Hepatic involvement in hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber disease)

Abstract Hepatic involvement in hereditary hemorrhagic telangiectasia is infrequent and poorly studied. We describe a 62-year-old woman with Rendu-Osler-Weber (ROW) disease and recurrent gastrointestinal bleeding episodes. Blood chemistry was consistent with the presence of cholestasis. Imaging studies revealed prominent vascular abnormalities in the liver and focal intrahepatic bile duct dilatations. The intimate anatomic relationship of the vascular abnormalities to the dilated bile ducts suggests that external vascular compression could have caused their dilatation. To our knowledge, this mechanism has not been proposed in the literature as a possible explanation of biliary dilatation in patients with ROW.

Keywords Rendu-Osler-Weber disease - Hepatic vascular malformations - Biliary dilatation

Introduction

Hereditary hemorrhagic telangiectasia, or Rendu-Osler-Weber disease (ROW), is a systemic familial fibrovascular dysplasia characterized by telangiectases, aneurysms and arteriovenous malformations. The skin and mucosa as well as blood vessels of the lung, liver and central nervous system may be involved [1, 2]. The prevalence of liver involvement in patients with ROW disease ranges from 8 to 31% in retrospective studies and includes dilatation of the hepatic arteries, telangiectases and intrahepatic arteriovenous malformations in the form of flatulas, with or without concomitant liver fibrosis or cirrhosis [2, 3, 4, 5].

This article describes the clinical and radiological features of a patient with ROW disease presenting with extensive involvement of the hepatic vessels and concomitant focal intrahepatic bile duct dilatation.

Case report

A 62-year-old woman with known ROW disease, diagnosed at the age of 30 years, was admitted to hospital due to intermittent melena and epigastric pain during the 2 days preceding admission. Her past medical history was significant for multiple episodes of epistaxis and gastric bleeding due to telangiectases, treated by laser coagulation. The patient suffered also from congestive cardiac failure. On admission physical examination revealed telangiectases on her lips and finger tips. She was pale but without evidence of jaun-
dice. A thrill was palpated and hum was auscultated over the right upper abdominal quadrant.

Laboratory tests were compatible with a sideropenic anaemia and revealed low values for haemoglobin (9.0 g/l), haematocrit (27.6%), mean corpuscular volume (79 fl), mean corpuscular haemoglobin (26 pg). Serum Fe (10 μg/dl) and serum ferritin (4.0 ng/ml). Blood coagulation tests were normal.

Liver function tests revealed elevated levels of serum alkaline phosphatase (150 IU) and γ-glutamyl transferase (110 IU). Bilirubin, albumin, alanin aminotransferase and aspartate aminotransferase values were normal. Autoantibodies, including antinuclear factor, smooth muscle antibody and antimitochondrial antibody, were absent. Hepatitis B and C viral markers were also negative.

Abdominal ultrasonography showed enlarged and marked tortuosity of the main hepatic and intrahepatic arteries as well as dilatation of the hepatic veins. Mild, focal dilatation of right and left intrahepatic bile ducts was also noted. Gallstones were not detected. The echogenicity of the liver parenchyma and the liver size were normal. Colour Doppler sonography revealed high-velocity flow in both, intra- and extrahepatic arteries, indicating the presence of arteriovenous shunts.

Upper gastrointestinal endoscopy disclosed a small quantity of blood in the stomach originating from a mucosal angiodysplasia of the lesser curvature of the stomach which was treated by injecting 10 cc of a 1:10,000 adrenaline solution with satisfactory haemostatic results. A second angiodyplastic lesion with an adjacent recent clot, detected at the horizontal portion of the duodenum, was also treated endoscopically by the same technique. In view of recurrent episodes of melena during the following days, angiography of the coeliac trunk and the superior mesenteric artery was performed. The superior mesenteric artery angiogram showed an angiodyplastic lesion supplied by the inferior pancreaticoduodenal artery corresponding to the anatomic region of the horizontal portion of the duodenum, without intraluminal contrast medium extravasation. Supraselective catheterization of the feeding artery was followed by a two-step embolization of the lesion with Contour particles and subsequent platinum coil (fibered platinum coil, 0.35-in. type, 3-mm diameter, 40-mm length, Target, Boston Scientific, Cork, Ireland) deposition. In view of the possibility of incomplete embolization of the angiodysplasia due to feeding arteries originating from the superior pancreaticoduodenal artery, hepatic and gastroduodenal artery catheterization were attempted. The hepatic artery angiogram showed dilated and tortuous common hepatic and intrahepatic arteries, multiple nodular hepatic vascular malformations and early opacification of the hepatic veins (Fig. 1). No definite bleeding source was found. Selective catheterization of the gastroduodenal artery was technically not possible.

Abdominal CT confirmed the findings of ultrasonography by showing a massively dilated, tortuous hepatic artery originating from a hypertrophic coeliac axis. The intrahepatic tortuous hepatic artery branches were also very prominent. Dilatation of the hepatic...
Fig. 4a, b Maximal intensity projection (MIP) image of MR angiography during the arterial phase demonstrating simultaneous enhancement of the hepatic arteries and the hepatic veins. Multiple vascular malformations disseminated throughout the right and left liver lobes.

Fig. 5 Coronal MIP reconstructed single-shot turbo spin-echo magnetic resonance cholangiopancreatography image demonstrating focal, intrahepatic bile duct dilatation in the eighth liver segment.

ic veins was also noted. Segmental dilatation of intrahepatic bile ducts was shown in the second and eighth liver segments without dilatation of the extrahepatic bile ducts. Dilated, tortuous intrahepatic vascular branches were demonstrated adjacent to the dilated bile ducts (Fig. 2).

Magnetic resonance cholangiopancreatography (MRCP) was requested in order to identify the cause of the bile duct dilatation. Abdominal MRI and a contrast-enhanced 3D abdominal MR angiography (MRA) were performed at the same session. The abdominal MRI (1.5 T; Siemens Vision, Siemens, Erlangen, Germany) showed the diffuse hypervascular pattern of the liver as multiple tubular, tortuous structures of signal void, in part continuous with the hepatic artery. Tubular high signal intensity structures on T2-weighted images, representing focal intrahepatic bile duct dilatation, were depicted in both liver lobes, abutting ectatic vascular loops. In fact, compression of the bile ducts by these abnormal vessels and subsequent upstream dilatation were demonstrated (Fig. 3). Three-dimensional contrast-enhanced MRA demonstrated simultaneous enhancement of the hepatic arteries and hepatic veins indicating the presence of arteriovenous shunts. The prominent, kinked hepatic artery communicated with multiple liver arteriovenous malformations which drained into dilated hepatic veins (Fig. 4). The MRCP (T2-weighted single-shot turbo spin echo) demonstrated the dilated intrahepatic bile ducts in the second and eighth liver segments. No filling defects were present. The common bile duct and the pancreatic ducts were normal (Fig. 5).

Discussion

Liver involvement is a rare but important manifestation of ROW disease and includes vascular malformations and connective tissue formation with fibrosis and atypical cirrhosis [3, 6, 7]. Halpern et al. described three varieties of vascular abnormalities in selective visceral angiographies of patients with ROW disease [8]; these are aneurysms, angiomata and arteriovenous malformations in the form of discrete arteriovenous fistulas, conglomerate masses of angiectasia, capillary angiodysplastic lesions and phlebectases. Vascular involvement of the liver can often be asymptomatic [6]. When symptomatic, liver involvement results in high-output cardiac failure [6, 9, 10]. Angiography may demonstrate massive dilatation and tortuosity of the hepatic artery and its branches, widespread parenchymal blushes of vascular ectasia, and early opacification of hepatic veins signifying arteriovenous shunting [1]. Alternatively, dynamic contrast-
enhanced MR angiograms provide a map of the anomalous vessels and allows analysis of filling kinetics [11]. Colour Doppler sonography, as well as 3D sonography, are noninvasive, readily available examinations, which may allow excellent analysis of the flow patterns of hepatic vascular malformations [11, 12, 13].

Acantotic cholestasis has been described in 73% (8 of 11) of a series of patients with ROW disease and hepatic involvement, whereas various liver function tests were normal and diverse causes of chronic cholestasis could be excluded in most cases [6]. There are proposals that abnormalities in the hepatic blood flow account for the hepatic fibrosis and nodular regeneration [14, 15]. Hepatic fibrosis and nodule formation, by causing stenosis and compression of the large intrahepatic bile ducts, result in biliary stasis. There are two reports of patients with ROW disease and biliary lithiasis in the literature [14, 16]. Biliary stasis and subsequent secondary infection is the hypothesized mechanism for intrahepatic calculi formation [14].

In another series of 19 patients, 5 symptomatic patients had elevated alkaline phosphatase levels and radiographic evidence of bile duct abnormalities similar to those of Caroli’s disease or those in primary sclerosing cholangitis [4]. Arteriovenous shunts may cause hypoperfusion of the peribiliary plexus which supplies the biliary tree, resulting in bile duct ischaemia with subsequent development of biliary strictures or biliary necrosis which induces the formation of bile-containing cysts [4, 17, 18]. Alternatively, it has been postulated that abnormalities in vascular formation at the ductal plate arrest the normal development of the bile duct system [4]. Diffuse intrahepatic arteriovenous fistulas can be the origin of secondary high-output ventricular failure and furthermore of pulmonary hypertension. In such cases, hepatic arterial embolization with coils or polyvinyl alcohol sponge can lead to minimally invasive treatment [19, 20]. This kind of treatment is usually of short-term success, because of the development of new arteriovenous malformations in the liver or recurrent cholangitis caused by ischaemia or necrosis of the biliary tree [21]. Better long-term results can be achieved after liver transplantation [21].

In our patient, segmental intrahepatic bile duct dilatation was shown in the second and eighth hepatic segments. The presence of dilated, tortuous vascular tangles effacing the bile duct lumen just proximal to the diluted ducts suggests the possibility of a mechanical, rather than an ischaemic/fibrotic, cause for their abnormal appearance. A similar mechanism has been described in biliary obstruction associated with peripoortal and pericholecodochal varices in patients with extraportal portal hypertension as well as in patients with hepatic artery aneurysms [22, 23]. In these reports the abnormal vessels exerted extrinsic compression on the extraportal bile ducts.

To our knowledge, this is the first report of a patient with ROW disease where intrahepatic bile duct dilatation was associated with external vascular compression due to tortuous and dilated intrahepatic arterial branches.

References


