selection, and to precipitously treat the illness when indicated. Hereby we report an extremely rare case of invasive CMV pneumonia and hepatitis in an immunocompetent young adult. At this time, to the best of our knowledge, no case of simultaneous CMV pneumonia and hepatitis was reported.

Case Report

This is the case of a 38-year-old previously healthy male patient presenting with a 5-day duration of a high-grade fever measuring 39 °C. He works as a tattoo artist and is a social smoker and alcohol user. The patient reported a persistently high-grade fever that dispersed throughout the day and was unresponsive to over-the-counter medications. He also reported a chronic cough, which he attributed to recurrent sinusitis. The patient exhibited diaphoresis, a bilateral frontal headache, and dark-colored urine. The patient denied phonophobia, photophobia, or altered mentation, dyspnea, chest pain, palpitations, nausea, vomiting, abdominal pain, altered bowel movements, and urinary symptoms.

On physical examination, no rashes, petechia, or purpura were noted. He has no recent history of weight loss or sick contacts. There is no pertinent family history. The patient reported traveling to Saudi Arabia four months prior to the presentation. The patient sought medical advice in an outpatient urgent care clinic where laboratory work-up was pertinent for elevated liver enzymes and abdominal ultrasound was remarkable for hepatomegaly. In the emergency room, the patient was found to be febrile and tachycardic. He was given hydration and pain management. Laboratory work-up as an inpatient showed: SGPT of 485 U/L, SGOT of 399 U/L, LDH of 1089 U/L, GGT of 469 U/L, CRP of 3.13 mg/L, direct bilirubin of 1.73 mg/dL, and alkaline phosphatase of 366 U/L, consistent with liver function abnormalities. Laboratory work-up was negative for EBV, CMV, HAV, HBV, HCV, and brucellosis. Blood cultures were taken. A CT scan of the abdomen and pelvis showed hepatosplenomegaly along with sub-centimetric mesenteric lymphadenopathy. Chest x-ray was normal. Initially, the patient was treated symptomatically. During his hospital stay, he developed pancytopenia. A blood smear showed 4% atypical lymphocytes and thrombocytopenia. A bone marrow biopsy was done, and a medullogram showed the presence of some erythrophagocytic cells. The viral workup was repeated after 1 week of hospitalization and showed: CMV viral load of 11280 c/ml (positive), CMV IgM of 9.6 c/ml (positive), CMV IgG of 2.76 c/ml (positive), EBV IgM of 22/7 c/ml (borderline), and EBV IgG of > 400 c/ml (positive). Herpes viridae panels for both EBV and CMV were positive. The workup for PPD, Toxoplasma IgM, and malaria was negative. The patient was eventually diagnosed with CMV hepatitis.

During his stay, he developed desaturation and a persistent fever. A CT scan of the chest showed patchy areas of ground glass opacities in both lower lobes and in the lingula, consolidation in the right lower lobe, and small bilateral pleural effusions. Sputum culture grew alfa hemolytic streptococcus; both respiratory viral and bacterial panels were negative. Bronchoscopy was done, and the cell count showed a WBC of 250/µL, an RBC of 2000 /µL, neutrophils of 43/µL, and lymphocytes of 47/µL. Bronchoalveolar lavage taken showed adequate smears with dense cellularity consisting of reactive mesothelial cells and mixed inflammatory infiltrates, negative for malignant cells.

The patient was found to have CMV pneumonia, for which he was given a ganciclovir course. Our patient was eventually diagnosed with severe CMV hepatitis along with CMV pneumonia which is rare in an immunocompetent young male.

Discussion

Cytomegalovirus (CMV) belongs to the herpes-viridiae family and is a double-stranded DNA virus. CMV causes enlargement of infected cells which results in the formation of inclusion bodies seen on microscopy [6]. The virus has an incubation period of 4 to 6 weeks and has multiple routes of infection: oropharyngeal, genital, blood, breast milk, peri-natal and occupational exposure [8].

It is common knowledge that CMV infection is symptomatic in immuno-compromised patients with increased morbidity and mortality, whereas it is subclinical and asymptomatic in immuno-competent patients. That being said, around 10% of CMV infections cause symptoms in non-immuno-suppressed patients [4]. Notably, CMV infection presents as a mononucleosis-like syndrome in immuno-competent patients with a wide range of symptoms and laboratory findings: fever, malaise, leukopenia, thrombocytopenia, hepatitis and tissue invasive disease.

CMV infection can have a systemic involvement by targeting multiple organ systems. The virus can cause esophagitis, colitis, pneumonia, encephalitis, retinitis, myocarditis, hemolytic anemia, and portal venous thrombosis. Notably, CMV has a predilection for the gastro-intestinal tract (GIT) and central nervous system (CNS) [5]. The GIT is most commonly targeted by CMV and infected patients can have gastroenteritis, colitis and proctitis [7]. CMV-induced CNS involvement can present as meningo-encephalitis, myelitis and meningo-radiculopathy. CMV can trigger thrombosis of the vascular system by directly invading endothelial cells and altering their membrane. Such membrane alteration results in coagulation and thrombosis [7]. Ocular and pulmonary involvement are less common manifestations of CMV infection [1]. Nonetheless, our patient had bilateral pneumonia due to CMV infection exemplified by patchy areas of ground-glass opacities in both lower lobes and consolidation in the right lower lobe. CMV pneumonia seen in our patient highlights the rarity of the case because lung infection represents an uncommon involvement of CMV.

Steroid use, recent blood transfusions and a history of sick contact and recent travel are common risk factors for CMV infections [5]. Our patient had only a history of recent travel to Saudi Arabia 4 months prior to presentation.

Diagnosis of CMV infection should be made in context of a high clinical suspicion coupled with positive anti-CMV IgM or elevated IgG titers along with qualitative or quantitative CMV-DNA polymerase chain reaction (PCR) assay [6]. For instance, our patient had CMV-DNA levels of 11280 c/ml (POSITIVE), CMV IgM of 9.6 c/ml (POSITIVE) and IgG titers of 2.76 c/ml (POSITIVE). In light of this, quantitative PCR for CMV-DNA remains the standard diagnostic modality for early detection of CMV infections [8].

Sporadic cases of acute CMV hepatitis have been reported in immuno-competent patients and that was demonstrated in our patient who presented with a clinical profile mimicking a mononucleosis-like syndrome. Hepatitis A, B and C were ruled out. Serologies for EBV and herpes simplex virus were negative. Human immunodeficiency virus (HIV) rapid test was negative. Workup for autoimmune hepatitis and Wilson disease were also negative. Drug-induced liver injury (DILI) and alcohol-induced hepatitis were excluded.

CMV infection is usually self-limited in immuno-competent patients and anti-viral therapy is not warranted [8]. When indicated, CMV infection treatment options may include ganciclovir, valganciclovir, foscarnet and cidofovir. Decompensation of the liver is an indication for anti-viral therapy in acute CMV infection in immuno-competent patients [8]. Anti-viral therapy is notably associated with side-effects, such as myelo-suppression and hepatotoxicity. Anti-viral therapy is teratogenic and should be deferred during pregnancy [5]. Patients should adhere to anti-viral therapy for 2 to 3 weeks followed by a documented clearance of the viral load from the blood [3]. For instance, our patient received ganciclovir for a total of 21 days with symptomatic recovery and normalization of his liver functions tests within a few days from initiating anti-viral therapy.

Conclusion

CMV infection in an immuno-competent patient can masquerade as a mononucleosis-like syndrome. Acute CMV hepatitis is not uncommon in immuno-competent patients. Therefore, physicians ought to be vigilant to make a diagnosis of CMV infection in case of non-specific prodromal symptoms associated with acute hepatitis of unknown etiology. There are widely available non-invasive tests to diagnose CMV infection. Nonetheless, DNA quantitative tests remain the standard diagnostic modality when highly suspecting a CMV infection. Viral illness is usually self-limited and anti-viral therapy is not always warranted. When indicated, anti-viral therapy should be given for 2 to 3 weeks followed by a documentation of CMV viral load clearance from blood. Patients usually exhibit clinical improvement and liver enzymes normalization after a few days following anti-viral therapy.

Disclosure

- **Conflicts of Interest:** Authors have no conflicts of interest to disclose or declare.

- **Informed consent:** A signed written informed consent was obtained from the patient prior to writing the manuscript attesting his permission to publish his clinical history.

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