Hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber disease) presenting with polymicrobial brain abscess

Case report

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A 26-year-old man presented with expressive aphasia, weakness of the right arm, and anemia but there was no family history of hereditary hemorrhagic telangiectasia. Computerized tomography (CT) of the head demonstrated an enhancing left frontal mass, which was aspirated and on culture yielded multiple organisms. Pulmonary arteriovenous fistulae identified in both lungs by chest radiography, CT, and angiography were treated with coil embolization. Treatment of pulmonary arteriovenous fistulae and prolonged surveillance are necessary to prevent future neurological complications.

Key Words: • brain abscess • hereditary hemorrhagic telangiectasia • Rendu-Osler-Weber disease

Hereditary hemorrhagic telangiectasia (HHT), or Rendu-Osler-Weber disease, is an autosomal dominant disorder characterized by recurrent episodes of epistaxis and gastrointestinal hemorrhage from mucocutaneous and visceral telangiectasias. Central nervous system (CNS) manifestations of HHT are rare and include brain abscess and cerebral and spinal vascular malformations. Brain abscess develops in the presence of a right-to-left pulmonary shunt with decreased arterial oxygen saturation. Vascular anomalies of the brain and spinal cord that have been associated with HHT are telangiectasias, angiomas, aneurysms, carotid-cavernous fistulae, and arteriovenous malformations. The management of patients with HHT should include the identification and treatment of neurological infectious or vascular diseases and the obliteration of pulmonary arteriovenous fistulae that may predispose to CNS involvement.

Case Report

This 26-year-old man presented to another hospital complaining of fatigue and weakness of the right arm for 1 week. He experienced a generalized seizure and cranial computerized tomography (CT) revealed an enhancing left frontal mass with surrounding edema (Fig. 1). He was then treated with anticonvulsant agents and corticosteroid medications before transfer to the University of Minnesota Hospital and Clinic.

Examination. Additional clinical history elicited on admission included frequent dyspnea on exertion with recurrent epistaxis since childhood, occurring approximately three times per week. There was no family history of HHT. The patient was afebrile with stable vital signs. His general physical examination was remarkable for multiple small telangiectasias on the mucosal surface of the mouth and digital clubbing of the hands and feet. No thoracic bruits were detected on auscultation of the lungs. Neurologically, he was lethargic but easily arousable. He would follow commands and had a severe expressive aphasia but could answer "yes" or "no" to questions. There was no papilledema and a left gaze preference was present. A right-sided hemiparesis was worse in the arm than in the leg and his reflexes were increased on the right, with an upgoing toe reflex on that side.

Laboratory evaluation was notable for a hemoglobin value of 7.2 gm/dl and a normal white blood cell count. Blood cultures were sterile and room air blood gas values were pH 7.48, pCO₂ 29 mm Hg, and pO₂ 57 mm Hg. A lumbar puncture was not performed because of the mass effect present on the CT scan. Chest films showed opacification in the left lower lobe of the lung. Magnetic resonance imaging of the head with and without intravenous infusion of contrast medium verified that the left frontal lesion projected to the cortical surface; no other infectious or vascular lesions were found.
Hereditary hemorrhagic telangiectasia and brain abscess

Fig. 1. Preoperative computerized tomography scan of the head showing an enhancing left frontal mass with surrounding cerebral edema.

Fig. 2. Postoperative contrast-enhanced computerized tomography scan of the chest demonstrating opacification (arrows) in both lungs that represented pulmonary arteriovenous fistulae on angiography.

Operation. Cranial CT was performed to identify the area directly over the lesion. A brain needle was passed through a burr hole into the lesion and 12 ml of pus was aspirated. Gram stain demonstrated multiple Gram-positive and Gram-negative organisms. *Streptococcus intermedius*, *Actinomyces meyeri*, *Fusobacterium nucleatum*, *Capnocytophaga species*, and *Staphylococcus epidermidis* grew on culture. Based on organism sensitivities, the patient was treated intravenously every 6 hours with 5,000,000 U penicillin G and 1500 mg chloramphenicol.

Postoperative Course. Chest CT scans confirmed the presence of arteriovenous fistulae in both lungs (Fig. 2). Two-dimensional echocardiography of the heart documented a large right-to-left shunt. Pulmonary angiography revealed three arteriovenous fistulae in the left lung and two in the right lung, which were embolized with coils 3 to 12 mm in length. Following embolization, the room air blood PaO2 level increased to 93 mm Hg. Colonoscopy showed multiple small arteriovenous malformations that were not actively bleeding; these were coagulated with the laser.

The patient’s expressive aphasia and right hemiparesis gradually improved with speech therapy and physical therapy. He was treated for 4 weeks with chloramphenicol and for 6 weeks with penicillin G. Follow-up CT of the head at 6 months showed complete resolution of the abscess. It was recommended that the patient undergo repeat pulmonary angiography every 6 months for 2 years.

Discussion

The diagnosis of HHT requires the presence of two of the following criteria: a positive family history, mucocutaneous telangiectasias, and recurrent epistaxis or gastrointestinal hemorrhage.6 In 15% to 30% of patients with HHT there is no family history of the disease,7 as was the case in the patient described here.

Neurological complications develop in 8% to 41% of family members of patients with HHT and include air embolism, transient ischemic attacks, paradoxical embolism, and brain abscess.1,5,7 The mechanism responsible for the development of brain abscess is septic embolization through the pulmonary capillary circulation into areas of cerebral microinfarction.6-8 Polycythemia and cerebral hypoxia due to imperfect oxygenation can predispose patients to vascular thrombosis and cerebral infarction.7 The patient reported here had systemic hypoxia and anemia due to recurrent epistaxis.

Brain abscess occurs in 3% to 5% of patients with cyanotic congenital heart disease and in 5% to 10% of those with pulmonary arteriovenous fistulae.1,7 Press and Ramsey6 found pulmonary arteriovenous fistulae in 29 (94%) of 31 patients with HHT who developed brain abscess or meningitis. Dyer6 estimated that 15% to 23% of patients with HHT have pulmonary arteriovenous fistulae and that 5% of these patients will develop brain abscess. The expected risk for developing brain abscess in patients with HHT is approximately 1% or 1000 times greater than the risk for developing CNS infection in the general population.6,9 As shown by this case, pulmonary arteriovenous fistulae can often be asymptomatic with brain abscess being the first clinical manifestation.

In a review of the literature, Román, et al.,7 identified 28 (13%) cases of brain abscess in more than 200 patients with HHT; multiple brain abscesses were present in two patients (7%) and meningitis developed in three (11%). Abscess locations were primarily supratentorial with the posterior fossa rarely involved in HHT or congenital heart disease.2,7 Anaerobic organisms such as *Streptococcus* species are isolated from most infections although sterile culture results are not uncommon, particularly if antibiotic agents have been administered.6,7 As in this case, polymicrobial infection was present in 41% of patients with a positive culture reported by Press and Ramsey.6

Symptoms associated with brain abscess are obturation, headache, visual disturbances, hemiplegia, and seizures.6 A body temperature above 38°C and an associated primary focus of infection are uncom-
Leukocytosis and positive blood cultures are infrequent and were not present in the case reported here. Clinical manifestations of pulmonary arteriovenous fistulae and arterial desaturation are cyanosis, digital clubbing, polycythemia, hypoxemia, and a lung bruit. Radiographic evaluation for pulmonary arteriovenous fistulae should include chest radiography which demonstrates vascular opacities in 86% of patients. Computerized tomography of the chest should be performed if a fistula is not visualized on chest radiography. Arteriovenous fistulae are best demonstrated by pulmonary angiography, which in the patient reported here was reserved until the time of embolization.

Patients with brain abscess and pulmonary arteriovenous fistulae should be treated first by aspiration of the abscess and then by obliteration of the lung malformation. Abscess aspiration provides rapid relief of intracranial pressure and enables identification of the causative organism. Aspiration of deep lesions may require stereotactic guidance. Pulmonary arteriovenous fistulae can be treated by surgical resection or by endovascular embolization. Patients with multiple malformations are best treated with balloon or coil embolization. Improvement of pulmonary function will often follow embolotherapy, as experienced by this patient. Endovascular occlusion of lung fistulae carries the risk of pulmonary infarction and paradoxical embolization if multiple feeding arteries with septated aneurysmal sacs are present.

Small, clinically silent fistulae can be followed to document enlargement; however, the smaller size does not preclude septic embolization to the brain. We prefer surgical or endovascular intervention to observation, except in patients with extensive disease where no treatment is available. Surgical excision of one pulmonary arteriovenous fistula can prompt the emergence of new or previously undetected lesions. Pulmonary surveillance is necessary to identify the sequential development of pulmonary fistulae which arise from defects in capillary loops that dilate and form ectatic thin-walled vascular channels.

As illustrated by this case, polymicrobial brain abscess can be the first manifestation of HHT. Because patients with HHT can experience fatal brain abscess following interval development of pulmonary arteriovenous fistulae in other segments, routine surveillance with chest CT or angiography should be performed every 6 to 12 months. Screening family members of patients with HHT by means of chest radiography and arterial blood gas measurements has been recommended.

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References