Case Report

Rendu-Osler-Weber Disease with Portosystemic Encephalopathy

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We treated a Japanese man with Rendu-Osler-Weber disease and a recurrent encephalopathy with hyperammonemia concomitant with recurrent epistaxis, GI bleeding, congestive heart failure with aortic and mitral regurgitation, and chronic renal failure. At peritoneoscopy, several telangiectasia were noted on the surface of the liver. Angiographical studies revealed widened and tortuous hepatic arteries with early filling of hepatic veins and small pools of contrast medium scattered throughout the parenchyma. The recurrent encephalopathy was attributed to the porto-systemic shunt formed in the liver.

Key Words: Rendu-Osler-Weber disease, Hereditary hemorrhagic telangiectasia, Porto-systemic encephalopathy

Hereditary hemorrhagic telangiectasia (HHT) or Rendu-Osler-Weber disease is a vascular disorder characterized by telangiectasia of the skin, mucous membranes or internal organs, and by recurrent hemorrhages that arise from rupture of the telangiectasic lesions. It is a familial disorder with an autosomal dominant heritance and both sexes seem to be affected with equal frequency. The clinical manifestation is variable with regard to the number of vascular lesions and severity of organ dysfunction secondary to these lesions. Arteriovenous malformations may be widespread and involve any organ or tissue of the body. Visceral telangiectasia may cause gastrointestinal hemorrhages and abdominal pain. Liver lesions have also been demonstrated. The cerebral symptoms are most often transient ischemic attacks which may be caused by cerebral telangiectasia, however, hepatic encephalopathy caused by porto-systemic fistulas is rare. We report here a case with HHT accompanying a disturbance of consciousness and hyperammonemia due to liver involvement.

CASE REPORT

A 57-year-old Japanese man was admitted in March 1986 because of a disturbance of consciousness. He had had recurrent epistaxis since childhood. He had been surgically treated for a vertebral disc hernia 22 years ago and had dysuria and constipation therafter. In 1965, at the age of 35 years, he had an episode of disturbance of consciousness and was admitted to a psychiatric hospital. He attempted suicide during this hospitalization. In 1982, chronic renal failure became apparent. The following year, he again experienced a disturbance of consciousness and was hospitalized for 3 months but a definite diagnosis was not made. In July, 1985, he again had a disturbance of consciousness and was admitted. At this time, a slight elevation of serum aminotransferase activity was noted. Three months later, hematemesis occurred and he was admitted to another hospital. An endoscopic examination disclosed no ulcerative lesions. One month later, hematemesis recurred. One night during admission, he became drowsy and his electroencephalogram revealed high δ with triphasic waves. He had a couple of episodes of
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abnormal behavior thereafter and was admitted to Kyushu University Hospital on March 5, 1986.

He drank approximately 120 g of alcohol per day for 20 years up to age 35 years and one bottle of beer per day thereafter. He had no history of blood transfusion. His father had died following hematemesis.

On admission this 162 cm, 60 kg man was pale but alert. His blood pressure was 150/90 mmHg; the pulse rate 72/min and irregular. He had a gait disturbance due to vertebral disc hernia. Several cherry red-like spots were present on the face, lips and tongue (Fig. 1). No vascular spiders were seen on the chest and palmar erythema was absent. A high pitched diastolic murmur, Levine 2/6, and holosystolic murmur, Levine 3/6, were audible at 2L and 4L, respectively. The liver was palpable 3 cm at the epigastrium. Neither spleen, nor abdominal mass were palpable, and no bruit was audible over the liver.

Laboratory examinations data were: red blood cell count $314 \times 10^6/\text{mm}^3$; hemoglobin 9.3 g/dl; white blood cell count $4800/\text{mm}^3$, platelet count $13.5 \times 10^4/\text{mm}^3$, prothrombin time 12.0 sec, normotest 101%; total bilirubin 0.6 mg/dl, albumin 3.2 g/dl, γ-globulin 15.4%, asparatic aminotransferase 25 IU/l; alanine aminotransferase 23 IU/l; lactic dehydrogenase 234 IU/l; alkaline phosphatase 139 IU/l, γ-glutamyl transpeptidase 105 IU/l, choline esterase 272 IU/l, indocyanine green 15-min retention rate 18.4%; total bile acid 28.6 μmol/l. Fasting blood ammonia and glucose level were 124 μg/dl and 87 mg/dl, respectively. Blood ammonia levels were elevated after each meal (Fig. 2). The oral glucose tolerance test (75 g) showed a normal pattern. The fasting aminogram showed mild elevation of serine, glutamine, glycine, alanine, citrulline, cystine, methionine, tyrosine, phenylalanine, ornithine and arginine, not a specific pattern for any known congenital hyperammonemia. HBs antigen and α-fetoprotein were both negative.

Renal function tests showed: blood urea nitrogen 30 mg/dl, creatinine 2.6 mg/dl, uric acid 9.0 mg/dl, endogenous creatinine clearance 25.1 ml/min, PSP test 7.3% (15 min) and 41% (120 min). The renogram showed a delayed pattern in the left kidney and a non-functional pattern in the right kidney. Serum electrolytes showed normal values.

On the chest X-ray there was an enlarged cardiac silhouette with signs of congestion. The cardiac thoracic ratio was 78%. The electrocardiogram revealed atrial fibrillation and left ventricular hypertrophy. The ultrasonocardiogram revealed aortic and mitral regurgitation. Tricuspid regurgitation was also suspected.

Ultrasonography, computed tomography and $^{99m}$Tc phytate scintigraphy of the liver revealed no findings of cirrhosis (Fig. 3) but the inferior vena cava was dilated. Upper gastrointestinal barium examination showed no abnormality. Gastrofiberscopic examination disclosed several cherry-red like telangiectasia in the stomach (Fig. 4) but no varices were observed either in the esophagus or

![Fig. 2. Circadian rhythm of blood ammonia levels.](image1)

![Fig. 3. $^{99m}$Tc-phytate hepatic scintigraphy.](image2)
Celiac angiography was performed to evaluate the existence of portal-systemic shunts. Selective hepatic arteriography revealed widened and tortuous hepatic arteries suggesting an increased hepatic arterial flow, and a rapid filling of hepatic veins suggesting the existence of intrahepatic arteriovenous shunts. Numerous irregular contrast pools were scattered throughout the liver parenchyma (Fig. 5A, B).

To rule out possible cirrhosis and a diffuse type hepatocellular carcinoma, peritoneoscopy was performed. As shown in Fig. 6, the liver surface was
slight uneven and a network of white fibrous bands with several vascular spider-like telangiectasias were seen. Neither cirrhosis nor diffuse type hepatoma were suggested. As diffusely distributed hemangioma could not be ruled out, a biopsy was not performed.

From these findings of telangiectasia in the stomach, on the surface of the liver as well as on the face and tongue, concomitant with recurrent episodes of epistaxis and G-I bleeding, plus the fact that his father had died of G-I bleeding, the diagnosis of HHT was made. The hyperammonemia and hepatic encephalopathy were attributed to intrahepatic portal-systemic shunts existing concomitant with the arterio-venous shunts.

One morning during admission, the patient became hazy after two-day constipation. The electroencephalogram revealed slow waves with typical triphasic waves. This consciousness disturbance was improved several hours later after the transfusion of an amino acid-solution, rich in branched chain-amino acids. The electroencephalogram taken the next day showed a normal pattern.

At present the patient is well without any mental disturbance by taking lactulose.

**DISCUSSION**

Our patient experienced repeated disturbances of consciousness following hematemesis or constipation, from the age of 35 years. Physical examinations and laboratory data revealed no evidence of cirrhosis or hepatoma, rather valvular disease with cardiac failure, chronic renal failure, lordoscoliosis and a neurogenic bladder were evident and a diagnosis of HHT was made. The disturbance in consciousness was attributed to hepatic encephalopathy caused by porto-systemic shunt formed in the liver.

Hepatic involvement is rather frequent in HHT and hepatomegaly is apparently common\(^{12}\). Most of the autopsy studies revealed evidence of hepatic involvement\(^2,3,8,9,14\). The lesions were generally fibrosis or cirrhosis and atypical forms of cirrhosis have been observed; telangiectasia-associated hepatic fibrosis of "pseudocirrhosis"\(^9\) or Osler's cirrhosis\(^3\). Characteristic of the histology are telangiectasic vessels surrounded by randomly scattered fibrovascular foci with no major parenchymal or inflammatory reaction\(^8\). Peliosis hepatitis, hepatic adenoma, or hepatocellular carcinoma secondary to long-term hormone therapy were also noted. Etiology of the hepatic lesions is variable because patients with HHT are at risk for the development of liver disease. Chronic hepatitis or an iron overload may be secondary to transfusions. Passive congestion is secondary to high output heart failure caused by chronic anemia and arteriovenous shunting\(^6,10\). Daly and Schiller\(^3\) emphasized the importance of recognizing the apparently common and seemingly benign hepatic involvement in this disease.

Our patient had never received a blood transfusion, hepatosplenomegaly was absent and serum aminotransferase levels were normal. In the liver function tests, indocyanine green test showed a mild retention and the serum level of total bile acids was slightly elevated. The former may be due to congestive heart failure or arterio-venous shunt present in the liver. The latter was highly suggestive of the presence of porto-systemic shunts in the liver\(^13\).

From the angiographic findings, diffuse-type hepatoma, hepatoma arising in a cirrhotic liver, metastases, and cavernous hemangioma should be excluded\(^1\). Filling of hepatic veins during hepatic angiography may appear in other conditions such as reduced portal flow, infantile hemangiomas, richly vascularized metastatic neoplasm and, rarely, during normal conditions\(^16\). Although direct portal venography was not done because of cardiac and renal failure, findings on the hepatic angiography were highly suggestive of the existence of porto-systemic shunts in the liver.

CNS manifestations have been observed in 8 to 12% of the members of families with HHT and most of the patients with CNS complications had pulmonary arteriovenous fistula\(^2,11\). The occurrence of porto-systemic encephalopathy due to hepatic telangiectasia is, however, rare. Since the report of Michaeli et al.\(^4\) in 1968, there have been apparently no reports of such cases in English literatures.

The disease process involves both large and small vessels. Pulmonary arteriovenous fistulas, aortic aneurysms, and aneurysms of the splenic and hepatic arteries have been reported. Our pa-
tient had mitral, aortic and suspected tricuspid regurgitation. The etiology of these valvular diseases is not clear, however, HHT itself has to be considered. Reilly and Nostrant reported that 
dence of right, left, or biventricular cardiac failure with no explanation other than a possible HHT. It was not clear at present whether these lesions are manifestations of this syndrome because the etiology of the lesions is unknown.

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REFERENCES