Hereditary Hemorrhagic Telangiectasia Induced Portosystemic Encephalopathy: A Case Report and Literature Review

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Abstract:
Hereditary hemorrhagic telangiectasia (HHT) is a rare disorder characterized by telangiectasias and arteriovenous malformations (AVMs), which can involve multiple organ systems. Although hepatic involvement is common, the development of portosystemic encephalopathy is extremely rare. We herein report a 72-year-old woman with HHT-induced portosystemic encephalopathy secondary to hepatic arteriovenous malformations. She presented with disturbance of consciousness, and her serum ammonia level was elevated at 270 mg/dL. Color Doppler ultrasonography and contrast-enhanced computed tomography showed hepatic AVMs and shunts, which were useful for making the definite diagnosis. Portosystemic encephalopathy should be considered as a differential diagnosis in HHT patients presenting with disturbance of consciousness.

Key words: hereditary hemorrhagic telangiectasia, portosystemic encephalopathy, arteriovenous malformation

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Introduction

Hereditary hemorrhagic telangiectasia (HHT), also known as Osler-Weber-Rendu disease, is a rare autosomal disorder characterized by telangiectasias and arteriovenous malformations (AVMs). The criteria of international guidelines are used to diagnose HHT: (i) recurrent and spontaneous epistaxis, (ii) mucocutaneous telangiectasias, (iii) visceral involvement, and (iv) a first-degree relative with HHT (1). If three or four are met, the patient has definite HHT. The prevalence has been reported to be between 1 in 5,000 and 1 in 10,000. HHT can involve the skin, mucous membranes of the head and upper extremities, respiratory tract, digestive tract, and liver (1, 2).

HHT patients with liver involvement are mostly asymptomatic, and a few have been reported to have high-output cardiac failure, portal hypertension, or biliary disease. Hepatic encephalopathy secondary to portosystemic shunts is an extremely rare complication (1, 3).

We herein report an HHT patient with portosystemic encephalopathy (PSE) secondary to hepatic AVMs.

Case Report

A 72-year-old woman with no remarkable family medical history was admitted to our hospital because of a disturbance of consciousness. The patient had a history of intermittent epistaxis and mild anemia. She had no other relevant medical history causing portal vein thrombosis, such as cholecystitis, cholangitis, pancreatitis, or abdominal surgery.

The patient had become less responsive and more confused two hours before her admission. The Glasgow Coma Scale score was 6 (E1V1M4), but other vital signs were normal. A physical examination showed cutaneous telangiectasias on the fingers (Fig. 1, arrows). Laboratory results on admission showed a slight elevation of hepatobiliary enzymes and mild anemia (Table 1). Serological testing for hepatitis B and C viruses was negative. Among hepatic fibrosis markers, only her hyaluronic acid level was slightly elevated. However, the serum ammonia level was elevated at 270 mg/dL. Brain magnetic resonance imaging (MRI) and magnetic

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Figure 1. Cutaneous telangiectasias were seen on the fingers (arrows).

Table 1. Laboratory Results on Admission.

| Laboratory item           | Value    | Normal range          | Laboratory item           | Value    | Normal range          |
|---------------------------|----------|-----------------------|---------------------------|----------|-----------------------|
| White blood cell counts (μL) | 3,300    | 3,300-8,600           | Total protein (g/dL)       | 6.2      | 6.6-8.1               |
| Red blood cell counts (μL) | 372      | 386-492×10^4          | Albumin (g/dL)             | 3.3      | 4.1-5.1               |
| Hemoglobin (g/dL)         | 10.9     | 11.6-14.8             | Total bilirubin (mg/dL)    | 2.2      | 0.4-1.5               |
| Platelet count (μL)       | 18.1     | 15.8-34.8×10^4        | Aspartate aminotransferase (IU/L) | 27      | 13-30                 |
|                           |          |                       | Alanine aminotransferase (IU/L) | 33      | 10-42                 |
| Prothrombin time (s)      | 12.8     | 11-14                 | Lactate dehydrogenase (IU/L) | 238     | 124-222               |
| Activated prothrombin time (s) | 31      | 25-35                | Alkaline phosphatase (IU/L) | 383     | 106-322               |
| Hyaluronic acid (ng/mL)   | 71.1     | 0-50                  | Urea nitrogen (mg/dL)      | 14.6     | 8-20                  |
| Type IV collagen (ng/mL)  | 119      | 0-140                 | Creatinine (mg/dL)         | 0.53     | 0.46-0.79             |
| Type IV collagen 7S (ng/mL) | 5.3      | 0-6                   | C-reactive protein (mg/dL) | 0.099    | 0-0.15                |

Discussion

The clinical symptoms of HHT are usually associated with bleeding, such as epistaxis or gastrointestinal hemorrhaging from telangiectasias. A previous report suggested that 32-78% of HHT patients have liver involvement, as the AVMs affect the destination of the portal venous and hepatic arterial blood flow (1). Three types of intrahepatic shunt may be attributable to the hepatic AVMs: hepatic artery to portal vein, hepatic artery to hepatic vein, and portal vein to hepatic vein. These shunts often co-exist and can result in several complications, such as high out-put cardiac failure, portal hypertension, biliary necrosis, encephalopathy, and mesenteric ischemia (4).

Among these three types of shunts, portal vein to hepatic vein shunts leading to hepatic encephalopathy are extremely rare (3). To our knowledge, only 12 cases of HHT patients with PSE have been reported, including our case (Table 2) (5-15). Reviewing these reports, there were 6 men
and 5 women including our case (case 4 was not described in detail and is not available), with ages ranging from 57 to 86 (median, 67) years old. Although HHT is a genetic and congenital disease, no cases of PSE have been reported at a young age. This suggests that hepatic AVMs are present early in life, but their symptoms do not appear until middle age or later, as vascular abnormalities progress with aging, and the shunt volume also increases (16). The HHT patients in all reported cases were treated with osmotic laxatives, such as lactulose, and there have been no reports of liver

Figure 2. Abdominal ultrasonography showed multiple anechoic structures in the liver (a). Flow was confirmed on color Doppler imaging, and the anechoic structures were considered to be dilated and tortuous vessels (b). Color Doppler imaging showed hepatic arteriovenous shunts with a turbulent flow (c, arrow).

Figure 3. Contrast-enhanced computed tomography showed dilation and tortuousness of the intrahepatic and extrahepatic arteries (a, arrows) and early enhancement of the hepatic vein in the early arterial phase (b, arrow). These findings were consistent with AVMs. AVMs: arteriovenous malformations.
Figure 4. Esophagogastroduodenoscopy showed multiple telangiectasias in the stomach.

Table 2. Literature Review of Hereditary Hemorrhagic Telangiectasia Induced Portosystemic Encephalopathy.

| Case number | Reference number | Age (years) | Sex  | Symptom                        | Ammonia level (μg/dL) | Diagnostic study                        | Treatment                           |
|-------------|------------------|-------------|------|---------------------------------|-----------------------|-----------------------------------------|--------------------------------------|
| 1           | 5                | 57          | Male | disturbance of consciousness   | 124                   | Ultrasonography                         | Lactulose                            |
|             |                  |             |      |                                 |                       | Computed tomography Angiography         | Branched-chain amino acids           |
| 2           | 6                | 64          | Female | abnormal behaviors              | 229                   | Angiography                             | Not available                        |
| 3           | 7                | 78          | Female | stupor                          | 198                   | Ultrasonography                         | Lactulose                            |
|             |                  |             |      |                                 |                       | Computed tomography Angiography         | Branched-chain amino acids           |
| 4           | 8                |             | Not available | abnormal behaviors              | Not available         | Not available                           |                                      |
| 5           | 9                | 71          | Female | abnormal behaviors              | 162                   | Computed tomography                     | Lactulose                            |
|             |                  |             |      |                                 |                       |                                         | Branched-chain amino acids           |
| 6           | 10               | 68          | Male | disturbance of consciousness   | 190                   | Ultrasonography                         | Osmotic laxatives                    |
|             |                  |             |      |                                 |                       | Computed tomography Angiography         | Branched-chain amino acids           |
| 7           | 11               | 78          | Male | disturbance of consciousness   | 224                   | Computed tomography                     | Branched-chain amino acids           |
| 8           | 12               | 75          | Female | altered mentality              | 137                   | Computed tomography                     | Lactulose                            |
| 9           | 13               | 64          | Male | confusion                       | 182                   | Ultrasonography                         | Not available                        |
|             |                  |             |      |                                 |                       | Computed tomography Angiography         | Branched-chain amino acids           |
| 10          | 14               | 86          | Male | disturbance of consciousness   | 128                   | Ultrasonography                         | Lactulose                            |
|             |                  |             |      |                                 |                       | Computed tomography Angiography         | Branched-chain amino acids           |
| 11          | 15               | 85          | Male | altered mentality              | 68                    | Ultrasonography                         | Lactulose                            |
|             |                  |             |      | disturbance of consciousness   |                       | Computed tomography Angiography         | Branched-chain amino acids           |
| 12          | Our case         | 73          | Female | disturbance of consciousness   | 270                   | Ultrasonography                         | Lactulose                            |
|             |                  |             |      |                                 |                       | Computed tomography Angiography         | Branched-chain amino acids Antibiotics |

transplants having been performed.

Hepatic angiography can be the best method of diagnosing hepatic AVMs, but less invasive modalities, such as Doppler US, CE-CT, and MRI, usually have been used for the diagnosis of hepatic AVMs in HHT patients (3). Doppler US is the optimal first-line investigation for the assessment of liver AVMs in HHT patients because of its safety, tolerability, low cost, and accuracy for detection. The caliber, course, and flow characteristics of the hepatic vessels evaluated by Doppler US support the diagnosis of hepatic AVMs and staging of their severity (17). A diagnosis using CE-CT can be achieved through diffuse liver telangiectasias and dilated hepatic vessels (3). However, the identification of portovenous shunts is usually difficult with these imaging mo-
The authors state that they have no Conflict of Interest (COI).

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