Medical Research Archives

ESMED
European Society of Medicine

OPEN ACCESS

Published: March 31, 2023

Citation: S Tougar, O Maghrabi, et al., 2023. Hepatitis and Pancreatitis Secondary to Cytomegalovirus Infection in Immunocompetent Patient, Medical Research Archives, [online] 11(3). https://doi.org/10.18103/mra.v11i3.3597

DOI
https://doi.org/10.18103/mra.v11i3.3597

ISSN: 2375-1924

CASE REPORT

Hepatitis and Pancreatitis Secondary to Cytomegalovirus Infection in Immunocompetent Patient

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ABSTRACT

Cytomegalovirus (CMV)is a member of the Herpes viridae family, its seroprevalence is high in the general population. CMV infection in the immunocompromised is a serious, sometimes fatal complication that can affect several organs. For immunocompetent patients, this infection is usually pauci- or asymptomatic, which evolves spontaneously favorably and does not require specific treatment. However, the primary infection can be exceptionally serious with multivisceral involvement, for which antiviral treatment is indicated with generally a quickly favorable response. In this article, we present an unusual case of hepatitis and pancreatitis due to CMV in an immunocompetent patient. The diagnosis was retained after excluding the most frequent and potential causes of acute hepatitis, with a brief review of the literature.

Keywords: Hepatitis, pancreatitis, Cytomegalovirus (CMV), immunocompetent, treatment.

Introduction:

Cytomegalovirus is double-stranded DNA virus that belongs to the Herpesviridae family. It is a highly prevalent and globally distributed virus, with a worldwide seroprevalence ranging from 60% to 100% [1] .

In immunocompetent individuals, CMV infection is usually asymptomatic or may cause a mild mononucleosis-like syndrome. In the other hand, CMV infection is responsible of significant morbidity and mortality in immunocompromised individuals [2]. In fact, Cytomegalovirus has the ability to disseminate throughout the haematogenous system, leading to acute inflammation in many different organs including severe hepatitis, colitis, meningitis and pneumonia[3,4].

While Cytomegalovirus is a well recognised pathogen in immunocompromised adults, the burden of the severe forms of CMV disease in immunocompetent adults is less well understood, especially its hepatic and pancreatic affection [5].

The aim of this article is to report an unusual case of hepatitis and pancreatitis due to CMV in an immunocompetent patient, in whom the diagnosis was confirmed after exclusion of other more common causes of the acute hepatitis.

Case presentation:

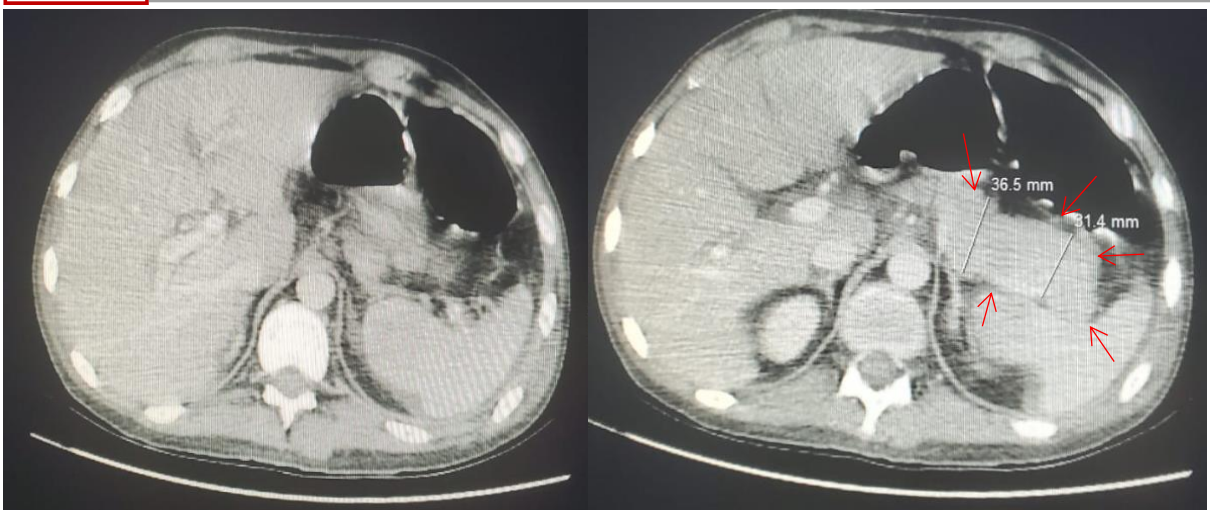
Patient X, 17 years old, with no significant medical history, was admitted for progressively worsening generalized muco-cutaneous jaundice dating up to a month before his admission without clinical signs of cholestasis, associated to an hemorragic syndrome comprised of gingival bleeding, epistaxis along with asthenia, anorexia and weight loss.

The clinical examination upon admission found a conscious patient with a Glasgow of 15/15, pupilles were symmetrical and reactive, he had no sensory or motor deficits, and was hemodynamically stable, abdominal examination revealed sensitivity of the right upper quadrant and the epigastric region with hepatomegaly and a negative murphy sign.

A biological workup found elevated liver enzymes aspartate transaminase(ASAT): 3896 UI/L, alanine transaminase (ALAT): 4021 UI/L (more than 10 times normal), mixed hyperbilirubinemia (direct bilirubin: 58mg/L, total bilirubin: 203 mg/L and indirect bilirubin: 144mg/l, 10 times normal), Lactate Dehydrogenase (LDH) LDH levels at 273 UI/L, with no signs of biological cholestasis, Albumine at 33g/l, low prothrombin time at 40%, factor V within normal range at 102%, and a serum lipase of 270 UI/l (4 times the normal range), C-reactive protein (CRP) at 33.2 mg/l, a complete blood count revealed pancytopenia, more specifically normochromic normocytic anemia at 10 g/dl of hemoglobine, leucocytopenia at 1120 elements/mm3 (neutrophils: 680 el/mm3, lymphocytes: 290 el/mm3) and thrombocytopenia at 88000 el/mm3 which prompted us to perform a bone marrow aspiration which confirmed the peripheral nature of the pancytopenia, a COVID19 PCR test was preformed and came back negative.

As for the imaging tests performed: An abdominal ultrasound showed acalculous cholecystitis as well as hyperechogenicity of the intrahepatic portal vessel walls, an aspect that is compatible with viral hepatitis.

An abdominal CT scan revealed pancreatitis that is graded B in the Balthazar score, along with homogenous hepatomegaly, completed by magnetic resonance cholangiopancreatography which found no obstuctions.



A **B**

Figure1: transversal Computed tomography (CT)scan showing, **A:** homogenous hepatomegaly and **B:** pancreas tumefied increases in size (red fleche), with loss of physiological lobulations enhanced homogeneous after injection of iodinated contrast agent (pancreatitis graded B in the Balthazar score).

Serologies of hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV), hepatitis E virus (HEV) and Epstein-Barr virus (EBV) all came back negative. All autoantibodies tested for autoimmune hepatitis are negative, while the cytomegalovirus PCR was positive at 753 UI/ml, an indirect ophthalmoscopy was preformed and was normal. Human immunodeficiency virus (HIV)screening was negative, immunoglobulin and complement levels were within normal range a lymphocyte subset panel was preformed and came back normal.

The patient was put on antiviral treatment: Ganciclovir 5mg/kg every 12 hours for a duration of 21 days. His progression was favorable with normalization of hepatic enzymes, CRP, serum lipase as well as the complete blood count (CBC). The patient was subsequently transferred to the infectious disease department.

Discussion:

The Cytomegalovirus (CMV) is a DNA virus belonging to the Herpesviridae group. Its seroprevalence is high within the general population (40 to 100%), with variations among ethnic groups and regions[6] CMV infections are usually mild or asymptomatic in immunocompetent adults and can clinically manifest during the primary infection or reactivation of the virus. Transmission can occur from mother to child in the perinatal or postnatal period, the virus can be acquired through saliva, sexual contact and blood, contamination through transplanted organs has been reported within literature[7], there have been no communicated cases of transmission through inhaled aerosols [8].

The most observed symptoms are malaise (67%), fever (46%), accompanied by disruptions of the liver function (69%), jaundice is found in 9% of immunocompetent patients. The symptomatology in our case is marked by the subacute onset and progression of the jaundice associated to an hemorrhagic syndrome. The Hepatomegaly and splenomegaly are exceptionally described in immunocompetent individuals [11,9].

As for biological findings, the elevation of liver enzymes is usually moderate (less than 5xN). LDH levels are high with a low ALAT/ LDH ratio. Cholestatic forms have been reported. In our case there was a significant elevation of liver enzymes (more than 10 times normal) without biomarkers of cholestasis and with a slightly high level of LDH. As for the cell blood count (CBC), Nolan et AL. have reported lymphocytosis in 68.8% of primary infections [12]. Our patient had pancytopenia up on admission.

Outcome is usually favorable within 8 weeks in adolescent and adult patients, prolonged forms have been reported in children. Most severe forms were those with gastrointestinal tract involvement (colitis) and central nervous system complications[9], CMV hepatitis has also been observed in pregnant woman and can be severe in this subgroup [10].

Our patient presented a severe form of CMV infection with both hepatic and pancreatic complications, which progressed favorably under treatment.

Diagnosis of CMV hepatitis is based on the detection of CMV IgM in an immunocompetent patient during primary infection, as well as through the detection of the virus or its antigens and detection of the viral genome[13].

In immunocompromised patients or in the case of reinfection, anti-CMV antibodies have no diagnostic value, making the diagnosis more difficult. CMV viremia is highly in favor of the diagnosis but is often insufficient for confirmation. A hepatic biopsy is usually necessary [7].

In our case, the confirmation was obtained through the detection of the viral genome using PCR.

We recognize the inconvenience of not being able to obtain definitive proof of the hepatitis and pancreatitis through histology as a biopsy was contraindicated due to the severe thrombocytopenia. The clinical improvement was quick after Ganciclovir was initiated and histology would not have changed management. we attempted to compensate the lack of histological proof by eliminating all other probable causes of hepatitis (viral, structural, vascular and autoimmune).

Antiviral treatment of CMV hepatitis is indicated in severe or prolonged forms in the immunocompetent and aways in the immunocompromised [14]. Protocols can use Ganciclovir, foscarnet and acyclovir sometimes in association with anti CMV gammaglobulines.

Ganciclovir is the corner stone of the treatment, with a dose of 5mg/kg/12h, given intravenously, during at least 21 days. Foscarnet is a secondary option, used mainly in case of neutropenia or resistance to Ganciclovir at a dose of 90mg/kg every 12 hours intravenously for a period of 14 to 21 days[9] owing to its potential toxicity, Ganciclovir is often reserved for severe infections [15].

Conclusion:

Cytomegalovirus pancreatitis and hepatitis are rare. The moral of this article is to look for viral infections other than those caused by hepatitis A, B or C, namely CMV, which can lead to fulminant hepatitis with non negligeable morbimortality, especially if it goes unnoticed. Treatment with Ganciclovir is generally reserved for severe CMV infections, due to the potential side effects. Early diagnosis and treatment of CMV hepatitis and pancreatitis may not only improve prognosis but can also spare the patient unnecessary and invasive procedures.

Conflict of interest:

The authors report no conflict of interests

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