

Severe Cytomegalovirus Meningitis in an Immunocompetent Patient; A Case Report

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Abstract: Cytomegalovirus (CMV) is a DNA virus and is a member of the Herpesviridae family. There are few reports of CMV meningitis in immunocompetent adults. We reported an immunocompetent patient presenting with CMV meningitis and discussed the important relevant management issues. A 37-year-old male patient with fever, headache, confusion, nuchal rigidity and vomiting was presented to the emergency department. Chest radiography, brain CT and MRI were normal. Subsequently, he underwent a lumbar puncture and examination of the cerebrospinal fluid revealed lymphocytic pleocytosis. Polymerase chain reaction (PCR) of CSF was positive for cytomegalovirus DNA (Viral load=1000copies/ml) and therefore, treated with intravenous ganciclovir. In immunocompetent patients with acute meningitis with predominance of lymphocytes, CMV meningitis has to be included in the differential diagnosis and has to be ruled out with PCR testing of the cerebrospinal fluid.

Key words: Cytomegalovirus • Immunocompetent • Meningitis

INTRODUCTION

Cytomegalovirus (CMV) is a double-stranded DNA virus that belongs to subfamily of Beta-herpesvirinae and family of Herpesviridae [1]. The sero-prevalence of CMV ranges from 40% to 100% in various communities [2]. Human cytomegalovirus has an ability to remain latent within the body over long periods because the viral genome encodes multiple proteins that interfere with MHC class-I presentation of viral antigens and can later be reactivated [3]. Reactivation usually occurs in immunocompromised patients and causes severe diseases [4]. However, reactivation of CMV has been reported in “non-immunocompromised patients” such as severe trauma, sepsis, shock, burns and other critically ill patients [5]. T lymphocyte cells and NK cells have important role in controlling CMV infection and hence reactivation of CMV in immunocompetent persons is rare but CMV possesses a series of genes by which it escapes from immunosurveillance [6]. CMV infection in the

immunocompetent host is generally asymptomatic. However, it can also present with flu-like symptoms or more commonly, it can present as a mononucleosis syndrome [7]. The illness is generally self-limited, with complete recovery over a period of days to weeks. Antiviral therapy is usually not indicated because CMV is seldom associated with mortality in immunocompetent patients (< 1%) but substantial morbidity may occur in patients, such as meningitis, encephalitis and pneumonitis; and thus, accurate diagnosis is necessary [8].

There are only a few reports of CMV meningitis in immunocompetent patients. Therefore, we reported an immunocompetent patient presenting with CMV meningitis and discussed the important relevant management issues.

Case Presentation: A 37-year-old male patient with fever, headache, confusion and vomiting was presented to the emergency department of teaching hospital of Arak

University of Medical Sciences. He had fronto-temporal headache, fever and weakness for the five days prior to admission and took Acetaminophen and Ibuprofen at home. He did not give any history of trauma, tuberculosis or other diseases. On examination, He was febrile with a temperature of 38.3°C. The blood pressure was 110/70 mmHg, pulse 90 per minute regular and 18 respirations per minute. He was confused, agitated. On examination he was found to have neck rigidity, normal reflexes and no focal neurologic signs. Examination of optic fundi and cranial nerves was normal. There were no abnormal respiratory and abdominal symptoms or signs. Chest radiography, brain CT and MRI were normal. Subsequently, he underwent a lumbar puncture and examination of the cerebrospinal fluid revealed 185 cells/mm³, 95% lymphocytes, 48 mg/dl glucose levels (Serum glucose levels: 105 mg/dl), protein 85 mg/dl. Gram stain of the cerebrospinal fluid (CSF) was negative, as was culture of the CSF.

The patient was empirically treated with acyclovir intravenously. On the third day of admission the level of consciousness was decreased with respiratory distress due to brain edema occurred therefore, the patient was intubated and admitted in ICU. Basic investigations were as follows; Na⁺ 128 mmol/l, K⁺ 4.1 mmol/l, Serum creatinine 1.6 mg/dL, blood urea 33 mg/dL, White cell count 10400/mm³(PMN=%69, Lymph=%25), platelet count 156000/mm³, Hemoglobin 13.4 g/dl, AST 35u/l, ALT 48u/l, Bilirubin 0.8 mg/dL, ESR 16 mm/hr, CRP 1.8 mg/dl. Wright Agglutination test and VDRL in serum and CSF were negative. Serum IgG antibodies against cytomegalovirus (CMV) were positive, whilst IgM were negative. PCR testing on peripheral blood to detect cytomegalovirus DNA was not performed. The Rheumatoid Factor (RF), Anti-nuclear antibody (ANA), HBS-Ag, anti-HCV and anti-HIV were negative. Serum immunoglobulin levels and C₃, C₄ and CH₅₀ were normal.

Polymerase chain reaction (PCR) testing to detect *Mycobacterium tuberculosis*, HSV₁, HSV₂, Epstein-Barr virus (EBV) in the CSF and cytopathology of CSF for malignancy were negative but results of PCR on CSF was positive for cytomegalovirus DNA (Viral load=1000copies/ml).

In accordance with these results, treatment was changed to Intravenous ganciclovir and continued for 3 weeks. A repeat lumbar puncture 10 days after admission (7 days after ganciclovir therapy) showed 60

cells/mm³ (99% lymphocytes) and a decrease in CSF protein (39.5 mg%). The patient made an uneventful recovery and when last seen at follow up (60 days after discharge) was in good health.

DISCUSSION

In developed countries as many as 60–80% of the population will be infected with CMV by adulthood but its actual prevalence rate in Iran remains unknown [9]. In the majority of hosts, primary CMV infection is clinically asymptomatic. When symptomatic, CMV disease in immunocompetent individuals may present as a mononucleosis syndrome or as flu-like symptoms [10]. The virus can spread by horizontal transmission (Direct contact with virus containing secretions such as semen, urine, cervical secretions or saliva) or vertically via transplacental route [11]. When CMV produces a mononucleosis-like syndrome, the most common manifestations are pharyngitis, adenopathy, fever, fatigue and hepatitis. Arthralgia, skin rash, Headache and abdominal pain with diarrhea, may also occur. Laboratory abnormalities include elevated transaminases, thrombocytopenia, lymphocytosis or lymphopenia. The drug of choice for treatment of CMV disease is intravenous ganciclovir however one challenge is to this view, because there isn't enough evidence for the effectiveness of antiviral treatment of CMV meningitis in the immunocompetent patient. It is not clear whether CMV meningitis is a self-limited disease or a disease with potential catastrophic consequences for the patient [12].

In our patient, the presence of serum anti-CMV IgG in the absence of anti-CMV IgM indicates a previous primary CMV infection. CMV can be latent in the central nervous system (CNS); then, the absence of serum anti-CMV IgM with presence of CMV in the CSF, should be indicated of local (CNS) reactivation. The most sensitive way of detecting CMV in blood or other fluids may be by PCR because IgM can persist up to one year after infection [13]. Despite of CMV meningitis is rare in immunocompetent patients [14]. Also, that may be due to moderate accuracy of some routinely available diagnostic methods, such as serological tests and as a result underdiagnosing of CMV infections. Nevertheless, the use of PCR is increasingly employed in various centers around the world and has facilitated the diagnosis of various types of CMV infection.

CONCLUSIONS

In conclusion, severe life-threatening complications of CMV infection in immune-competent patients may not be as rare as previously thought. In immunocompetent patients with acute meningitis with predominance of lymphocytes, CMV meningitis has to be included in the differential diagnosis and has to be ruled out with PCR testing of the cerebrospinal fluid. Until prospective trials will clarify whether the disease needs treatment or not, we would suggest to treatment is probably warranted for patients with severe diseases such as meningitis.

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