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BRIEF REPORT

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Effective therapy for hepatic M. Osler with systemic hypercirculation by ligation of the hepatic artery and subsequent liver transplantation

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Abstract Hereditary hemorrhagic teleangiectasia, or M. Osler (Osler-Weber-Rendu disease), is an autosomal dominant, systemic fibrovascular dysplasia. This may lead to increased liver blood flow from arteriovenous fistulas. A 45-year-old woman with a known M. Osler was admitted for liver transplantation. On admission, exertional dyspnea was the predominant symptom. Radiological investigations revealed multiple intrahepatic arteriovenous fistulas and consecutive high-output heart failure. Laboratory findings revealed remarkably elevated bilirubin and alkaline phosphatase. To alleviate the high-output cardiac failure, the hepatic artery was ligated. Fourteen months later, the patient presented again with increased levels of bilirubin and recurrent bleeding episodes from esophageal varices grade IV. The patient underwent liver transplantation and post-transplant recovery was excellent. A hyperdynamic circulatory state due to a hepatic M. Osler has been treated in several cases by ligation or embolization of the hepatic artery. This procedure, however, is recommended only for patients with normal liver function and carries a considerable risk of bile duct necrosis.

Key words Osler-Weber-Rendu disease, liver transplantation · Liver transplantation, Osler-Weber-Rendu disease

Introduction

Hereditary hemorrhagic teleangiectasia or M. Osler (Osler-Weber-Rendu disease), is an autosomal dominant, systemic fibrovascular dysplasia that is characterized by teleangiectatic lesions of the naso- and oropharynx, lungs, and visceral organs. Recurrent epistaxis and gastrointestinal bleeding episodes represent common, life-threatening manifestations of M. Osler [16]. During these hemorrhagic episodes, platelet function and coagulation are apparently unaffected; however, in some cases, Von Willebrandt syndrome has been associated with M. Osler [1].

The incidence of liver involvement in M. Osler is unknown [13]. Arteriovenous malformations of the liver in this disease are distinctive lesions in that dilated vascular channels and thickened arterial walls in portal and parenchymal areas are embedded in varying degrees of dense fibrous tissue [3, 4]. Fibrovascular infiltration of the liver can increase total liver blood flow due to arteriovenous fistulas and lead to hepatomegaly and right upper quadrant pain. In rare cases, a significant arteriovenous shunting through fistulas in the liver may cause a hyperdynamic circulatory state with subsequent high-output heart failure, portal hypertension, and hepatic encephalopathy [12]. These symptoms are potentially curable by ligation or embolization of the hepatic artery [6, 11]. We report a case of intrahepatic M. Osler with high-output cardiac failure that was treated initially with hepatic artery ligation and later, successfully, with liver transplantation.

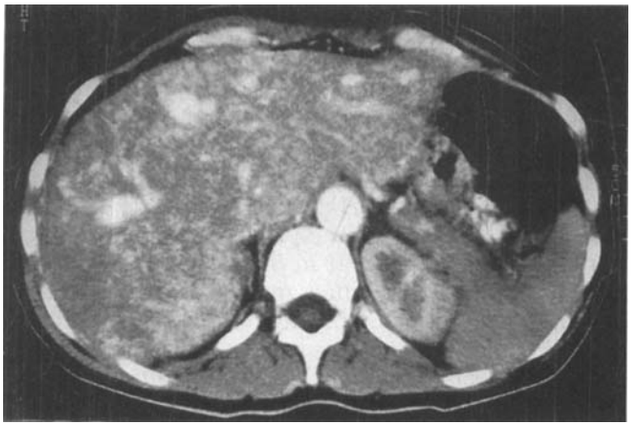


Fig. 1 Spiral CT (arterioportovenous phase). Note the multiple arteriovenous fistulas distributed over the entire liver, leading to a patchy enhancement before ligation of the hepatic artery

Case report

A 45-year-old woman was admitted to our clinic with heart failure, abdominal pain, and weight loss. Her past medical history included a partial left pulmonectomy at the age of 15 years due to M. Osler with arteriovenous fistulas. On admission, dyspnea was the predominant symptom. Clinical examinations showed signs of hepatic dysfunction with jaundice, palmar erythema, and spider naevi. Intestinal pathology was excluded by radiological and endoscopic procedures. The chest X-ray showed cardiac enlargement. Abdominal ultrasound revealed hepatomegaly, gallstones, and changes consistent with liver cirrhosis. Pulsed Doppler analysis documented an increased blood flow through the hepatic artery (90 cm/s) and the portal vein (70 cm/s). Magnetic resonance imaging and computer tomography (CT; Fig. 1) revealed multiple intrahepatic arteriovenous fistulas with simultaneous enhancement of hepatic arteries and veins. Cardiomegaly prompted cardiac catheterization with selective angiography of the coronary vessels. Right and left atrial and ventricular pressures were within the normal range. Cardiac output was 8.8 l/min and increased during exercise conditions up to 17 l/min. A hepatic arteriogram confirmed the presence of intrahepatic arteriovenous fistulas nourished by the hepatic artery associated with 50% shunting of cardiac output. Despite elevated bilirubin levels, overall hepatic function with normal albumin and clotting factors had not deteriorated to a point to justify a liver transplantation.

To alleviate the exertional dyspnea caused by the high-output cardiac failure, complete dearterialization of the liver was carried out. This included a division of triangular ligaments and of the small omentum, and ligation of the proper hepatic artery and an accessory left hepatic artery. In addition, a cholecystectomy was performed. Red, arterialized areas on the liver surface returned to the normal color of liver parenchyma after ligation of the hepatic arteries. Cardiac output dropped from 8.8 l/min to 5.8 l/min. During the peri- and postoperative course, peak levels of total bilirubin and alkaline phosphatase reached 36 mg/dl and 2300 U/l, respectively. Recurrent cholangitis with fever up to 38 °C required antibiotic treatment with oral application of ciprofloxacin. During the 1st postoperative week, two units of fresh frozen plasma were substituted daily to maintain an acceptable coagulation profile. Ultrasound and CT of the liver revealed inhomogeneous areas of the hepatic parenchyma indicative of bile duct necroses. This finding was subsequently confirmed by biopsy. The patient showed no clinical signs of acute liver failure at that time. After further improvement, the patient was discharged from the hospital with continued oral ciprofloxacin treatment. Eight months after the ligation of the hepatic artery, the physical state of the patient was satisfactory with decreasing bilirubin and alkaline phosphatase levels (Fig. 2).

Fourteen months after hepatic arterial ligation, the patient once again developed cholestasis and recurrent esophageal bleeding episodes. Endoscopic and radiological investigations revealed

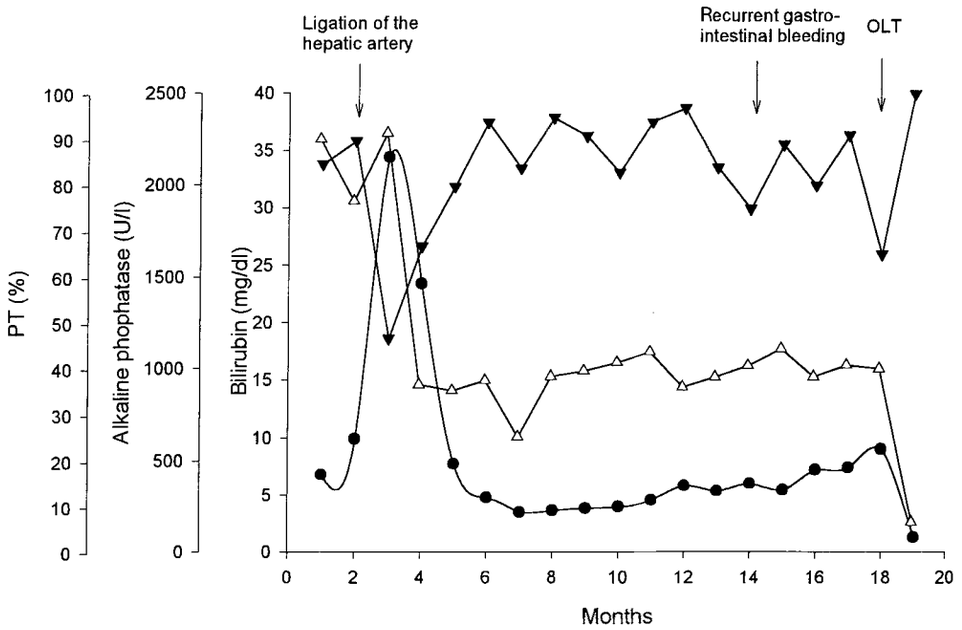
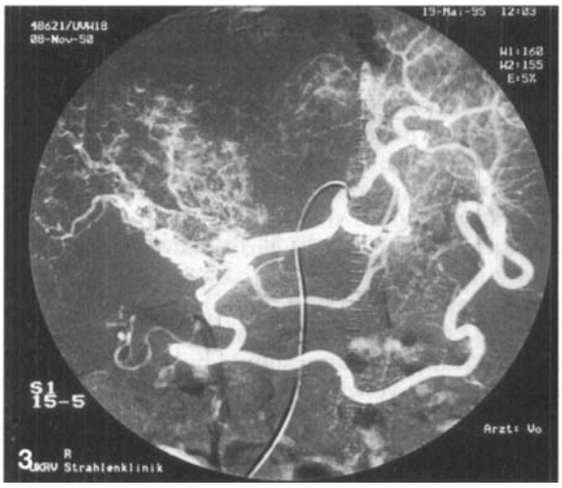


Fig. 2 Course of the cholestatic parameters and PT of the patient. ●—● Bilirubin; Δ—Δ alkaline phosphatase; ▼—▼ PT



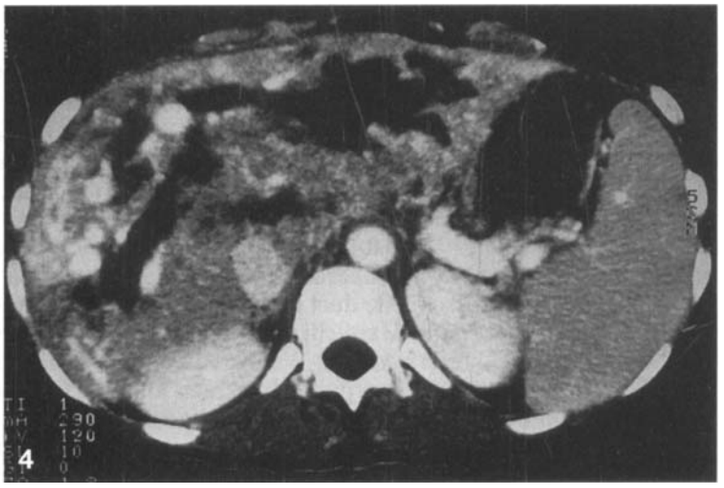


Fig. 3 Pretransplantation selective angiography of the celiac trunk revealing a prominent common hepatic artery with a short stump of the hepatic artery and tortuous pancreatic arcades. Note the multiple arteriovenous intrahepatic fistulas with the consequence of a patchy enhancement of the entire liver volume

Fig. 4 Spiral CT (arteriovenous phase). Characteristic CT findings of multiple arteriovenous fistulas and confluent areas of low density corresponding to bile necrosis after ligation of the common hepatic artery

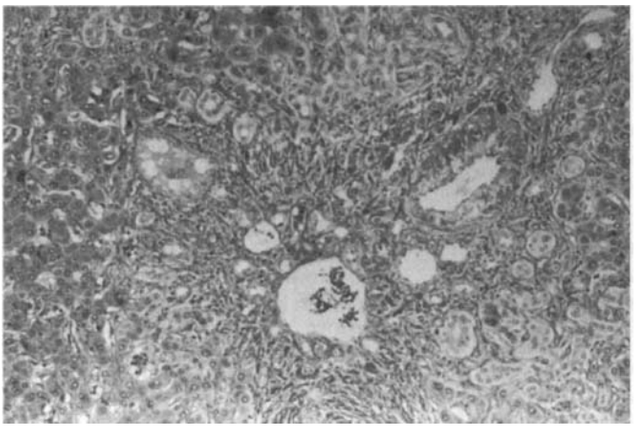


Fig. 5 Pathological examination of the liver showing typical findings of M. Osler-Weber-Rendu disease with enlarged portal tracts with distinctive fibrosis and development of porto- portal septal and perisinusoidal fibrosis. The portal tracts revealed dilated and thickened vascular channels (Masson-Goldner × 220)

esophageal and gastric varices grade IV. Angiography of the liver presented recurrence of multiple arteriovenous shunts with collateral vessels along the common bile duct (Fig. 3). Faced with the prospect of gastrointestinal bleeding and increasing bilirubin and alkaline phosphatase levels reflecting bile duct necrosis (Fig. 4), the patient underwent liver transplantation. Post-transplant recovery of the patient was excellent. Immunosuppressive therapy was based on FK 506 and steroids. Complications did not occur. The patient returned home in excellent clinical condition with normal liver function.

Pathological examination of the recipient liver showed typical findings of M. Osler-Weber-Rendu disease. Portal tracts were enlarged with distinctive fibrosis and development of portoportal septal and perisinusoidal fibrosis. The portal tracts revealed dilated and thickened vascular channels (Fig. 5).

Discussion

M. Osler is an autosomal dominant disorder [10] characterized by the classical triad of mucocutaneous and visceral teleangiectasia, recurrent epistaxis, and a positive family history. Liver involvement with typical arteriovenous fistulas and teleangiectasias has been reported in more than 50 cases [5, 10]. In a few cases, these pathological features were also associated with fibrosis and cirrhosis [8].

Arteriovenous fistulas in the liver leading to a hyperdynamic circulatory state have been successfully treated by ligation or embolization of the hepatic artery. In the cases reported, no serious complications occurred after ligation or chemoembolization. Therapeutic arterial embolization of the hepatic artery has been described as a safe and effective treatment for several diseases [2], including high cardiac output due to intrahepatic arteriovenous malformation in the course of an M. Osler [14]. However, the recruitment of collateral vessels after either a ligation or embolization procedure and the new formation of arteriovenous fistulae may lead to recurrence of the intrahepatic shunts, as shown in our case. Since perfusion of the biliary tree depends mainly on the hepatic artery, intrahepatic bile duct damage can be expected [9]. This finding has been described in patients after liver transplantation with hepatic artery thrombosis and consecutive necrosis and destruction of the bile ducts [15]. According to the literature, these complica-

tions did not occur in cases with high-output heart failure due to arteriovenous malformations in the liver and ligation or embolization of the hepatic artery [11]. Embolization of the hepatic artery may not dearterialize the liver completely since small arterial vessels are still present within the perihepatic ligaments. In the setting of liver transplantation, however, the liver is completely dearterialized and depends solely on the surgically dissected arterial pedicle. Therefore, a thrombosis of the hepatic artery in the early postoperative course after liver transplantation results in bile duct necrosis. As shown in our case, the complete dearterilization of the liver leads to multiple bile duct necrosis. We were able to ligate the hepatic artery in our patient because of the good synthetic liver function preoperatively. Postoperatively, the patient suffered from recurrent cholangitis and mild destruction of bile ducts, but she recovered from this severe complication.

Ligation of the hepatic artery has been shown to be an effective procedure to reduce the high cardiac output in M. Osler with intrahepatic shunting. In our opinion, however, this procedure should be recommended only for patients with unaffected liver function. Postoperatively, these patients run a high risk of developing bile duct necrosis and should be monitored closely. When the synthetic capacity of the liver is already compromised, a liver transplantation should be considered as a therapeutic alternative with excellent results [7].

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