Liver Transplantation for Recurrent Cholangitis From Von Meyenburg Complexes

Nikhil Panda, MD,1 Diane Brackett, MD,2 Corey Eymard, MD,1 Tatsuo Kawai, MD, PhD,1 James Markmann, MD, PhD,1 Camille N. Kotton, MD,3 Karin Andersson, MD,4 and Heidi Yeh, MD1

Abstract. Von Meyenburg complexes, or multiple biliary hamartomas, are often asymptomatic lesions incidentally discovered during abdominal or hepatic imaging. The presentation of clinically significant Von Meyenburg complexes ranges from cholestasis and self-limited episodes of cholangitis to malignant degeneration into cholangiocarcinoma. In cases of persistent or recurrent cholangitis, treatment is a significant challenge. Definitive source control with liver transplantation, as in other cases of cholestatic liver disease, may be necessary.

CASE DESCRIPTION

A 62-year-old female presented with cholangitis from presumed choleodocholithiasis and underwent successful common bile duct decompression via endoscopic retrograde cholangiopancreatography with sphincterotomy and subsequent cholecystectomy. No ductal abnormalities were seen on the cholangiogram, and the pathology from the cholecystectomy showed cholecystitis without cholelithiasis. Of note, she had been diagnosed incidentally with biliary hamartomas 3 years previously when undergoing abdominal imaging for perforated appendicitis.

Over the subsequent 3 years, she was admitted for 6 episodes of cholangitis with bacteremia from multidrug-resistant organisms, including Klebsiella pneumoniae, Enterobacter cloacae, extended spectrum beta-lactamase Escherichia coli, and vancomycin-resistant Enterococcus faecium. Several of these episodes occurred despite various courses of suppressive antibiotics, including amoxicillin clavulanate, doxycycline, and trimethoprim-sulfamethoxazole. The patient also developed Clostridium difficile colitis for which she completed treatment and received prophylactic oral vancomycin during subsequent recurrences of cholangitis.

Her recurrent episodes of cholangitis prompted repeat endoscopic retrograde cholangiopancreatography with sphincterotomy extension and balloon dilation. Cholangiography did not reveal any ductal abnormalities (Figure 1A). Cross-sectional MRI of the abdomen demonstrated innumerable stable lesions throughout the liver (Figure 1B). Serial imaging revealed the development of a small and nodular liver consistent with a radiographic diagnosis of cirrhosis (Figure 1C). Liver biopsy confirmed biliary hamartomas (VMC) without histologic evidence of advanced fibrosis. There were no drainable hepatic abscesses or collections. During these 3 years of recurrent episodes of cholangitis, her biochemical profile remained remarkable only for an elevated alkaline phosphatase with normal platelets, albumin, and international normalized ratio.

At the time, given the paucity of literature on the septic complications of VMC, it was postulated that these recurrent infections may represent seeding of the hamartomas from...
bacteremia during cholangitis. Given her recurrent infections with multidrug-resistant organisms despite antibiotic prophylaxis, hospitalizations, and invasive procedures, she was listed for liver transplantation as a means of source control. Her Model for End-stage Liver Disease score at the time of listing was 7; however, we petitioned for exception points given her recurrent bacteremia and associated impact on her overall health-related quality of life. She ultimately was matched with a standard-criteria organ donor approximately 3 years later at which time her Model for End-stage Liver Disease score, with exception points, was 30.

At liver transplantation, small abscesses were seen throughout the liver (Figure 2A and B), purulence was observed on transection of the common bile duct, and dense adhesions to the
E. coli, vancomycin-resistant E. faecium, and Staphylococcus hominis. The remainder of the patient’s post-operative infectious tests, including multiple blood and urine cultures, was negative. Postoperative prophylaxis included linezolid and meropenem for 5 days, fluconazole for 3 days, and oral vancomycin as C. difficile colitis prophylaxis extending 1 week after completion of other antibiotics. She also received postoperative trimethoprim-sulfamethoxazole and valganciclovir for prophylaxis against opportunistic infections.

The patient was discharged after an uncomplicated inpatient hospital stay on the fifth postoperative day. Over the 6 months after her transplant, she has remained clinically well with stable allograft function, no evidence of rejection, and without new or recurrent infectious complications.

**DISCUSSION**

VMC were first described in the early 20th century and represent abnormalities of the embryonic ductal plate within the intrahepatic biliary tree. They are associated with polycystic kidney disease and other congenital biliary tree abnormalities, such as Caroli disease. The majority of VMC were identified incidentally or at the time of autopsy; however, with improving imaging modalities, these lesions are more frequently being identified radiographically. On MRI, VMC appear as nonenhancing lesions, which are hypointense on T1-weighted imaging and hyperintense on T2-weighted imaging. Notably, the extrahepatic and intrahepatic biliary tree is normal, which is better appreciated on magnetic resonance cholangiopancreatography. Liver biopsy remains the gold standard for diagnosing and distinguishing VMC from other hepatic lesions, with key histologic features, including cystic bile duct dilation within a dense, fibrous stroma.

There are fewer than 10 case reports in the literature describing cholangitis caused by VMC. In 8 of these cases, the patients were successfully treated with a single brief course of antibiotics. However, in 2 cases, treatment failure or recurrent cholangitis required multiple prolonged attempts at sterilization. These reports have also proposed the pathophysiology of cholangitis from VMC, describing the bacterial colonization of numerous foci of biliary stasis. Clinicians should be aware of VMC not only to distinguish them from other hepatic lesions, such as multiple hepatic metastases or cysts, but also to recognize their ability to cause recurrent cholangitis, portal hypertension, and to undergo malignant degeneration into cholangiocarcinoma.

Unlike prior reports describing a single or self-limited episode of cholangitis from VMC, our case emphasizes that sterilization with antibiotics alone is challenging in patients with recurrent cholangitis secondary to VMC given the significant burden of infected hepatic parenchyma. For patients who similarly develop recurrent cholangitis from other hepatic parenchymal lesions, as in the case of cholestatic liver diseases (eg, primary sclerosing cholangitis and Caroli disease), liver transplant remains the only durable treatment approach. Unlike the majority of patients who undergo liver transplantation for chronic liver disease in the United States, approximately 50% of these patients with recurrent cholangitis from cholestatic liver disease have no clinical manifestations of portal hypertension or evidence of cirrhosis. Notably, the synthetic function and structure of their liver is generally preserved, as underscored in this case by the patient’s unremarkable biochemical profile and the lack of advanced fibrosis on liver biopsy and final explant histology, despite cirrhotic morphology on MRI. However, given the impact of recurrent hospitalizations, invasive procedures, and both direct and indirect healthcare costs on quality of life, patients may gain exception points when listed for transplantation in the absence of decompensated liver failure.

The postoperative management of antibiotics and immunosuppression in this patient with a history of recurrent cholangitis from highly resistant organisms represented a critical challenge, given that posttransplantation infection is a major source of morbidity and mortality. It should be noted that care was taken to avoid abscess rupture at surgery and that omentum was used to buttress the fresh anastomoses, which were fashioned within a chronically inflamed and infected field. The patient was placed on a brief course of antibiotics, despite achieving source control via native liver explant with minimal bile spillage given her history of recurrent cholangitis and initiation of multiple immunosuppressing medications.

Given the rarity of clinically significant VMC, transplantation for this disease entity in adult patients has not been previously described. This case represents the first reported successful liver transplant for the treatment of recurrent cholangitis secondary to VMC. Clinicians should be aware of the life-threatening infectious complications of diffuse structural biliary ductal abnormalities and, in cases where sterilization with suppressive antibiotics fail, the approach to source control with liver transplantation.

**REFERENCES**

1. Sinakos E, Papalavrentios L, Chourmouzi D, et al. The clinical presentation of Von Meyenburg complexes. Hippokratia. 2011;15:170–173.
2. Nagano Y, Matsuo K, Gorai K, et al. Bile duct hamartomas (von Meyenburg complexes) mimicking liver metastases from bile duct cancer: MRC findings. World J Gastroenterol. 2006;12:1321–1323.
3. Zheng PQ, Zhang B, Kudo M, et al. Imagining findings of biliary hamartomas. World J Gastroenterol. 2005;11:6354–6359.
4. Salies VJ, Marotta A, Netto JM, et al. Bile duct hamartomas—the von Meyenburg complex. Hepatobiliary Pancreat Dis Int. 2007;6:108–109.
5. Kosy DSC, Leow WQ, Tan TT, et al. Recurrent hepatobiliary sepsis in a patient with von Meyenburg complexes: a case report and review of the literature. Proc Singapore Healthc. 2016;26:133–136.
6. Khungar V, Goldberg DS. Liver transplantation for cholestatic liver diseases in adults. Clin Liver Dis. 2016;20:191–203.