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A rare case of peliosis hepatis in primary immune deficiency

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Abstract

Peliosis hepatis is a rare condition characterized by blackish-blue blood-filled cavities in hepatic parenchyma caused by dilatation of hepatic sinusoids. Peliosis hepatis has been described in secondary immunodeficiencies and certain medications. We present the first case of peliosis hepatis in a patient with a primary immunodeficiency, common variable immunodeficiency. A 44-year-old African-American male presented with gastrointestinal bleeding and elevated liver function tests. His medical history included common variable immunodeficiency and chronic kidney disease. The patient had jaundice, regenerative nodules on liver pathology, and low immunoglobulin levels. A magnetic resonance imaging of the abdomen with contrast revealed a cirrhotic liver, a 5×3 cm lesion, and poorly defined nodules which had decreased enhancement. A computed tomography-guided liver biopsy revealed peliosis hepatis, focal nodular hyperplasia, and fibrosis. No other etiology of his liver disease was found. The etiology of peliosis hepatis in patients with primary immunodeficiencies remains unclear. Additional studies are needed to understand the underlying mechanisms.

Keywords

Peliosis hepatis, common variable immunodeficiency, focal nodular hyperplasia

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Introduction

Peliosis hepatis is a term used to describe blackish-blue blood-filled cavities in the hepatic parenchyma caused by dilatation of hepatic sinusoids. Certain patients with peliosis hepatis may be at risk for portal hypertension, peritoneal hemorrhage, and variceal bleeding. In particular patients, the condition may progress to eventually require liver transplantation or death. Peliosis hepatis is a relatively rare condition, and a diagnosis made solely on pathological examination. Peliosis hepatis was first termed by Schoenlank in 1916. Peliosis hepatis had been previously described in patients with secondary immunodeficiency, such as in patients with HIV, patients on chronic steroids, or patients who were ill with underlying cancer or tuberculosis.[1,2] *Bartonella* infections have also been implicated and are believed to be a cause of peliosis hepatis, particularly in HIV patients. We present a case of peliosis hepatis in a patient with common variable immunodeficiency (CVID), a primary immunodeficiency. This case highlights the importance of including primary immunodeficiencies in the differential diagnosis for peliosis hepatis.

Case report

A 44-year-old African-American male presented to our hospital, transferred from an outside hospital, with gastrointestinal bleeding and elevated liver function tests. The patient had a prior history of chronic kidney disease, common variable immunodeficiency (CVID), and had been previously diagnosed with cryptogenic cirrhosis. The patient was diagnosed with CVID in 2012 after presenting with jaundice, regenerative nodules on liver pathology and low

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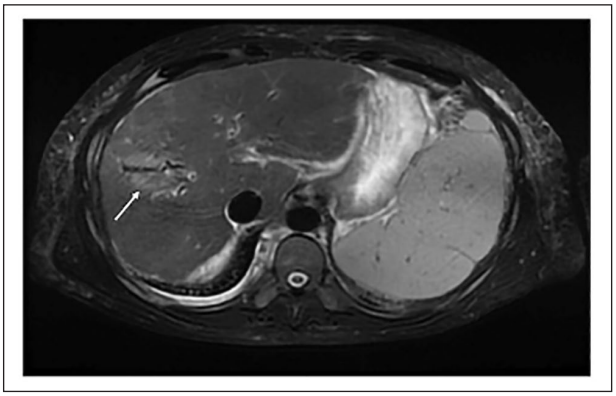

Figure 1. MRI abdomen: 5 × 3 cm liver lesion and numerous poorly defined nodules.

immunoglobulin levels: IgM, IgA, and IgG. He reported a history of multiple pneumonias and was started on Intravenous immunoglobulin (IVIG) treatment but was not adherent to this therapy. Records from 3 years prior revealed his liver was previously functional and pathology results from 3 years prior did not reveal cirrhotic morphology. On admission to the hospital lab values revealed the following: alanine transaminase (ALT) = 33 U/L, aspartate aminotransferase (AST) = 93 U/L, alkaline phosphatase = 262 U/L, total bilirubin = 25.6 mg/dL, direct bilirubin = 14.1 mg/dL, international normalized ratio (INR) = 1.3, platelets = 78,000 × 10^3/μL, and hemoglobin = 7.6 g/dL. Prior to transfer to our hospital, immunoglobulin levels were as follows: IgG = 285 mg/dL, therefore, he was given IVIG dosed at 400 mg/kg. On arrival at our hospital, his other immunoglobulin values were as follows: IgG = 839 mg/dL, IgM = 104 mg/dL, IgA < 6 mg/dL (15 days post-IVIG infusion). Magnetic resonance imaging (MRI) with and without contrast of the abdomen was performed which revealed a cirrhotic liver, a slightly T2 hyperdense 5 × 3 cm liver lesion (Figure 1). After contrast administration, this lesion was hypodense compared to the liver parenchyma along with numerous poorly defined nodules throughout the liver. To identify the etiology of his liver abnormalities, the patient underwent computed tomography (CT)-guided liver biopsy. Histopathology revealed peliosis hepatis and nodular regenerative hyperplasia (NRH), along with fibrosis not consistent with cirrhosis.

Patient underwent esophagogastroduodenoscopy (EGD), which revealed portal hypertensive gastropathy and a pyloric ulcer. This was treated with local epinephrine and cautery. Further evaluations of causes of liver disease were performed, although were not diagnostic of an underlying cause (see Table 1). The patient denied alcohol use, drug abuse, was HIV Ab negative and *Bartonella* IgM and IgG were negative. The reliability of *Bartonella* immunoglobulin levels in this patient is low due to his CVID. A Warthin–Starry stain for *Bartonella* was negative. No other etiology of his liver disease was found. During his hospitalization, the patient had experienced recurrent fevers yet no infectious source could be identified. The patient continued treatment with monthly IVIG treatment.

Table 1. Additional studies performed to evaluate cause of liver disease.

Transthoracic echocardiogram
CT chest
CT abdomen
Right heart catheterization
Quantiferon

CT: computed tomography.

The patient's liver function continued to deteriorate. The patient was listed for a liver transplant, but was found not to be a candidate due to social issues. He continued to require multiple hospitalizations for treatment of gastrointestinal (GI) bleeding, lower extremity cellulitis, and *C difficile* colitis. The patient was ultimately placed into hospice care and succumbed to complications of his NRH 3 weeks later.

Discussion

Peliosis hepatis is a rare condition, identified by the dilatation of the space of Disse, leading to blood-filled cavities spread randomly throughout the hepatic parenchyma. On pathologic evaluation (Figure 2), it is noted that our patient's sinusoidal cavities were enlarged and filled with red blood cells. Trichrome staining of this sample revealed perisinusoidal fibrosis (Figure 3). These findings are typical of peliosis hepatis.[3–5] Two histologic patterns of peliosis hepatis have been identified: phlebectatic peliosis which characterized by distended cavities lined by fibrosis or endothelium while in the parenchymal peliosis, the cavities are not lined by fibrous tissue or sinusoidal cells but may be associated with hemorrhagic necrosis.[6] Some consider both patterns to be one process that started by distended cavities (parenchymal pattern) and then re-endothelialize and progressed to the phlebectatic pattern. In our case, the cavities were lined by endothelial cells consistent with phlebectatic pattern. There is no evidence in the literature that the histologic patterns play a role in the clinical course of the disease. The clinical course is determined by the underlying disease that caused the peliosis. Our patient's pathology result read a final diagnosis of peliosis hepatis with NRH. NRH is also known to present in patients with CVID. It is estimated that between 5% and 12% of patients with CVID may have NRH.[7,8] NRH may be a severe complication in patients with CVID, with a potential to lead to fatal liver disease.

The etiology of peliosis hepatis remains unclear. Peliosis hepatis has only been once mentioned to have occurred in a patient with CVID.[8] The more frequent occurrence of it among patients with secondary immunodeficiency and patients who begin immunosuppression, suggests that this condition is allowed by the malfunction of the immune system. Additional studies are needed to understand the underlying mechanisms

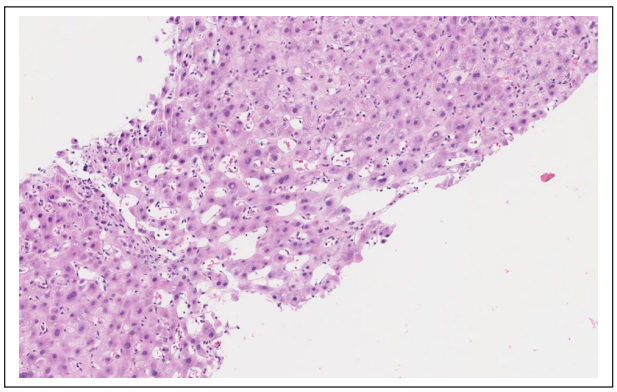

Figure 2. Sinusoidal dilatation.

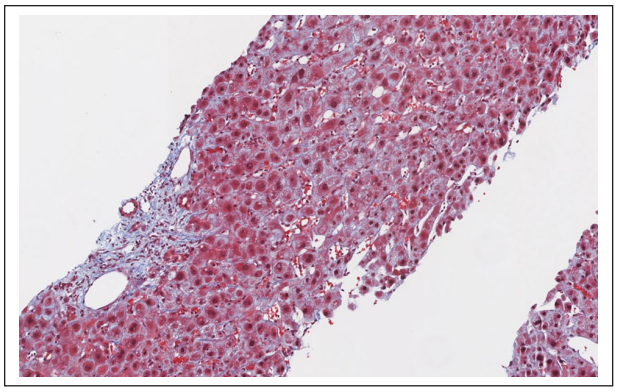

Figure 3. Perisinusoidal fibrosis.

in those with primary immunodeficiency are needed. Peliotic lesions have been reported in the liver, spleen, and lungs. These cavities are known to lead to organ dysfunction in the affected organ. Reports of fatalities secondary to ruptured peliotic lesions have also been documented.[2,4,5] By studying cadmium acute hepatotoxicity in a mouse model, it has been recognized that sinusoidal cell apoptosis is likely a precursor for peliotic lesions.

Infections have been implicated as factors for peliosis hepatis, particularly in patients with HIV.[9–11] *Bartonella* species have been identified in HIV patients within sinusoidal epithelial cells which may ultimately lead to damage to the sinusoidal epithelial cell lining. Titers can be used to assist in the diagnosis and identification of *Bartonella* infection, although in a patient with CVID, these results are unreliable due to IVIG therapy. Warthin–Starry stain may be used to assist in the identification of *Bartonella* species.[9] This patient's samples were stained per Warthin–Starry protocol and were negative. Scanning electron microscopy is another method in which tissue may be examined for *Bartonella* infection. Peliosis hepatis is rarely identified in healthy immunocompetent individuals with *Bartonella* infection as these patients tend to present with cat scratch disease.[12] It has also been shown that HIV patients may acquire peliosis hepatis in association with other chronic infections such as tuberculosis.[11] Medications have been reported to be inciting factors for peliosis hepatis. Reports indicate that azathioprine, cyclosporine, oral contraceptives, steroids, and many other medications have all been associated with new cases.

Lesions of peliosis hepatis can be suggested on imaging such as MRI combined with diffusion weighted imaging and positron emission tomography (PET)/CT.[13–15] Definitive diagnosis is still made using histopathology. These blood-filled lesions can appear similar to hemangiomas on imaging, although hemangiomas highly over-express CD34, which is a marker for reticulin and fibrous tissue.[16–18] CD34 positivity is also noted in normal liver tissue. This patient's pathology is not consistent with hemangioma (Figure 2).

Conclusion

This case report features the incidence of peliosis hepatis in a patient with CVID and nodular regenerating hyperplasia. This case also highlights the fact that one should consider primary immunodeficiency in the differential diagnosis of peliosis hepatis. Diagnostic work up of a patient with peliotic lesions should include *Bartonella* immunoglobulin testing (if applicable) and/or tissue examination using Warthin–starry staining of biopsy sample or SEM.

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Ethical approval

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Informed consent

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