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CASE REPORT

Late-onset cytomegalovirus cholangiopathy in a renal transplant patient: Case report and review of the literature

Nicole Min Hui Loh,* Bhavesh Doshi† and Ning Qi Pang‡,§

*Yong Loo Lin School of Medicine, National University of Singapore, †Division of Gastroenterology and Hepatology, Department of Medicine, National University Hospital, ‡Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery and §National University Centre for Organ Transplantation, National University Health System, Singapore

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Correspondence
Dr Ning Qi Pang, Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, National University Hospital, 1E, Kent Ridge Road, NUHS Tower Block, Level 8, 119228 Singapore.
Email: pangningqi@gmail.com

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Abstract

This case report highlights the investigation and treatment of a 70-year-old male with cytomegalovirus (CMV) cholangiopathy. The patient underwent a kidney transplant in 2016 and presented 3 years later with the atypical presentation of left shoulder pain associated with dilated biliary tree and mild transaminitis. Initial endoscopic retrograde cholangiopancreatography (ERCP) showed diffuse stricture of the common bile duct, requiring stenting, and over the course of a year multiple stent changes were required to prevent cholestasis. CMV polymerase chain reaction (PCR) tests were conducted on bile duct brushings and found to be positive. Oral valganciclovir was given for 6 weeks but the strictures did not resolve. He underwent a laparoscopic total choledochectomy and hepaticojejunostomy as definitive treatment. CMV involvement of the biliary tract has rarely been reported in kidney transplant patients. Antiviral therapy in the form of ganciclovir or valganciclovir is often sufficient to eradicate CMV infection and improve clinical disease. Surgical management should be considered only if the patient has failed medical therapy, or if there is suspicion of malignancy. This case shows that in renal transplant patients presenting with cholangiopathy, CMV disease should be considered as a possible differential even in patients without early CMV infection or with prior CMV prophylaxis.

Introduction

Cytomegalovirus (CMV) reactivation is common in patients who have undergone kidney transplantation and frequently associated with graft failure and death.[1] Almost two-thirds of CMV infections are symptomatic, with symptoms often occurring by the first year of transplantation.[2] However, late-onset CMV infection, which is defined as that occurring beyond 12 months after kidney transplantation, is uncommon.[3]

We report a rare case of a kidney transplant patient who presented with late-onset CMV infection manifesting as cholangitis and complicated by common bile duct (CBD) strictures refractory to medical therapy.

Case report

A 70-year-old male with end-stage renal failure (ESRF) who was on hemodialysis for 2 years underwent kidney transplantation in 2016. The procedure was performed at an overseas center. The donor was a healthy 33-year-old male. Comorbidities of our patient included ischemic heart disease, diabetes mellitus, recurrent idiopathic portal vein thrombosis, and a previous left cerebellar stroke with good functional recovery. The CMV serostatus of both the patient and donor was unknown then, and there was no record of CMV prophylaxis therapy. No rejection episodes occurred after the transplant, and the patient was placed on a triple immunosuppression regimen for daily maintenance, consisting of 500 mg mycophenolate mofetil (MMF), 5 mg prednisolone, and 150 mg cyclosporin A.

The patient presented to us 3 years later, in December 2019, with acute onset of left shoulder pain associated with fever. Ultrasound of the hepatobiliary system showed dilation of the biliary tree, but no gallstones were seen. Biochemical investigations showed raised bilirubin of 41 μmol/L, with conjugated bilirubin of 21 μmol/L. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels were 687 and 240 U/L, respectively, and alkaline phosphatase (ALP) was 262 U/L.

The patient was treated for cholangitis and started on IV ceftriaxone and metronidazole. He underwent endoscopic retrograde cholangiopancreatography (ERCP), which showed an abnormal CBD distally, suggestive of strictures. Initial brushings showed reactive-type cell atypia and inflammation. The CBD was stented, and the patient was discharged after resolution of liver enzyme derangements and symptoms.

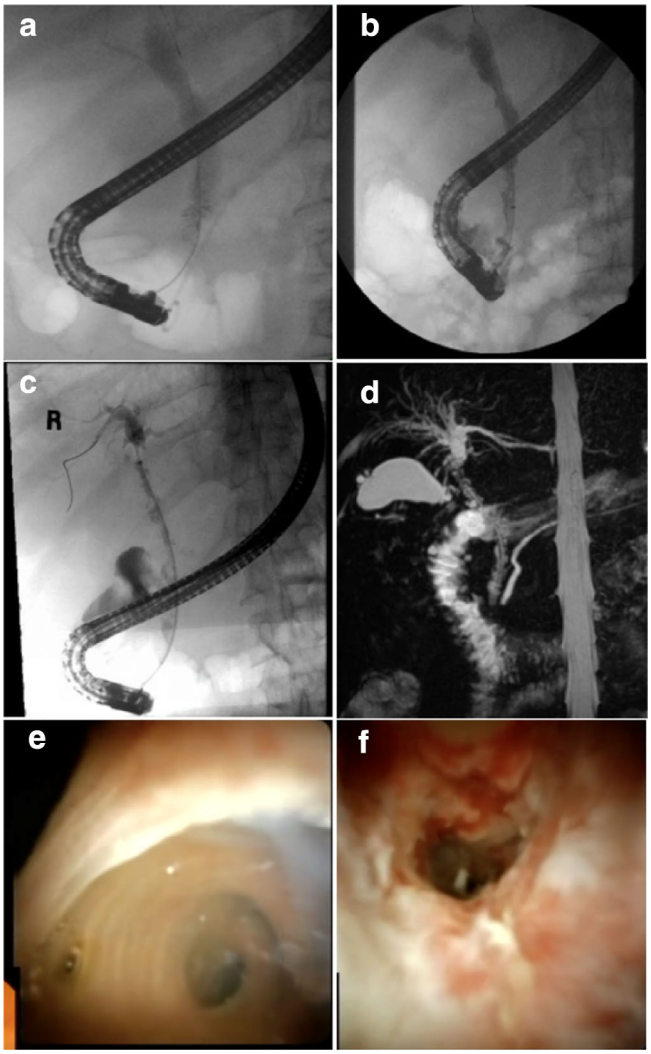

Figure 1 Radiologic and endoscopic images demonstrating cytomegalovirus cholangiopathy. (a) Endoscopic retrograde cholangiopancreatography (ERCP) image of the common bile duct in December 2019. (b) ERCP image of the common bile duct in March 2020. (c) ERCP image of the common bile duct in December 2020 showing worsening strictures. (d) Magnetic Resonance Cholangiopancreatogram (MRCP) findings in January 2021, delineating the extent of bile duct stricture and dilated proximal hepatic ducts. (e) Spyglass during ERCP showing normal mucosa of the hepatic duct at the hilar confluence. (f) Spyglass image during ERCP showing diseased extrahepatic bile duct.

The patient was re-assessed with ERCPs in March, July, October, and December 2020. Liver function tests on follow-up were normal, and the patient remained asymptomatic. However, the stricture persisted despite repeated balloon dilatation and stentings at each ERCP. Figure 1 shows the sequence of ERCP images (a–c) revealing stricture of the CBD till the hepatic ductal bifurcation, while image (d) shows the corresponding Magnetic Resonance Cholangiopancreatogram (MRCP) image of severe CBD stricture with intrahepatic ductal dilatation. Images (e) and (f) show the spyglass pictures and reveal intraductal disease in the CBD but normal ductal mucosa at the hilar confluence.

Differentials that could account for the presentation of cholangitis and recurrent biliary stricture such as IgG4 cholangiopathy, sclerosing cholangitis, drug-induced cholangiopathy, and cholangiocarcinoma were considered but ruled out via histology and biochemical investigations. CMV polymerase chain reaction (PCR) tests were conducted on bile duct brushings and found to be positive in a bile duct brushing, in October 2020, during which the diagnosis of CMV cholangiopathy was made.

Antiviral therapy consisting of a 6-week course of oral valganciclovir 450 mg BID was started, and ERCP was repeated afterward in December 2020 (Fig. 1). Despite negative CMV PCR of bile duct brushings and completion of antiviral therapy, the bile duct stricture did not resolve. In view of the persistence of the CBD stricture despite endoscopic and pharmacologic therapy, the patient was advised to undergo surgical intervention. The patient underwent a laparoscopic total choledochectomy and hepaticojejunostomy as definitive treatment.

Intraoperative choledochoscopy showed strictured and unhealthy bile duct mucosa down to the ampulla and up to 1–2 cm from the hepatic duct confluence. The bile duct was thickened and dilated at 1 cm. The final histology from the specimen returned negative for malignancy, and therefore no further intervention was required. The operation was successful with no complications, and the patient was discharged well with no recurrence of symptoms until the time of writing (21 months post operation).

Discussion

This is a rare case of a renal transplant patient who was diagnosed with CMV cholangiopathy 3 years after transplantation. The presentation was atypical with left shoulder pain and fever, which delayed diagnosis and antiviral treatment. The patient eventually required surgical resection of the unresolving bile duct stricture, which was found to be benign on histologic examination.

CMV cholangiopathy is defined as CMV infection of the biliary tract. It is more commonly found in HIV-infected patients with advanced immunosuppression (CD4 count < 100 cells/μL)[4] or patients undergoing chemotherapy for leukemia.

However, CMV involvement of the biliary tract has rarely been reported in kidney transplant patients. A review of the literature showed only two cases reporting multiorgan involvement[5,6] and three cases presenting with acute CMV cholangitis with resolution upon antiviral treatment.[7–9] Cholestasis mainly occurs as a result of a functional stricture (e.g., inflamed oedematous papilla) rather than a true chronic stricture, occurring with concomitant papillitis or pancreatitis. Unlike our patient, none of the reported cases so far required surgical intervention for definitive management.

The pathophysiology of CMV infection of the hepatobiliary tract could be similar to that in HIV patients. CMV has been proposed to cause vascular injury to cholangiocytes, typically involving the large intrahepatic ducts. Cello described AIDS cholangiopathy to mainly follow four patterns: sclerosing cholangitis and papillary stenosis, papillary stenosis alone, intrahepatic sclerosing cholangitis alone, and long extrahepatic bile duct strictures with or without intrahepatic sclerosing cholangitis.[10] Typical presentation of CMV cholangitis include abdominal pain, fever, and cholestatic jaundice with elevated gamma-glutamyl transferase (GGT) and ALP. Our patient presented with elevated AST, ALT, and ALP, as is typical.

Antiviral therapy in the form of ganciclovir or valganciclovir is often sufficient to eradicate CMV infection and improve clinical disease. Oral ganciclovir has been shown to be equivalent to its IV counterpart in the management of CMV disease in renal patients and is thus considered an acceptable form of management, with the duration of its course altered to cater to the individual being treated.[11] Surgical management should be considered only if the patient has failed medical therapy, or if there is suspicion of malignancy. Surgical options include resection of the bile duct stricture or inflamed segments of the biliary system, especially if malignancy is suspected.

In summary, we report a rare case of late-onset chronic CMV infection in a renal transplant patient, leading to cholangitis and unresolving strictures of the CBD that required eventual surgical intervention. In renal transplant patients presenting with cholangiopathy, CMV disease should be considered as a possible differential even in patients without early CMV infection or with prior CMV prophylaxis. Regular follow-ups and imaging of the biliary tract should be considered in chronic CMV cholangitis, as antiviral treatment alone may be insufficient to resolve strictures caused by CMV infection.

Patient consent

The patient involved in this report was informed of the writing of this paper and has given his explicit consent for publication of his condition.

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