CLINICAL VIGNETTE

Pulmonary Arteriovenous Malformation as the Initial Manifestation of Hereditary Hemorrhagic Telangiectasia

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Case Presentation

A 39-year-old female with asthma and hypothyroidism presented to the emergency room with dyspnea on exertion. She reported gradual dyspnea on exertion for several months with intermittent chest tightness. She denied dyspnea at rest, cough, or hemoptysis. She was very active previously but now unable to climb a flight of stairs due to dyspnea. For asthma treatment, she only used prn albuterol inhaler but used it more often over the past several weeks, up to four times a week. She had never been hospitalized for asthma or needed to be intubated for an asthma exacerbation. She reported several episodes of epistaxis every month since childhood. She denied history of skin telangiectasias, gastrointestinal bleeding, liver problems, or history of stroke, brain abscess, or seizure. Her brother had frequent epistaxis since childhood.

The patient's initial vitals were temperature of 36.7 degrees Celsius, heart rate 61/min, blood pressure 111/63 mmHg, respiratory rate 19 breaths/min with room air oxygen saturation of 87%. On physical examination, her lungs were clear to auscultation, and no increased work of breathing. No telangiectasias were noted on her skin. Laboratories included normal basic metabolic panel (BMP) and a complete blood count (CBC) with elevated hemoglobin of 15.8 g/dL (normal range 11.6 - 15.2 g/dL). Computed tomography angiography (CTA) chest was negative for pulmonary embolism (PE) but was notable for 4 pulmonary arteriovenous malformations (AVMs) in the right lung. Pulmonary and Interventional radiology were consulted, and she underwent three coil embolizations with subsequent improvement in her breathing and resolution of her hypoxia.

Given concern for hereditary hemorrhagic telangiectasia (HHT), genetics was consulted, and genetic panel ordered. Otolaryngology performed nasal endoscopy that did not show telangiectasias. CTA liver did not show any large vascular malformations. Magnetic resonance imaging (MRI) brain did not show cerebral AVMs. The patient was discharged with scheduled follow-up with genetics. Her genetic testing later returned positive for ENG, also known as HHT, a highly suspicious variant. Given that she already met clinical diagnostic criteria for HHT, this was diagnostic.

Discussion

HHT, or Osler-Weber-Rendu syndrome, is an autosomal dominant disorder of blood vessels with reported worldwide prevalence of 1 in 5,000 to 1 in 10,000.[1] The most common manifestation is epistaxis that begins during childhood or adolescence. Telangiectasias are dilated blood vessels that appear as thin, spiderweb-like red and dark purple lesions, usually appear after puberty. Patients can also develop AVMs, abnormal connections between arteries and veins that bypass the capillary system, in lungs, brain, and liver. Pulmonary AVMs can cause hypoxemia and cerebral abscesses or strokes due to paradoxical emboli. Cerebral AVMs can cause intracranial hemorrhage. Liver AVMs are usually asymptomatic but can lead to high-output heart failure, biliary disease, and portal hypertension.

The Curaçao diagnostic criteria for HHT include four findings: recurrent and spontaneous epistaxis, multiple skin telangiectasias, AVMs in one or more internal organs, and a first degree relative with HHT.[2] A patient who has two of the criteria has possible HHT, and definite HHT if three or four criteria are met. This patient had at least two criteria, with epistaxis and pulmonary AVMs, and possible family history of HHT given recurrent epistaxis in her brother. In children and young adults, the Curacao criteria has limited value, as clinical manifestations of HHT develop with age. It is believed that over 90% of HHT patients in the United States are undiagnosed.[3] This may be due to physicians failing to connect HHT's diverse manifestations as part of the underlying syndrome.

HHT is caused by mutations in one of two genes, and now is subclassified into types 1 and 2. Type 1 HHT is caused by a mutation in the ENG gene, as the presented patient had. With this type, patients, especially women, are at a higher risk of forming pulmonary and cerebral AVMs. Type 2 HHT is caused by a mutation in the ACVRL1 gene. These patients have a higher risk of forming liver AVMs. Studies report HHT as clinically diagnosed by the Curaçao criteria is highly predictive of a causative variant in either ENG or ACVRL1.[4] After the diagnosis of HHT, family members should undergo genetic testing.

Approximately 90% of pulmonary AVMs occur in patients with HHT, though AVMs can also be acquired through trauma, infection, hepatopulmonary syndrome, or after surgical repair

of congenital heart disease.[5] Pulmonary AVMs present with a wide variety of clinical manifestations including dyspnea or hypoxemia. However, in asymptomatic individuals, thrombi or bacteria can shunt through the AVM and bypass the filtering capabilities of the lung, leading to serious complications such as stroke or brain abscess.[6] Pulmonary AVMs do not have malignant potential but can enlarge with time. Treatment with embolization is recommended with AVMs >3 mm, due to potential neurological complications. After successful embolization, patients should have lifelong CT follow-up in 3-to-5-year intervals.[7]

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