HEREDITARY HEMORRHAGIC TELANGIECTASIA WITH
A PULMONARY ARTERIOVENOUS FISTULA

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HEREDITARY hemorrhagic telangiectasia (Rendu-Osler-Weber disease) characterized by cutaneous, mucosal and visceral telangiectasia, angioma, hemorrhages and a hereditary transmission was first described by Babington in 1865.

Telangiectasia may involve almost all of organs of the body and a pulmonary arteriovenous fistula is found in 60% of the cases. The latter anomaly may be interpreted to be a manifestation of pleiotropic effects of a mutant allele with incomplete penetrance which is responsible for hereditary telangiectasia. Surgery is indicated in selected patients who have localized lesions. The prognosis for patients with pulmonary arteriovenous fistula is determined by the magnitude of the right-to-left shunt, the possibility of complications and the chance of progression of the lesion.

Recently, we examined two patients having pulmonary arteriovenous fistula at Seoul National University Hospital. They had multiple cutaneous and visceral telangiectasia. There was no definite family history of hemorrhagic telangiectasia.

About 20 percent of hereditary hemorrhagic telangiectasia cases have no family history.

Hereditary hemorrhagic telangiectasia is a rare disease and the initial presentation is similar to that of congenital heart disease. It is important for clinicians to differentiate these two morbid conditions in the early stages.

CASE REPORTS

Case I

An 11-year-old girl was admitted to the pediatric ward of Seoul National University Hospital with a chief complaint of cyanosis on March 15, 1982. At 5 years of age, cyanosis of the lips was first noticed by her parents especially in the cold weather. And soon, exertional dyspnea and squatting developed. About 2 years prior to admission, cyanosis became intense and about 1 year prior to admission, multiple purplish telangiectatic spots developed on the bilateral cheeks.

Epistaxis and lip bleeding were frequently noticed, and clubbing of the fingers gradually developed. Therefore, she was brought to a local clinic where she was found to have congenital heart disease.

She was admitted to the pediatric ward under the assumption of congenital heart disease on November 23, 1981, but cardiac catheterization and right ventricular angiography revealed no abnormal findings. After discharge, intermittent mild chest pain and headache developed. So she was readmitted to this ward for the further evaluation of cyanosis. There had been a history of hemoptysis and melena. The family history was not contributory.

Physical examination on admission revealed the following findings: She looked deeply cyanotic but not dyspneic in the resting state. Her body weight was 24 kg, on the 3rd to 10th percentile.

Vital signs were stable

Multiple telangiectatic lesions with purplish tone were noted on her cheeks, buccal mucosa, and nasal mucosa. The conjunctivae were

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injected, and the sclerae were not icteric. Purplish papillae were prominent on the tongue. Her chest cage expanded symmetrically without deformity. Breath sound was diminished slightly on the both sides of lung fields, especially on the right side. Heart beat was regular and neither bruit nor murmur was audible. Her abdomen was soft and not tender, and her liver and spleen were not palpable. Cyanosis was deeper on her lips and finger tips than on her toes.

Laboratory data: Hemoglobin 22.8 g/dl, red blood cells 6,710,000/mm³, hematocrit 72%, white blood cells 7,900/mm³ (stab 2, seg 71, eosino 8, baso 1, lympho 18%), platelet 120,000/mm³.

The radial artery was sampled for blood gas analysis, which showed pH 7.392, PaCO₂ 31.9 mmHg, PaO₂ 41.5 mmHg, HCO₃⁻ 19.7 mEq/L. On breathing 100% oxygen, PaO₂ 51.7 mmHg and after O₂ removal, PaO₂ was 44 mmHg. A chest x-ray revealed a normal heart size with a slightly increased density in the right upper lung field. ECG and echocardiography showed no abnormal findings.

A pulmonary function test showed a restrictive pattern. A lung scan with ⁹⁹ᵐTc-MAA showed a perfusion defect in the right upper lung field. A heart scan with ⁹⁹ᵐTc-HSA revealed rapid transit time (RV to lung, 2.25 sec, lung to LV 1 sec, RV to LV 3.25 sec) and early visualization of the abdominal aorta. Assuming the presence of a pulmonary arteriovenous fistula, pulmonary arteriography was done. As a result, bilateral diffuse pulmonary arterio-venous fistula were found (Fig. 1). Celiac and superior mesenteric arteriography showed multiple irregular vessels existing in the right lobe of the liver, the head of the pancreas, and the jejunum (Fig. 2). Early venous drainage was noted.

Case II

A 4-year-old boy with cyanosis was admitted in a semicomatose state to the pediatric ward of Seoul National University Hospital on May 12, 1982. Since his early infancy, he was known to have a cyanotic congenital heart disease. On September 3, 1981, he visited Seoul National University Hospital where dyspnea at rest, cyanosis and clubbing of the fingers and toes were noted. His liver was palpable by 7 cm width in the epigastrium and his spleen was finger breadth palpable at that time. One week prior to admission ear discharge from both ears was noted.

Two days prior to admission, his fever subsided.

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but irritability developed. He vomited once. One day prior to admission, he became drowsy and lost his consciousness. He was brought to our emergency room, where hematochezia was noted. Physical examinations on admission were as follows: He looked cyanotic and dyspneic in the resting state. His body weight was 13 kg, on the 10th to 25th percentile. His body temperature was 36°C, pulse rate 112/min, respiration rate 50/min, and blood pressure 90/70 mmHg. Telangiectatic lesions were noted on his cheeks. The conjunctiva were slightly anemic and the sclerae were slightly icteric. Pupils were isocoric and light reaction was present. Ear discharges were noted in both ears. Both tympanic membranes were perforated. Venous engorgement and precordial bulging were noted. Breathing sounds were coarse with rales in the right lung field. Heart beats were regular without murmurs. His abdomen was soft and distended. His liver was palpable deeply by 10 cm span in the epigastrium being hard in consistency and lobulated. His spleen was 1 finger bedth palpable below the left subcostal margin.

Cyanosis and clubbing of the fingers and toes were noted. Neurologic examination showed an unconscious state with pain sense. The knee and ankle jerk were increased on the left side. Ankle clonus and Babinski reflexes were noted bilaterally. The right extremities were slightly paretic.

Meningeal irritation signs were absent. Laboratory data: Hemoglobin 10.2 g/dl, hematocrit 44%, white blood cells; 11700 mm$^3$ (seg 92, lympho 7%, immature cell 1%), platelet 98,000/mm$^3$, corrected ESR; 20 mm/hr. Stool occult blood was +3 positive. Blood chemistry showed the following findings: protein/albumin 6.8/2.8 gm/dl, SGOT/SGPT 21/5 IU/L, BUN/Cr 13/0.9 mg/dl, bilirubin (total/direct) 3.0/1.5 mg/dl, alkaline phosphatase 180 IU/L. Prothrombin time was 15 seconds (60% of the control). Blood gas analysis showed pH 7.45, PaCO$_2$ 34 mmHg, PaO$_2$ 38 mmHg, and HCO$_3^-$ 24 mEq/L. On breathing 100% oxygen, PaO$_2$ increased to 50 mmHg. CSF examination revealed no pleocytoses. Chest X-ray revealed a slightly enlarged heart size with decreased pulmonary vascularity. EKG and echocardiography were normal.

Under the assumption of a brain abscess as a complication of cyanotic congenital heart disease, antibiotics and mannitol were given initially.

On the 3rd hospital day, his consciousness returned to normal. Brain CT and brain radioisotope scan revealed no abnormal findings. A liver scan with $^{99m}$Tc-phytate revealed shrinkage of the right lobe of the liver with a decreased uptake and splenomegaly with an increased splenic uptake. Esophagography showed an

Fig. 2. Celiac and superior mesenteric arteriogram showing multiple irregular vessels in right lobe of liver, head of pancreas and jejunum.
esophageal varix. On the 10th hospital day, cardiac catheterization was performed. But no intrinsic pathology was found in the heart. Pulmonary arteriography revealed diffuse fine nodular density in both lungs and early visualization of the peripheral branches of pulmonary vein. A lung scan revealed perfusion defects in the upper portion of the left lung field. Visualization of radionuclide in the liver, the kidney and other sites suggested right to left shunt.

Abdominal aortography revealed no evidence of an arteriovenous shunt of the visceral organs. On the 14th hospital day, celiac angiography revealed collateral from the main portal vein to the dilated, tortuous coronary vein and an inferior mesenteric vein. These findings suggested portal hypertension, most likely due to liver cirrhosis. In order to differentiate pulmonary arteriovenous fistula due to liver disease from fibrosis of the liver due to Rendu-Osler-Weber disease, an open liver biopsy was done under a general anesthesia on the 15th hospital day.

A liver wedge biopsy showed an irregular surface with a focal connective tissue scar having a nodular appearance. Microscopically the liver was divided into numerous lobules that varied in size from unilobular to multilobular. Some of the lobules included central veins in the middle of them. These central veins showed sclerosis and were surrounded by congested dilated sinusoids, only to stop rather abruptly in the midzone where dilated empty sinusoids were seen. The liver cells cords were relatively well maintained in the remaining portions. The connective tissue septa extended into the lobule forming either definite pseudolobule or incomplete ones. The portal spaces were mildly infiltrated by small round cells. Dilated capillaries were seen, but bile duct proliferation or vascular thickening were not seen. No regenerative activity was found. Some portal spaces did not contain a bile duct. No fatty changes were present. Operative findings were as follows: The left lobe of the liver was macronodular cirrhotic. The right lobe of the liver was shrunken. The spleen was palpable. A moderate amount of ascites was found. The portal pressure was

37 cm H₂O.

DISCUSSION

The present two cases showed symptoms suggesting congenital heart disease such as cyanosis, exertional dyspnea, and clubbing. Cyanosis was out of proportion to the dyspnea. Cyanotic congenital heart disease was considered first. However, thorough examination including cardiac catheterization and angiography revealed no cardiac abnormalities. Multiple telangiectatic spots and epistaxis developed. Pulmonary arteriography revealed bilateral diffuse pulmonary arterio-venous fistulas. Surgical treatment was not recommended for this abnormality. Case I also had telangiectatic lesions in the liver, pancreas and jejunum, and case II had liver cirrhosis accompanied by esophageal varix and splenomegaly.

No definite evidence of familial occurrence was obtained in the both cases. The pulmonary arterio-venous fistula may be interpreted to be a manifestation of pleiotropic effects of a mutant allele with incomplete penetrance which is responsible for hereditary telangiectasia.

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