A missed case of hereditary hemorrhagic telangiectasia: A case report

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Abstract
Hereditary hemorrhagic telangiectasia is a rare autosomal dominant disorder characterized by abnormal blood vessel formation. When an abnormal vascular architecture affects the lungs and central nervous system, serious complications can occur. We report a missed case of hereditary hemorrhagic telangiectasia with pulmonary arteriovenous malformations and cerebral arteriovenous malformations. A 22-year-old Chinese female was taken to the emergency room because of unconsciousness. Emergency head contrast-enhanced computed tomography and transthoracic contrast echocardiography showed that she had cerebral arteriovenous malformations and pulmonary arteriovenous malformations. The patient experienced multiple spontaneous epistaxis since childhood, for which she was treated at a local hospital for a brief period. Her mother also had pulmonary arteriovenous malformations. The patient was diagnosed with hereditary hemorrhagic telangiectasia according to the consensus Curacao diagnostic criteria and eventually died of hereditary hemorrhagic telangiectasia. The case report highlights the importance of early diagnosis and intervention for hereditary hemorrhagic telangiectasia. Given that hereditary hemorrhagic telangiectasia is frequently undiagnosed, increasing the physician’s awareness of hereditary hemorrhagic telangiectasia can play an important role in the timely diagnosis and treatment of these patients.

Keywords
Hereditary hemorrhagic telangiectasia, cerebral arteriovenous malformations, pulmonary arteriovenous malformations

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Introduction
Hereditary hemorrhagic telangiectasia (HHT) is a rare autosomal dominant disorder, occurring in approximately 0.02% of the general population.1 The visceral and mucocutaneous manifestations of HHT are the result of an abnormal vascular architecture. HHT is characterized by mucocutaneous telangiectasia, epistaxis, and visceral arteriovenous malformations, which can lead to serious complications when it affects the lungs and central nervous system.2

The clinical diagnosis of HHT is based on the Curacao criteria and includes recurrent epistaxis, multiple telangiectasias, visceral lesions, and family history.3 Patients who meet at least three of the four criteria are diagnosed with HHT.3 The early symptoms of HHT are mild and atypical, resulting in frequent misdiagnosis of HHT. Pulmonary arteriovenous malformations (PAVMs) are visceral lesions associated with HHT and have a natural tendency to enlarge over time. The penetrance of PAVMs is age-related and almost complete at age 40.4 Studies have shown that the time lag between the onset of HHT-related clinical
manifestations and the final diagnosis is approximately 29 years.\(^5\) Because the clinical manifestations of HHT develop with age, the clinical diagnostic criteria of Curacao lack sensitivity in young adults.\(^6\) We report a missed case of HHT with PA VMs and cerebral arteriovenous malformations (CA VMs).

**Case presentation**

A 22-year-old Chinese female was taken to the emergency room because of unconsciousness. Bedside monitoring showed a blood pressure of 90/60 mmHg, heart rate of 122 bpm, pulse SpO\(_2\) of 90%, and respiratory rate of 41 bpm. Emergency head contrast-enhanced computed tomography (CT) showed a left frontal hematoma with rupture into the ventricular system and CA VMs in the left-middle cerebral artery (Figure 1). She was immediately taken to the operating room for emergency treatment involving intracranial hematoma removal, arteriovenous malformation repair, and bone plate decompression surgery. The patient had hypoxemia, and blood gas analysis showed pH: 7.48, PaCO\(_2\): 28 mmHg, PaO\(_2\): 54 mmHg, and SaO\(_2\): 90%. We suspected that she had PAVMs; however, the patient’s condition was severely unstable and too high risk for chest CT angiography (CTA), so we performed a transthoracic contrast echocardiography (TTCE). Five milliliters of agitated saline was injected into the patient’s venous system within 3 s while projecting the four-chamber apical view.\(^7\) TTCE confirmed our hypothesis and showed that the contrast agent entered the left heart from the pulmonary veins at the beginning of the third cardiac cycle and that the left heart was completely filled with the dense microbubbles.

The patient experienced multiple spontaneous epistaxis since childhood, for which she was treated at a local hospital for a brief period. Her mother also had hypoxemia and TTCE (Figure 2), and chest contrast-enhanced CT (Figure 3) confirmed PAVMs. The patient was diagnosed with HHT according to the consensus diagnostic Curacao criteria.\(^3\) Given the rapid deterioration of the patient’s condition and poor prognosis, a legally authorized representative of the patient finally decided to forgo further treatment, and the patient eventually died of HHT.

**Discussion**

HHT is a rare autosomal dominant disorder. The most common symptom of HHT is epistaxis, which occurs in more than 90% of HHT patients.\(^8,9\) HHT-related epistaxis is caused by the presence of several dilated capillaries in the nasal mucosa, and the rupture of these dilated capillaries can lead to repeated instances of epistaxis,\(^10\) as seen in our patient.\(^11\) Many factors often trigger epistaxis, such as certain foods, low humidity, activity, and changes in external temperature and posture.\(^12\)

PAVMs are structurally abnormal vessels that provide direct capillary-free communication between the pulmonary and systemic circulations, thus creating right-to-left shunts.\(^13\) Although isolated PAVMs are occasionally present, 90% of all PAVMs are associated with HHT.\(^14\) Well-tolerated daily activities in the early stage may be associated with slower progression of PAVMs. The right-to-left shunt may lead to respiratory symptoms, which also affect the patient’s quality of life.\(^15\) HHT patients with PAVMs are at risk of neurological complications due to paradoxical embolism. Such complications may even be the first symptoms of PAVMs. In addition to paradoxical embolism, neurological symptoms in HHT patients may also be caused by CAVMs.\(^16\) CAVMs occur in 1% of HHT patients, compared with approximately...
Figure 2. The red arrows on TTCE show the pulmonary right-to-left shunt. (a) No pulmonary right-to-left shunt, (b) pulmonary right-to-left shunt grade 1, (c) pulmonary right-to-left shunt grade 2, (d) pulmonary right-to-left shunt grade 3.

Figure 3. The red arrows on chest contrast-enhanced CT show that angiogenic lesions were PAVMs.

0.01% of the general population. CAVMs can occur and lead to high-pressure vascular channels that are at risk of rupture, thus increasing the risk of morbidity or death. In addition, primary pulmonary hypertension is increasingly recognized as a complication of HHT. In the presence of unexplained tachypnea with features of right ventricular pressure or volume overload, the presence of primary pulmonary hypertension should be considered.
The patient was diagnosed with HHT according to the consensus diagnostic Curaçao criteria. The Curaçao criteria include (1) spontaneous recurrent epistaxis, (2) family history, (3) multiple telangiectasias, and (4) visceral lesions such as PAVMs and CAVMs. HHT can be confirmed if the patient presents at least three of the above four criteria. Different mutations may affect the clinical presentation of HHT. We recommended genetic testing for the patient and her mother to further clarify the clinical classification of HHT. Unfortunately, genetic testing was refused.

Conclusion

Our case report highlights the importance of early diagnosis and intervention for HHT. The early symptoms of HHT are mild and atypical, but when an abnormal vascular architecture affects the lungs and central nervous system, it can lead to serious complications and even death. Given that HHT is frequently undiagnosed, increasing the physicians’ awareness of HHT can play an important role in the timely diagnosis and treatment of these patients.

Declaration of conflicting interests

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Ethics approval

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Informed consent

Written informed consent was obtained from the legally authorized representative of the patient for her anonymized information to be published in this article.

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