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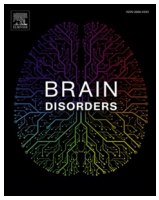

A case of hereditary hemorrhagic telangiectasia presenting with brain abscess

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ABSTRACT

Background: Hereditary hemorrhagic telangiectasia (HHT), characterized by telangiectases and arteriovenous malformations that can occur in any organ but primarily the lungs, liver, and brain, is an autosomal dominant disorder. Brain abscess, though a rare and potentially fatal complication, can be an initial presentation of this condition.

Case summary: A 60-year-old man presented with anemia and black tarry stools, then developed right-sided weakness initially misdiagnosed as an ischemic stroke. Subsequent onset of headaches and high-grade fever led to the diagnosis of brain abscess, and HHT was subsequently identified.

Conclusion: This case underscores that brain abscess can be an initial symptom of HHT. Prompt diagnosis and treatment are vital, which requires physicians to maintain a high index of suspicion and conduct appropriate investigations promptly.

Introduction

Hereditary hemorrhagic telangiectasia (HHT), also known as Rendu-Osler-Weber disease, is an autosomal dominant disorder of fibrovascular tissue with an estimated prevalence of approximately 1 in 5000 [1–3]. It is primarily caused by mutations in the endoglin gene on chromosome 9 or the activin receptor-like kinase 1 gene on chromosome 12. Additionally, a mutation in the SMAD4 gene can lead to a combination of juvenile polyposis syndrome and HHT, and a mutation in the GDF2/BMP9 gene can also result in an HHT phenotype [4].

HHT is characterized by the presence of multiple arteriovenous malformations (AVMs) that lack intervening capillaries and result in direct connections between arteries and veins [1,2]. The most common clinical manifestation is spontaneous and recurrent nosebleeds (epistaxis) beginning on average at age 12 years. Telangiectases (small AVMs) are characteristically found on the lips, tongue, buccal and gastrointestinal (GI) mucosa, face, and fingers [2]. The appearance of telangiectases is generally later than epistaxis but may be during childhood [2]. Large AVMs occur most often in the lungs, liver, or brain; complications from bleeding or shunting may be sudden and catastrophic [1]. A minority of individuals with HHT have GI bleeding, which is rarely seen before age 50 years [1].

It is estimated that between 1% and 10% of patients with HHT have cerebral AVMs, and between 15% and 45% develop pulmonary AVMs [1]. Neurologic complications of HHT attributed to these AVMs include embolic stroke, cerebral abscess, migraine, hemorrhagic stroke, and seizures [2]. Although relatively rare compared with other causes of stroke, AVMs are causally important because they have the potential to be identified and treated in high-risk patients before complications develop [1,2].

In this context, we present a case of a 60-year-old man with HHT who developed a brain abscess, a known but potentially devastating complication of the disease. The case underscores the importance of adhering to the international guidelines for the diagnosis and management of HHT in order to prevent such severe complications [3].

Case presentation

A 60-year-old male patient presented with anemia and black tarry stool following minor head trauma without immediate complications. Three days later, he developed right-sided weakness, initially misdiagnosed as an ischemic stroke due to CT scan findings of a hypodense

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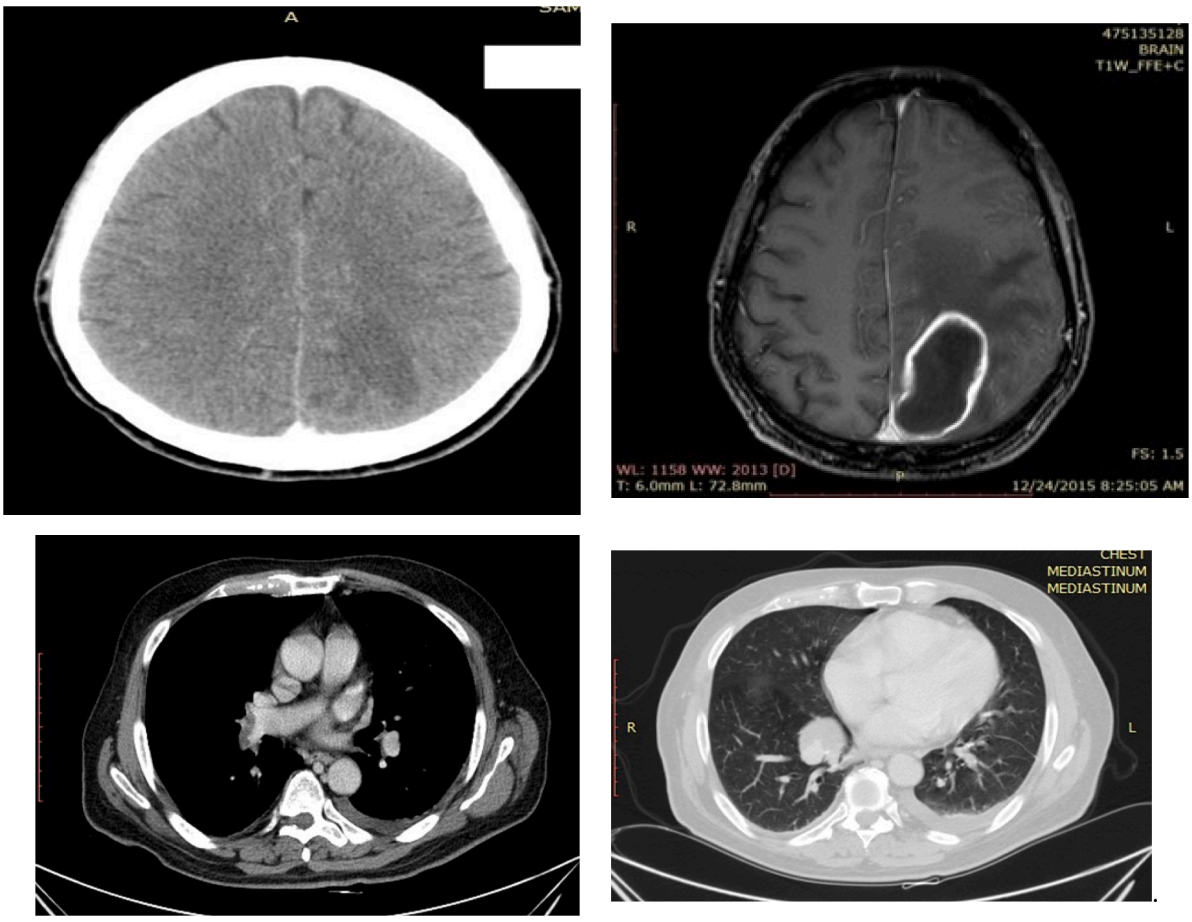

Fig. 1. (a): CT head showing hypodense area in the left parietal and temporal lobe. **(b):** T1 post-contrast brain MRI showing ring enhancing lesion in the left parietal and temporal lobe consistent with brain abscess. **(c):** CT angiography chest showing a filling defect in the right lower pulmonary artery that indicates pulmonary embolism. **(d):** Chest CT showing pulmonary arteriovenous malformations (PAVM), in the posteromedial segment of the right lower lobe.

area in the left parietal and temporal regions. Despite treatment with aspirin and statins, and later the addition of clopidogrel, his condition worsened, accompanied by headaches and a high-grade fever. A subsequent MRI revealed a brain abscess in the left parietal lobe, which was managed with surgical evacuation. A culture test grew Streptococcus pneumoniae, leading to a 6-week treatment with oral clindamycin (600 mg) and intravenous ceftriaxone (1 g, twice daily).

During his hospitalization, he experienced shortness of breath and chest pain. A CT angiography revealed a filling defect in the right lower pulmonary artery, as well as three pulmonary arteriovenous malformations (PAVMs) in the right lower lobe, with the largest measuring 5.3 $\times$ 3.5 $\times$ 4.6 cm. No AVMs were found elsewhere, including the liver, on abdominal CT. Family history revealed his son had recently been diagnosed with HHT, and his daughter underwent lung lobectomy due to massive hemoptysis. His-mother, a sister, a brother, an uncle, two daughters, and a son all reported frequent epistaxis.

Laboratory tests showed hemoglobin of 9.2 g/dl, hematocrit of 27%, mean corpuscular volume 77 Fl, white blood cell count of 6.2 $\times$ 10^3 /ul, platelet count of 248 $\times$ 10^3 /ul. Coagulation profile, serum electrolytes, liver functions, and kidney parameters were all within normal limits.

Following discharge with a diagnosis of pulmonary embolism and treatment with rivaroxaban, the patient returned to the hospital with anemia and black tarry stools. Physical examination revealed right-sided weakness, diffuse telangiectasia over the chest, lower lip, tongue, cheek mucosa, nasal mucosa, and clubbed nails. Upper and lower GI endoscopies revealed multiple small AVMs in the distal part of the esophagus, a single small AVM in the fundus of the stomach, multiple AVMs at the duodenal bulb and the second part of the duodenum, and AVMs in the descending colon.

Three months post-surgery, a brain MRI showed an irregular area of abnormal enhancement in the posterior aspect of the left parietal region, likely representing postoperative changes. The patient was diagnosed with HHT based on the clinical presentation, radiological evidence of multiple AVMs, and a strong family history. After obtaining informed consent, a genetic study revealed compound heterozygous mutations in the ENG gene consistent with hereditary hemorrhagic telangiectasia type 1. Genetic studies of his family revealed that two daughters and his granddaughter also had the disease.

The patient underwent argon plasma coagulation for gastrointestinal telangiectatic lesions and transcatheter embolization therapy for lung AVMs. He was discharged in good general condition and placed on iron replacement therapy.

Discussion

In this manuscript, we describe a patient who presented with a brain abscess that was eventually diagnosed with HHT that was confirmed to have a novel gene mutation on the ENG gene and lung AVM. HHT is a rare disease with an abnormal spectrum of clinical presentation. The most common manifestation of HHT is epistaxis (95%), PAVM (50%), liver AVM (30%), gastrointestinal bleeding (20%) and central nervous system AVMs (10%) [5]. Although central nervous system manifestation is rare, it has a 40% death rate, as previous studies showed [6].

Potential mechanisms to develop brain abscesses in HHT patients would be pulmonary vascular malformation that causes the pulmonary artery to flow into the venous return directly and bypasses the capillary

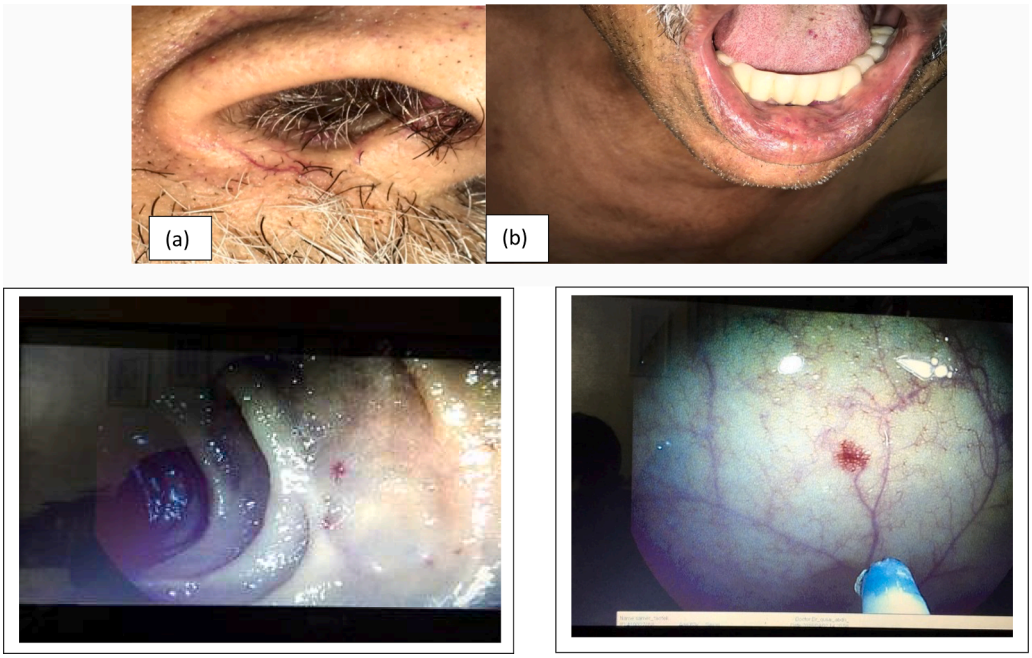

Fig. 2. **(a):** Diffuse telangiectatic lesions spread through the nasal mucosa. **(b):** Diffuse telangiectatic lesions spread through the lower lip, tongue, and cheek mucosa. **(c):** Upper GI endoscopy showing multiple small telangiectatic lesions located in the distal part of Esophagus. **(d):** Lower GI endoscopy showing few Lt side of Colon telangiectatic lesions.

circulation, allowing microparticles such as bacteria to break through the capillary bed barrier, resulting in the formation of cerebral abscesses [7,8]. Kjeldsen et al. estimated the risk of cerebral abscess among patients with HHT. The risk of cerebral abscesses in patients with HHT with PAVM was found to be high and reaching 7.8% which is more than 100 times the risk in the background population [9].

HHT can still present with brain and spinal cord vascular malformation that could cause hemorrhagic complications [10], however brain abscess occurs in around 1% of the patients with HHT with relatively high mortality rate [6,11], though survivors have relatively good prognosis with mild weakness to complete recovery [12]. Therefore, early diagnosis and treatment is critical. In our case, the patient was treated immediately after making the diagnosis, fortunately with overall reasonable outcome. Figs 1 and 2

Conclusions

In conclusion, this case demonstrates that a brain abscess could be the first symptom of HHT. This shows how critical it is to recognize and appropriately manage brain abscess, especially if there is no obvious entry source of infection, and to keep HHT in the differential diagnosis.

Ethics approval and consent to participate

Ethics committee approval was not applicable as the information was analyzed in a retrospective manner and had no effect on treatment.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. No identifying patient information was used.

Availability of data and materials

All the data supporting our findings is contained within the manuscript. Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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CRediT authorship contribution statement

MZ, BM, MA & QA were responsible for the clinical management of the patient. MZ, BM, MA, MG & QA were responsible for drafting the manuscript. All authors: critical revision of the manuscript for important intellectual content, read and approved the final manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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