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Case Report

A rare case of cytomegalovirus hepatitis mimicking malignancy in an immunocompetent adult ☆

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ABSTRACT

Cytomegalovirus (CMV) is a highly prevalent pathogen that remains dormant in majority of the cases. Severe CMV infection is generally limited to immunocompromised hosts. While occasional cases of CMV hepatitis are observed in healthy immunocompetent hosts, it is very rare to find this associated with focal liver lesions mimicking malignancy. Cases of non-immunosuppressed CMV reactivation, CMV-associated liver lesions, and CMV-associated portal vein thrombosis have all been reported individually, we present a single case of CMV with all of these rare manifestations.

Introduction

CMV hepatitis is commonly encountered in immunocompromised hosts, but only sporadic cases of severe CMV hepatitis are reported in immunocompetent hosts [1].

We present a case of a 76-year-old immunocompetent male with nonspecific constitutional symptoms whose CT abdomen showed liver lesions that were highly suspicious for a neoplastic process. Further investigations with liver biopsy, liver MRI, and CMV viral load established CMV hepatitis as the cause. Treatment with antiviral therapy resulted in reduction in the CMV viral load and near-resolution of the liver lesions on follow-up imaging. Additionally, portal venous thrombosis was demonstrated on CT scan, which is a known but rare complication of CMV [2].

Case report

A 76-year-old male with no prior history of immunosuppression or malignancy presented to the emergency department

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with constitutional symptoms of lethargy, reduced exercise tolerance, loss of appetite and weight loss of about 4-kg over a period of 3-4 weeks. He was an ex-smoker with a significant 50-pack-year smoking history and consumed between 50 and 70 g of alcohol (5-7 standard drinks) daily. He reported family history of pancreatic cancer in his brother.

There was no subjective or documented fever, and no peripheral stigmata of chronic liver disease, jaundice, palpable organomegaly or lymphadenopathy. Laboratory tests showed mild derangement of liver function tests with elevated liver enzymes, normal bilirubin, low albumin, normal APTT, slightly raised prothrombin time, and INR of 1.4.

A contrast-enhanced CT scan of the head, chest, abdomen and pelvis was performed to screen for an occult malignancy, which was the topmost differential diagnosis based on the history of weight loss and nonspecific constitutional symptoms in an elderly patient.

CT head showed no intracranial mass or region of abnormal enhancement; and CT chest showed no suspicious pulmonary nodules or mass.

CT abdomen showed a large mass measuring approximately 7.5 × 6.3 × 8.0 cm with ill-defined margins and heterogeneous low density within hepatic segments 5 and 6 and extending to the hilar region (Fig. 1A). A further region of wedge-shaped heterogeneous low-density was noted in segment 8 (Fig. 1B).There was marked intrahepatic biliary dilatation, but no extrahepatic biliary dilatation. Additionally, thrombi were noted in both the right (Fig. 1C) and left portal veins. There was mild to moderate ascites. There was no evidence of pathologically enlarged lymph nodes, primary malignancy outside the liver or metastatic disease.

These findings were highly suspicious for a primary hepatobiliary malignancy.

Tumor marker assay was negative for alfa fetoprotein and carcinoembryonic antigen but showed raised CA19.9 at 51 IU/mL (ref. range <37).

A liver biopsy was performed from the largest lesion in the right hepatic lobe. Histopathology showed partly necrotic cores of liver tissue with loss of normal liver parenchyma, which was replaced by fibrotic stroma containing a polymorphous inflammatory infiltrate. Cytomegalovirus (CMV) inclusions were seen involving hepatocytes, biliary epithelium and endothelial cells, which were confirmed on CMV immunohistochemistry (IHC) stain (Fig. 4). There was no evidence of malignancy. An ascitic fluid aspiration was concurrently undertaken which demonstrated leucocytosis (predominantly monocytosis) on cell count with lymphocytosis on cytology.

MRI of liver with gadolinium contrast was performed for further clarification. The largest liver lesion (59.2 × 43.9 mm) involving segment 5 and 6 was hypointense on T1, moderately hyperintense on T2 (Fig. 2A), with enhancement increasing across the phases. There was no associated diffusion restriction. Areas with similar characteristics were also seen within segments 2, 5, 6 and 8 along the peri-vasculobiliary tracts, associated with marked intrahepatic biliary duct dilatation (Fig. 2B). The impression was of presumed inflammatory mass-like lesions secondary to CMV hepatitis.

Subsequently testing for CMV was performed which showed a positive CMV IgM antibody and a positive CMV DNA PCR. CMV viral load was 14,481 copies/mL.

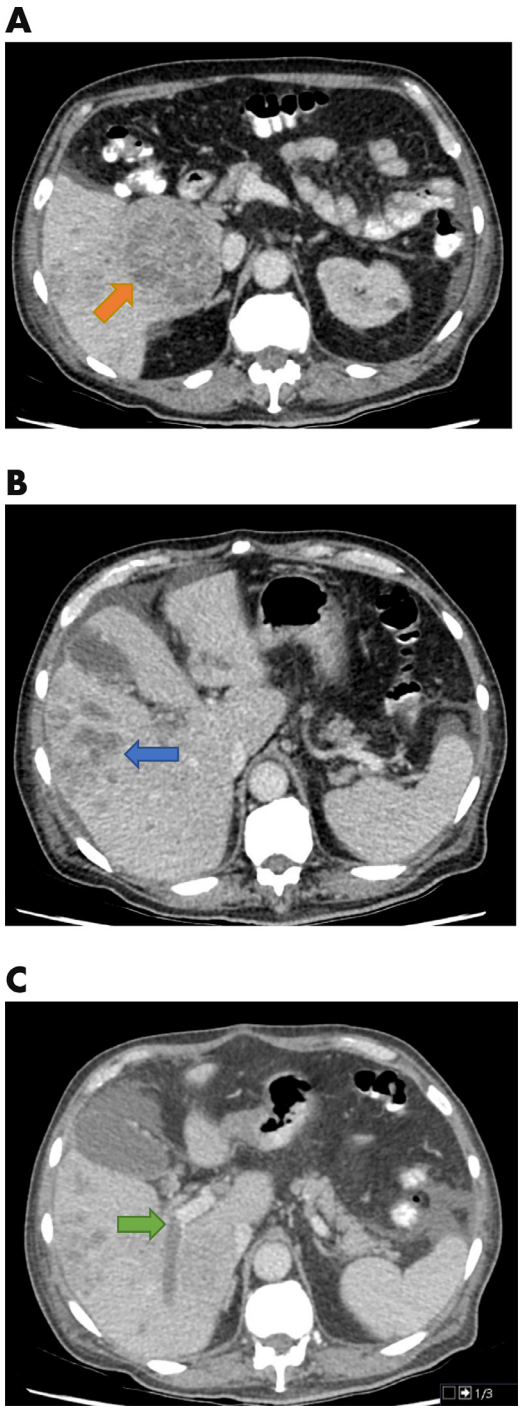

Fig. 1 – (A) Axial CT abdomen image after administration of intravenous iodinated contrast in portal venous phase showing a large ill-defined mass-like region of heterogeneous low density in hepatic segments 5 and 6 measuring approximately 7.5 x 6.3 x 8.0 cm, extending to the hilar region (orange arrow). (B) Wedge-shaped heterogeneous density lesion involving segment 8 (blue arrow). (C) Thrombus within the right portal vein (green arrow).

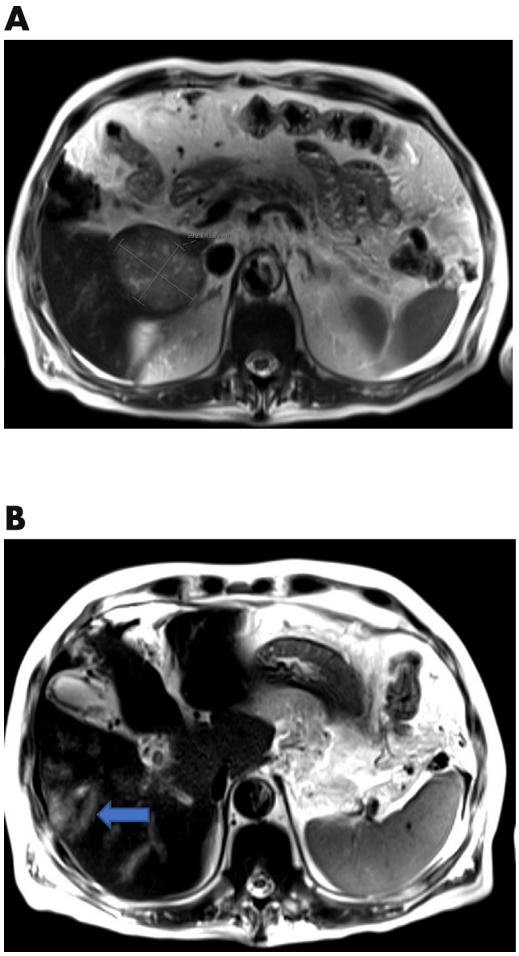

Fig. 2 – MRI liver with intravenous gadolinium contrast on axial T2 sequence showing moderately hyperintense 59.2 x 43.9 mm mass within hepatic segments 5 and 6 (A) and within segment 8 (B) along perivasculobiliary tracts (blue arrow).

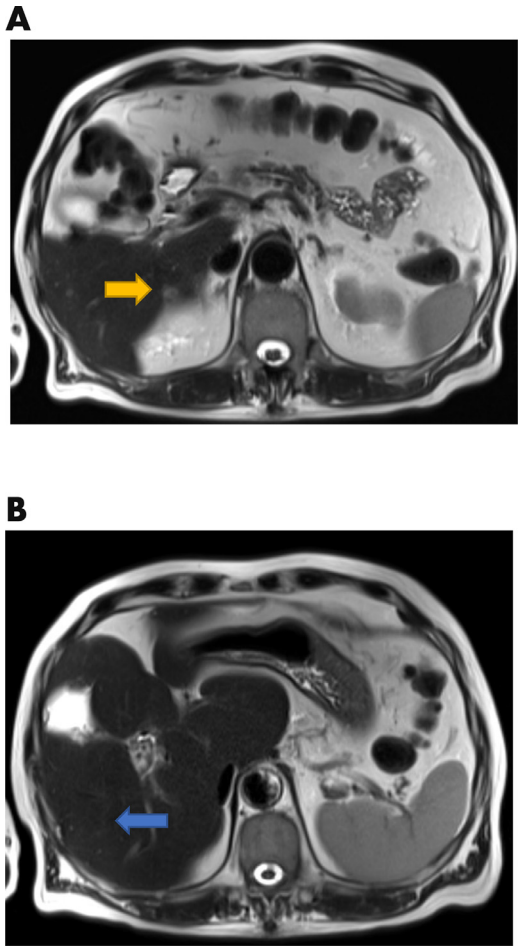

Fig. 3 – Follow-up MRI liver on axial T2 sequence showing near-resolution of segment 5 and 6 liver lesion (A) (yellow arrow) and segment 8 lesions (B) (blue arrow).

He was commenced on antiviral therapy with Valganaciclovir 900 mg orally twice daily for a total duration of 4 weeks. He was also commenced on anticoagulation with warfarin for portal venous thrombosis.

Viral load performed after 2 weeks of antiviral therapy showed a significant reduction in the count to less than 150 copies/mL. At 2-month follow-up, the patient was completely asymptomatic and had returned to his premorbid function. Follow-up MRI was performed at 3 months, which showed resolution of portal venous thrombosis and near-complete resolution of the liver lesions (Fig. 3).

Discussion

CMV is a member of the Herpesviridae family with its nomenclature related to the fact that it causes cell enlargement and the presence of characteristic inclusion bodies within the infected cells [3]. Like other herpes viruses, CMV is capable of creating an optimal environment for its continuous replication, permitting a lifelong latent infection [1]. Despite its high prevalence, it follows an asymptomatic course in the vast majority of the cases, and severe illness is usually limited to immunocompromised hosts [1].

CMV hepatitis is commonly encountered in immunocompromised hosts but is a relatively rare entity in immunocompetent hosts [1]. Most cases present with malaise, abdominal pain and fever [1]. Cases of fulminant hepatitis with cholestasis, ascites and portal venous thrombosis requiring antiviral therapy and anticoagulation therapy are rare in immunocompetent patients [2,4].

The precise mechanism of liver damage from CMV-hepatitis is not well-understood and the most accepted hypothesis suggest tissue damage through indirect cytopathogenicity, including activation of cytotoxic T cell reactions against CMV-infected cells [1]. Hepatocytes are most commonly infected, and bile duct cells are rarely involved [1]. One case study has described intrahepatic and common bile duct dilatation related to CMV infection [5]. Case reports exist of CMV causing hepatitis alone, granulomatous hepatitis, necrotizing hepatitis and portal vein thrombosis [1,2]. CMV

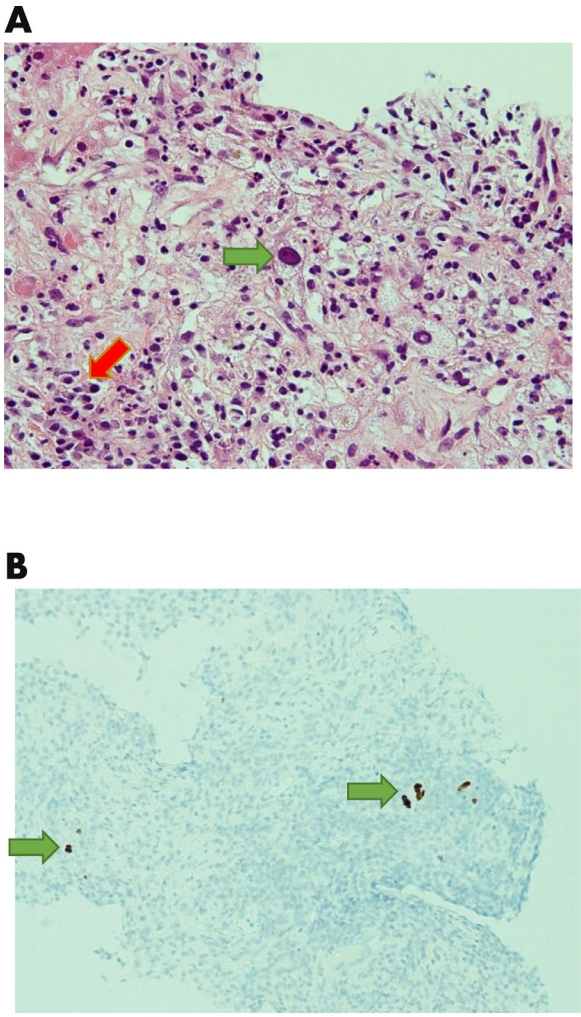

Fig. 4 – Histopathology from liver biopsy. (A) H&E high power image, x400 (Hematoxylin and eosin) demonstrating CMV inclusion bodies (green arrow), and infiltrate of inflammatory cells which include plasma cells (red arrow). (B) CMV IHC stain, x200 (immunohistochemistry staining) demonstrating inclusion bodies which stain a distinctive brown (green arrows).

has shown to have a procoagulant effect from direct infection of endothelial cells and systemic inflammatory response [6].

Diagnosis of CMV hepatitis, like other acute viral hepatitis, is primarily based on clinical, laboratory and virological findings [7]. CMV infection is established by serology, polymerase chain reaction test and immunostaining [5–8]. Imaging is generally performed to exclude other pathologies such as malignancy or cirrhosis (21-11). Imaging findings of acute viral hepatitis are nonspecific and consist of hepatomegaly, periportal edema, gall bladder wall edema, and occasionally ascites [7]. Imaging findings in cases of CMV hepatitis are generally inconspicuous [3,9]. One case in literature has reported multifocal fatty infiltration caused by CMV in a patient known to have AIDS [10]. And a hepatic mass related to CMV has been reported in a pediatric patient [11].

In our case the combination of nonspecific constitutional symptoms and weight loss in an elderly male with imaging findings of hepatic mass, intrahepatic biliary dilation in the absence of gall stones [12], portal venous thrombosis and ascites would be in keeping with a hepatobiliary malignancy [13]. On contrast-enhanced MRI the liver lesions demonstrated T2 hyperintensity with enhancement increasing across all the phases, without associated diffusion restriction. While these findings are not typical of a hepatocellular carcinoma, they can be seen in cases of intrahepatic cholangiocarcinoma [13,14].

Subsequently, histopathology and immunohistochemistry unequivocally suggested CMV as the cause and showed the absence of malignant cells. This was further supported by a positive CMV IgM antibody and positive CMV DNA PCR, along with high CMV viral load. In the light of these findings, MRI changes can be explained by inflammation resulting caused by CMV.

After completing 4 weeks of antiviral treatment the patient was asymptomatic and there was a significant drop in CMV viral load. Follow-up MRI at 3 months showed near-resolution of liver lesions. These findings confirm CMV hepatitis as the diagnosis and exclude malignancy.

While cases of non-immunosuppressed CMV reactivation [9], CMV-associated liver lesions simulating metastases [10], CMV-hepatitis presenting as a hepatic mass [11], and CMV-associated portal vein thrombosis [2] have all been reported individually, to have all these occur in the same patient would be very rare, and hence this case brings attention to this uncommon manifestation of a common disease.

Patient consent

A written, informed consent was obtained from the patient for publication of this case and any accompanying images.

REFERENCES

[1] Da Cunha T, Wu GY. Cytomegalovirus hepatitis in immunocompetent and immunocompromised hosts. J Clin Transl Hepatol 2021:1–10. doi:10.14218/jcth.2020.00088.
[2] Burkey C, Teng C, Hussein KI, Sabetta J. Cytomegalovirus (CMV)-associated portal vein thrombosis in a healthy, immunocompetent man. BMJ Case Rep 2020;13(12):e238645. doi:10.1136/bcr-2020-238645.
[3] Zahid M, Ali N, Saad M, Kelly P, Ortiz A. Acute cytomegalovirus (CMV) hepatitis in an immunocompetent adult. Am J Case Rep 2020;21 e925495-1e925495-5. doi:10.12659/AJCR.925495.
[4] Qian J-Y, Bai X-Y, Feng Y-L, Zhu W-J, Yao F, Li J-N, et al. Cholestasis, ascites and pancytopenia in an immunocompetent adult with severe cytomegalovirus hepatitis. World J Gastroenterol 2015;21(43):12505. doi:10.3748/wjg.v21.i43.12505.
[5] Win M, Myat T. S1515 acute cytomegalovirus infection can present with acute obstructive cholangitis. Am J Gastroenterol 2021;116:S690. doi:10.14309/01.ajg.0000779592.63649.4c.
[6] Squizzato A, Ageno W, Cattaneo A, Brumana N. A case report and literature review of portal vein thrombosis associated

with cytomegalovirus infection in immunocompetent patients. Clin Infect Dis 2007;44(2):e13–16. doi:10.1086/509641.
[7] Ros PR. Imaging of diffuse and inflammatory liver disease. In: IDKD Springer Series; 2018. p. 237–46. doi:10.1007/978-3-319-75019-4_22.
[8] Moreno-Treviño MG, Garza-Garza GG, Ulloa-Ortiz Ó, Rivera-Silva G. Acute cytomegalovirus hepatitis in a non-immunosuppressed patient: a case report. Rev Latinoam Patol Clin Med Lab 2017;64(2):60–2.
[9] Gupta P, Suryadevara M, Das A. Cytomegalovirus-induced hepatitis in an immunocompetent patient. Am J Case Rep 2014;15:447–9. doi:10.12659/ajcr.890945.
[10] Vieco PT, Rochon L, Lisbona A. Multifocal cytomegalovirus-associated hepatic lesions simulating metastases in AIDS. Radiology 1990;176(1):123–4. doi:10.1148/radiology.176.1.2162068.
[11] Wagoner M, Saliba C, Melkonian V, Miyata M, Blewett C, Greenspon J. A rare case of cytomegalovirus-induced hepatitis presenting in a pediatric patient as a hepatic mass. J Pediatr Surg Case Rep 2022;79:102212. doi:10.1016/j.epsc.2022.102212.
[12] Jhaveri KS, Halankar J, Aguirre D, Haider M, Lockwood G, Guindi M, et al. Intrahepatic bile duct dilatation due to liver metastases from colorectal carcinoma. Am J Roentgenol 2009;193(3):752–6. doi:10.2214/ajr.08.2182.
[13] Balogh J, Victor D, Asham EH, Burroughs SG, Boktour M, Saharia A, et al. Hepatocellular carcinoma: a review. J Hepatocell Carcinoma 2016;3:41–53. doi:10.2147/jhc.s61146.
[14] Vanderveen KA, Hussain HK. Magnetic resonance imaging of cholangiocarcinoma. Cancer Imaging 2004;4(2):104–15. doi:10.1102/1470-7330.2004.0018.