Acute cytomegalovirus hepatitis in a non-immunosuppressed patient: a case report

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ABSTRACT

Cytomegalovirus (CMV) has high rates of seroprevalence and subclinical infection in the general population. The infection is habitually recognized in immunocompromised patients. However, in a state of immunocompetence, CMV usually presents as asymptomatic and is often revealed fortuitously on routine tests. A case of a 53-year-old female immunocompetent patient with CMV hepatitis is presented. Eight days prior to admission, the patient presented occasional fever, fatigue, myalgia and arthralgia associated with prior upper respiratory tract distress. The percutaneous liver biopsy revealed CMV inclusion bodies; CMV serology and the CMV DNA qualitative PCR test were positives. She was treated with ganciclovir.

When patients present non-specific prodromal symptoms pertaining to acute hepatitis with an unclear etiology, CMV infection should be considered.

BACKGROUND

Cytomegalovirus (CMV) is member of the family Herpesviridae and subfamily beta Herpesviridae that contains a large DNA genome of around 235 kb coding for over 200 genes. Adult infection is transmitted through vaginal secretions, sperm, urine, blood, breast milk, oropharyngeal secretions and iatrogenically. CMV infection is a significant cause of mortality in immunocompromised hosts. However, after primary infection with CMV, the virus becomes latent in several tissues and can later be reactivated and possibly cause esophagitis, colitis, pneumonia, retinitis, encephalitis, myocarditis, portal vein thrombosis, hemolytic anemia and pulmonary embolisms. CMV has high seroprevalence (40-100%) in the general population. Usually, the infection generated by this virus presents as asymptomatic in immunocompetent individuals and is often revealed fortuitously on routine examinations, suggesting high rates of subclinical infections. However, severe illness could be developed by primary CMV infection in such patients. Immune-competent adult patients infrequently present liver involvement; nonetheless, viral hepatitis is the most common cause of liver inflammation.

CASE REPORT

A 53-year-old female, full-time faculty professor, presented with an 8-day history of occasional fevers, fatigue, myalgia and arthralgia associated with prior upper respiratory tract discomfort. Medical records indicated primary hypothyroidism that is controlled with levothyroxine (125 μg/day). Patient denied use of alcohol, smoking, drugs, or contact with other harmful substances. General physical examination was normal, with the exception of
mild abdominal distension and fever of 105 °F. Laboratory exams showed chemistry and urinalysis without alterations. The complete blood count revealed leukocytes of 12.53 k/μL (4.50-11.50 k/μL), lymphocytes of 43% (18.0-42.0%), monocytes of 13% (2.0-11%) and normal platelet count. A normal CD4 count (1,600 cell/mm³). The serum liver profile revealed her bilirubin and prothrombin levels within normal parameters; however, serum aspartate aminotransferase (AST) was of 203 U/L (0-32 U/L), serum alanine aminotransferase (ALT) was of 286 U/L (0-33 U/L) and serum alkaline phosphatase (ALP) was of 160 U/L (35-105 U/L). HIV RNA test, Widal test and hepatitis A, B, and C serology were all negative. Hepatobiliar ultrasound and abdominal CT were normal. Following admission, patient continued to have arthralgia, temperature spikes ranging from 103 to 105 °F not responding to antipyretics, and semicomatose state. Blood, stool, urine and M. tuberculosis cultures showed no bacterial growth. C reactive protein was 44.9 mg/L (0-5 mg/L), erythrocyte sedimentation was 34 mm/h (0-15 mm/h), and liver enzyme levels remained high. Subsequently, her Epstein-Barr, influenza, chikungunya, dengue, adenovirus and herpes virus tests were negatives; however, CMV serology was positive with an IgM titre of 2.5 (0-0.99 Index), IgG of 213.9 (0-6 AU/mL), and also positive for a CMV DNA qualitative PCR test. Antinuclear antibody, ceruloplasmin level, liver-kidney microsomal antibody, anti-smooth muscle antibody determinations were negatives; thus, systemic lupus erythematosus, Wilson’s disease and autoimmune hepatitis were discarded. A percutaneous liver biopsy was then performed, revealing lobular and periportal infiltration of mononuclear cells (figure 1A) and minimal hepatic necrosis with CMV inclusion bodies (figure 1B).

Patient was treated with ganciclovir (5 mg/kd q12hr, x 14d) and intravenous hydration and was checked for fever patterns and liver-renal functions routinely. Fever subsided 10 days after her hospitalization. Repeated hepatic profiles revealed serum AST of 30 IU/L (0-32 U/L), serum ALT of 20 IU/L (0-33 U/L) and serum ALP of 64 IU/L (35-105 U/L). Titres of CMV IgM and IgG performed 15 days after discharge were 0.81 (0-0.99 Index) and 2.20 AU/mL (0-6 AU/mL) respectively, coherent with seroconversion. Two months after hospitalization, hepatic enzymes have remained constant at normal range.

DISCUSSION
CMV has high seroprevalence (40-100%) in the general population. Usually, the infection generated by this virus presents as asymptomatic in immunocompetent individuals and is often revealed fortuitously on routine examinations, suggesting high rates of subclinical infections. However, severe illness could be developed by primary CMV infection in such patients. Immunocompetent adult patients infrequently present liver involvement;

### Table I. Some cases of cytomegalovirus hepatitis in immunocompetent patients treated with antivirals

<table>
<thead>
<tr>
<th>Distinctive clinical manifestations</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td>Serum anti-CMV Ig M + serum pp65 antigenemia</td>
<td>Serum anti-CMV IgM + DNA qualitative PCR + in serum and cerebrospinal fluid</td>
<td>Serum CMV antigen+, Serum DNA qualitative PCR+ and +CMV antigen stain on liver biopsy</td>
</tr>
<tr>
<td>Antiviral</td>
<td>Valganciclovir</td>
<td>Acyclovir</td>
<td>Ganciclovir</td>
</tr>
<tr>
<td>Recovery time in days</td>
<td>28-35</td>
<td>21</td>
<td>84</td>
</tr>
<tr>
<td>Complication</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

Figure 1. A. Periportal infiltration of mononuclear inflammatory cells (200 μm, haematoxylin and eosin stain). B. Cytomegalovirus inclusion bodies were identified. (50 μm, haematoxylin and eosin stain).
Nevertheless, viral hepatitis is the most common cause of liver inflammation.\(^9\)

CMV infection can be detected by a positive anti-CMV IgM or an elevation in IgG titre, qualitative or quantitative PCR, immunofluorescence assay of CMV pp65 antigen in blood or in situ hybridization, and by cytopathology (CMV inclusion bodies).\(^{10,11}\) In this case, diagnosis of acute CMV hepatitis was made by positive CMV serology and PCR associated with increased rates of liver enzymes (ALT and AST).

Treatment of CMV hepatitis should be adjusted regarding individual patient needs, thus allowing for a personalized treatment approach. Some individuals respond to conservative management;\(^{12}\) however, in grave cases, the use of antiviral therapy is warranted, in our case the patient presented persistent fever an he was treated with ganciclovir (table I).\(^{13-15}\) Currently, guidelines for the treatment of CMV hepatitis in immunocompetent patients does not exist.

Essentially, when immunocompetent patients present non-specific prodromal symptoms associate with acute hepatitis from an unknown etiology, CMV hepatitis should be considered as a fundamental diagnosis.

REFERENCES