Osler-Weber-Rendu Disease with Esophageal Varices and Hepatic Nodular Change

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Abstract

A 72-year-old male visited our hospital for further evaluation of esophageal varices. Telangiectasias were present in the stomach. He had recurrent epistaxis, which was also confirmed in his family’s medical history. We diagnosed this case as Osler-Weber-Rendu disease. He had concomitant with hepatic nodular change. Abdominal angiography showed arterio-portal (A-P) shunts, superior mesenteric artery (SMA)-superior mesenteric vein (SMV) shunt, extension of SMV, and dilated and meandering portal vein. Esophageal varices were treated by endoscopic variceral ligation (EVL) and argon plasma coagulation (APC) therapy for prophylaxis of bleeding.

Key words: Osler-Weber-Rendu disease, esophageal varices, arterio-portal shunt, SMA-SMV shunt, hepatic involvement

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Introduction

Osler-Weber-Rendu disease, i.e., hereditary hemorrhagic telangiectasia (HHT), is an autosomal-dominant disorder of the fibrovascular tissue. It is characterized by epistaxis, muco-cutaneous telangiectasias, visceral telangiectasia, and inheritance. In more than 90% of the patients, epistaxis is the first predominant symptom. Apart from affecting the nose, arteriovenous malformations (AVMs) may also affect the skin, lungs, brain, liver and gastrointestinal tract. The two known genes that are implicated in Osler-Weber-Rendu disease are endoglin (ENG), located on chromosome 9q33-q34, and activin receptor-like kinase (ALK1), located on chromosome 12q13. Mutations of ENG are observed in HHT type 1 with an incidence up to 40% for pulmonary AVMs, whereas mutations of ALK1 are observed in HHT type 2 with an incidence of only 14% for pulmonary AVMs, which clinically distinguish these two types of mutation.

A common feature of Osler-Weber-Rendu disease is that it is more common than previously thought and shows a broad range of different clinical organ manifestations that can be sources of substantial morbidity and mortality, making this disease a continuing challenge for many sub-specialties where interdisciplinary diagnostic screening is mandatory in the management of the disease (1).

AVMs often remain clinically silent until provoking sudden serious complications, and they are responsible for important morbidity and mortality that can occur both in adulthood and children. The incidence of AVMs in pediatric populations with Osler-Weber-Rendu disease is unknown. Liver involvement in Osler-Weber-Rendu disease is almost always asymptomatic, while hepatic vascular malformations can induce severe complications, depending on the predominant venous side of the arteriovenous fistulas high-output cardiac failure in the case of hepatohepatic fistulas, and portal hypertension in the case of hepatoporal fistulas. Here we report a case of Osler-Weber-Rendu disease with esophageal varices and hepatic nodular change.
Figure 1. Six members of the family tree had episodes of recurrent epistaxis. Solid symbols indicate members suffering from recurrent epistaxis.

Case Report

A 72-year-old male visited our hospital for further evaluation of esophageal varices. On admission, he was 166.0 cm tall and weighed 66.3 kg. His pulse rate was 80/min, and blood pressure was 116/76 mmHg. Normal vesicular breath sounds were heard over the lungs, and no cardiac murmurs were audible. The abdomen was full of ascites, without hepatosplenomegaly or a palpable mass. There were no telangiectasias on the face, mouth, lips, and fingers, but the upper gastrointestinal endoscopy showed telangiectasias in the stomach. He had episodes of recurrent epistaxis, which were also confirmed in his family’s medical history (Fig. 1). We diagnosed this case as Osler-Weber-Rendu disease because of recurrent epistaxis, family history, and visceral telangiectasias. He had concomitant hepatic nodular change diagnosed by abdominal ultrasonography (US) and computed tomography (CT). But concomitant liver disease was ruled out by the absence of risk factors for chronic liver disease, such as alcoholism, intravenous drug use, and inflammatory bowel disease, and by negative results of tests for hepatitis B and hepatitis C viral markers and antinuclear and antimitochondrial antibodies (Table 1). He underwent cholecystectomy at the age of 43 years old and nephrectomy at 71 years old, but he did not have a blood transfusion. Abdominal CT showed hepatic nodular change, massive ascites, dilatation of capillaries in the liver, extension of the superior mesenteric vein (SMV), and a shunt between the SMV and the superior mesenteric artery (SMA). Abdominal angiography showed multiple small arterio-portal (A-P) shunts, SMA-SMV shunt, and extension of the SMV. Portography showed a very dilated and meandering portal vein (Fig. 2). Doppler color flow imaging showed peripheral hypervascularization, tortuous small vessel (arrow) and dilated portal vein without turbulent flow (Fig. 3A). Abundant blood flow was observed in the structure of vessel thought to SMA-SMV shunt (Fig. 3B). Some reddish telangiectasias were observed on the gastric endoscopy. Endoscopy showed telangiectasia appearing as cherry-red hillock (arrowhead) in the stomach, esophageal varices with telangiectasia, and gastric varices (Fig. 4). Endoscopic ultrasonography (EUS) showed thick varices in the submucosal layer without a perforating vessel (Fig. 5). Massive ascites disappeared after treatment with furosemide and spironolactone. Esophageal varices were treated by endoscopic variceral ligation (EVL) and argon plasma coagulation (APC) therapy for prophylaxis of bleeding.

Discussion

In Osler-Weber-Rendu disease, visceral and hepatic lesions have been described frequently in patients with hepatic involvement. The proportion of patients with hepatic involvement ranges from 8% to 31% (2). But liver involvement in patients with Osler-Weber-Rendu disease is a rare complication with a potentially life-threatening outcome due to the massive increase of cardiac output (3-5). The gold standard to diagnose hepatic involvement in Osler-Weber-Rendu disease is selective angiography of the hepatic artery (6, 7).

The present patient had episodes of recurrent epistaxis, which were also confirmed in his family’s medical history, and telangiectasias in the stomach. Angiography showed
Figure 2. Abdominal angiography showed multiple small arterio-portal (A-P) shunts (A) in the right hepatic artery (arrowhead), and (B) in the left hepatic artery (arrowhead). (C) Superior mesenteric artery (SMA)-superior mesenteric vein (SMV) shunt was observed between SMA (black arrow) and extensive SMV (white arrow). (D) Extensive and meandering portal vein and dilatation of capillaries in the liver were also observed.

dilatation of capillaries in the liver. We diagnosed this case as Osler-Weber-Rendu disease. Additionally, abdominal angiography showed arterio-portal (A-P) shunts, SMA-SMV shunt, extension of the SMV, and a very dilated and meandering portal vein. He had esophageal varices associated with portal hypertension because of hepatic nodular change, A-P shunts, and SMA-SMV shunt.

Martini (8) classified patients with hepatic disease due to Osler-Weber-Rendu disease into three subgroups according to the histologic features of the hepatic disease: patients who had telangiectasias with fibrosis or cirrhosis, those who had cirrhosis without telangiectasias, and those who had telangiectasias without fibrosis or cirrhosis. The patients in the second group probably had chronic post-transfusion hepatitis that was unrelated to Osler-Weber-Rendu disease. In the present case, telangiectasias were present in the stomach but we did not have a chance to investigate the histology of the liver. Through CT and US, he was diagnosed with hepatic nodular change. Our case underwent cholecystectomy at the age of 43 years old and nephrectomy at 71 years old, but he did not have a blood transfusion. Concomitant liver disease was ruled out by the absence of risk factors for chronic liver disease, such as alcoholism, intravenous drug use, and inflammatory bowel disease, and by negative results of tests for hepatitis B and hepatitis C viral markers and antinuclear and antimitochondrial antibodies. Osler-Weber-Rendu disease might be a candidate for the cause of cryptogenic cirrhosis. Further investigations between Osler-Weber-Rendu disease and cases of liver cirrhosis are needed.

Garcia-Tsao et al reviewed 83 patients with Osler-Weber-Rendu disease and liver involvement (7). Forty-four of the symptomatic patients could be classified as having one of the three presentations they identified in their study, 32 had heart failure, 7 had portal hypertension, and 5 had biliary disease. Of the nine patients who could not be classified, four presented with encephalopathy as a result of portal to hepatic vein shunting, two presented with abdominal angina due to mesenteric arterial steal through pancreaticoduodenal arteries, and three had clinical findings that were difficult to characterize, although one of the three may have had biliary disease. The particular clinical manifestation of liver involvement in patients with Osler-Weber-Rendu disease may depend on the predominant type and size of shunt as well as on the effects of an abnormal hepatic blood supply. The majority of such patients have a hyperdynamic circulation resulting from arterio-venous shunting, porto-venous shunting, or both. A shunt from the hepatic artery to the portal vein leads to portal hypertension. Increased sinusoidal blood flow can lead to increased deposition of fibrous tissue and nodularity, which are findings associated with the arterialization
of the portal vein. An alternative and perhaps more likely explanation is that the liver undergoes nodular transformation, also known as pseudocirrhosis. Nodular hyperplasia is characterized by the presence of regenerative nodules that compress the surrounding liver parenchyma. These nodules, unlike those in true cirrhosis, are not delimited by fibrous septa. An association between Osler-Weber-Rendu disease and nodular hyperplasia of the liver has been reported. Chronic ischemia which occurred with an arteriovenous or portovenous shunt, causes atrophy of the involved liver acinus. Adjacent acini, with an intact blood supply, undergo compensatory hyperplasia, resulting in micronodularity and portal hypertension.

Hisamatsu et al summarized 25 cases of treatments for the hepatic arteriovenous malformation in Osler-Weber-Rendu disease (9). In the twenty cases, embolization of the hepatic artery using metallic coils, gelatin sponge and polymer particle was added to the choice of treatments. After embolization, one died due to gastro-intestinal (GI) bleeding, one repeated hemorrhage, one died 3 weeks after the second embolization due to massive GI bleeding, one suffered biliary necrosis and hepatic failure, one suffered cholangitis, one died from variceral bleeding, one suffered ischemic cholangitis and one died of sepsis. In their case, two series of hepatic arterial coil embolization temporarily improved the

Figure 3. (A) Doppler color flow imaging showed peripheral hypervascularization, tortuous small vessel (arrow) and dilated portal vein without turbulent flow. (B) Abundant blood flow was observed in the structure of vessel thought to SMA-SMV shunt.

Figure 4. Some reddish telangiectasias were observed on gastric endoscopy. Endoscopy showed (A) telangiectasia appearing as cherry-red hilllock (arrowhead) in the stomach, (B) esophageal varices with telangiectasia, and (C) gastric varices.

Figure 5. Endoscopic ultrasonography (EUS) showed thick varices in the submucosal layer without a perforating vessel.
patient’s cardiac condition, but gradually induced progressive hepatic failure due to intrahepatic cholangitis. They concluded that peripheral arterial coil embolization might be temporarily useful for high output heart failure, but it was harmful to the liver. Buscarini et al reviewed patients with Osler-Weber-Rendu disease and hepatic vascular malformation, and reported that complications of portal hypertension (bleeding from gastro-esophageal varices, ascites) should be treated with consolidated medical and endoscopic treatments (10). In the present case, massive ascites disappeared after treatment with furosemide and spironolactone. We thought that main cause of esophageal varices might be portal hypertension due to SMA-SMV shunt. We had some choices for the treatment of esophageal varices, such as embolization of SMA, endoscopic injection sclerotherapy, and EVL and APC. We chose EVL and APC therapy because the hemodynamics of our patient may have been complicated and we could not forecast new hemodynamics after embolization. We followed this case for more than six months after EVL and APC therapy and did not find relapse of esophageal varices.

Although in the traditional view, it was thought that Osler-Weber-Rendu disease was rare among Asians, but Dakeishi et al reported the population prevalence of Osler-Weber-Rendu disease in the county of Akita Prefecture, located in the northern part of Japan, to be estimated at 1:8,000–1:5,000, which is roughly comparable with the reported prevalence in Europe and the United States (11). They suggested that the traditional view might be associated with a poor recognition of Osler-Weber-Rendu disease by physicians. The present case has lived in an area other than Akita Prefecture from childhood and the rate of prevalence might be in a similar range of Dakeishi’s report. He had episodes of recurrent epistaxis up to age 72, liver involvement and gastro-esophageal varices. Osler-Weber-Rendu disease displays age-related penetrance with manifestations developing throughout life and varying between affected individuals even within the same pedigree. Garcia-Tsao et al reported that 19 patients with Osler-Weber-Rendu disease for liver involvement had a median age of 55 years, with a range of 34 to 74 years (7). They identified three distinct clinical presentations, high-output heart failure, portal hypertension, and biliary disease. Median age of group of portal hypertension was 67 years, with a range of 56-74 years, and was the eldest among these three groups. There was no specific symptom in liver involvement and gastro-esophageal varices accompanying Osler-Weber-Rendu disease. But rupture of varices was a serious risk factor in his prognosis. Especially in elderly patients with Osler-Weber-Rendu disease, checking for liver involvement and gastro-esophageal varices is very important. Having no hesitation about selective angiography of the hepatic artery, understanding the hemodynamics of portal hypertension, and prophylaxis of rupture of varices had therapeutic value in these cases.

references

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