Brain Abscess as a Manifestation of Hereditary Hemorrhagic Telangiectasia in a Pediatric Patient: A Case Report

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Brain Abscess as a Manifestation of Hereditary Hemorrhagic Telangiectasia in a Pediatric Patient

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ABSTRACT

Hereditary Hemorrhagic Telangiectasia (HHT) is a disease defined by abnormal endothelial cell development that manifests as cutaneous telangiectasias, recurrent epistaxis, and visceral organ arteriovenous malformations. This report's objective is to exhibit a unique presentation of an uncommon disease within the pediatric population. It also provides excellent educational value through prioritizing the investigation of alternative diagnoses in a pediatric patient who develops a brain abscess without any known risk factors. Herein we report the case of a previously healthy 17-year-old female who developed sudden aphasia and a new onset tonic-clonic seizure after 3 days of headache and shortness of breath. She had a past medical history of migraines and recurrent epistaxis. Imaging confirmed a ring-enhancing lesion in her frontal lobe, which suggested a brain abscess. She was treated with intravenous antibiotics and steroids. Her neurological symptoms subsided and she was discharged home. Continued work-up revealed numerous arteriovenous malformations, which likely contributed to her brain abscess, and she was diagnosed with HHT. HHT should be suspected in pediatric patients who develop brain abscess without any other risk factors. Additionally, new onset neurological symptoms in pediatric patients should be investigated promptly with head imaging. Timely identification and initiation of therapy is crucial due to the high morbidity and mortality associated with brain abscess, especially in HHT patients.

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CASE PRESENTATION

A 17-year-old female was transported to the emergency department after suffering from a sudden episode of inability to speak followed by a single seizure episode at school. While in her classroom, she reported a difficulty "finding words" and stood up in panic from her desk. She approached the teacher to ask permission to leave the room. Unable to speak, she began to write on a sheet of paper, but her writing soon became incoherent to both the teacher and to herself. Her teacher sent her to the nurse's office, where she suffered a new-onset generalized tonic-clonic seizure and the emergency medical

service (EMS) was called. This seizure lasted a few minutes and resolved by the time the EMS arrived. During the seizure, she also suffered an episode of epistaxis. She was able to communicate on arrival to the ED, although with some difficulty, and stated that she had a 3-day history of headaches and shortness of breath. She also reported a history of headaches since the age of twelve. She stated her headaches usually begin with an aura of "shimmering prisms and cones of lights." The pain is typically unilateral and acetaminophen provides some relief. These headaches were sometimes associated with nausea and mild photophobia. They typically resolved with sleep. Over the last three days, however, the headaches had worsened, and ibuprofen became ineffective. She denied any recent head trauma.

Her vital signs included a blood pressure of 120/73 mmHg, heart rate of 117 beats/minute, respiratory rate of 16 breaths/minute, temperature of 99.6° Fahrenheit. On exam, she appeared anxious and in mild distress. Her cranial nerves II-XII were grossly intact, and her pupils were equally round and reactive to light. Dried blood was found in both of her nostrils; there was no active bleeding. There were no meningeal signs during her neck exam. Her cardiovascular, pulmonary, and abdominal exams were all within normal limits. Her neurological exam was also grossly normal with a Glasgow Coma Scale score of 15, but she continued having difficulty "finding words." A complete blood count with differential was drawn: hemoglobin was 14.8 g/dL, hematocrit was 45.7%, white blood cells were 14.8 cells/mcL (71% neutrophils, 18% lymphocytes, 6% monocytes, 5% eosinophils), and platelets were 245,000/mcL. A computed tomography (CT) scan of her head without contrast (Figure 1) showed an area of abnormally low density in the left frontal lobe that was suggestive of vasogenic edema as the grey-white matter differentiation was maintained and the edema primarily involved the white matter. No evidence of intracranial hemorrhage was found. While air or maturing hematomas may also cause low density on CT scans, these were ruled out due to the lack of a history of head trauma. Given the history of rapid onset neurologic symptoms and the elevated white blood cell count, as well as imaging that suggested an area of edema without obvious intracranial bleeding, a brain abscess was suspected. Therefore, she was admitted to the pediatric intensive care unit and started on empiric intravenous antibiotic therapy with ceftriaxone, metronidazole, and vancomycin as well as levetiracetam for seizure prophylaxis.

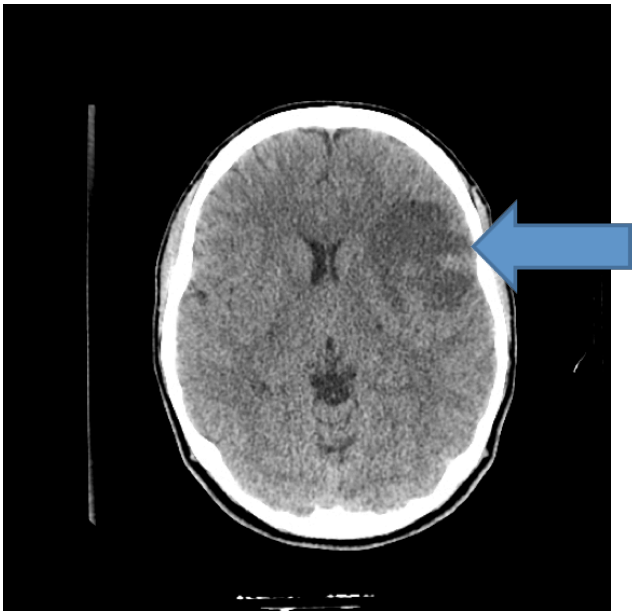

Figure 1. Initial CT scan taken at presentation to the hospital showing an area suggestive of vasogenic edema in the left frontal lobe (arrow) and mild midline shift.

A magnetic resonance imaging (MRI) scan with and without contrast (Figures 2 and 3) confirmed an area of vasogenic edema surrounding a ring-enhancing lesion in the left frontal lobe. The midline shift seen on the earlier CT scan was also evident on these MRI images. Although the differential diagnosis for ring-enhancing lesions includes glioblastoma multiforme, brain metastasis, infarct, contusion, and neurocysticerosis,

these were ruled out due to history and age of the patient. A follow up magnetic resonance angiogram (MRA) of the head (Figure 4) demonstrated mass effect of the lesion on the medial cerebral artery branches on the left side, but there was no evidence of aneurysms, arteriovenous malformations, or major vessel occlusion. These findings were also consistent with a brain abscess.

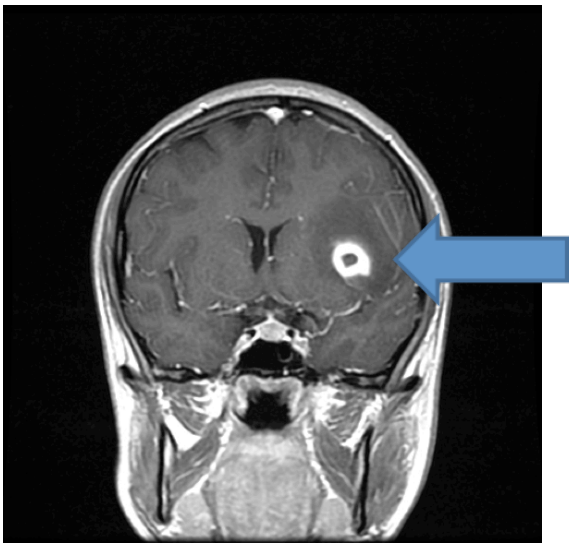

Figure 2. T1-weighted coronal MRI with contrast demonstrating a left sided ring-enhancing lesion (arrow) surrounded by vasogenic edema and also a midline shift.

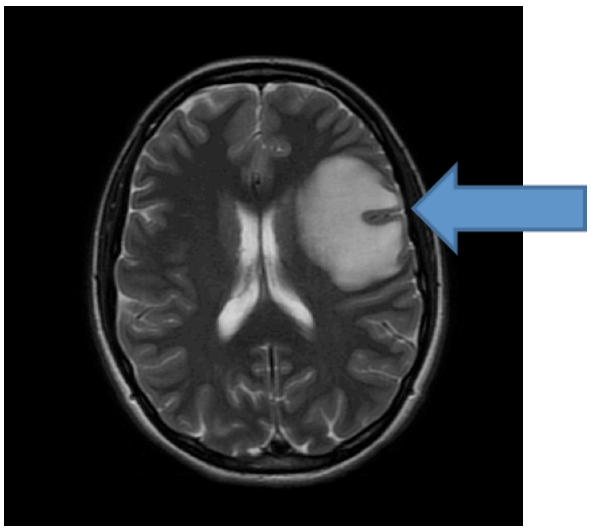

Figure 3. T2-weighted transverse MRI with contrast that highlights the area of vasogenic edema (arrow) and also further demonstrates the midline shift seen in previous images.

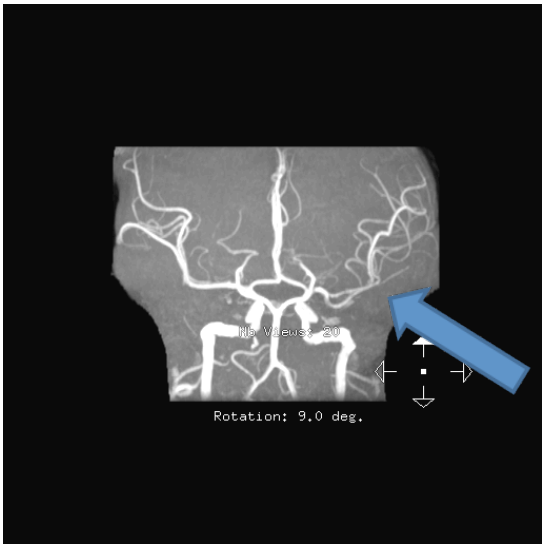

Figure 4. Coronal MRA of the head showing mass effect of the lesion on the branches of the left middle cerebral artery (arrow).

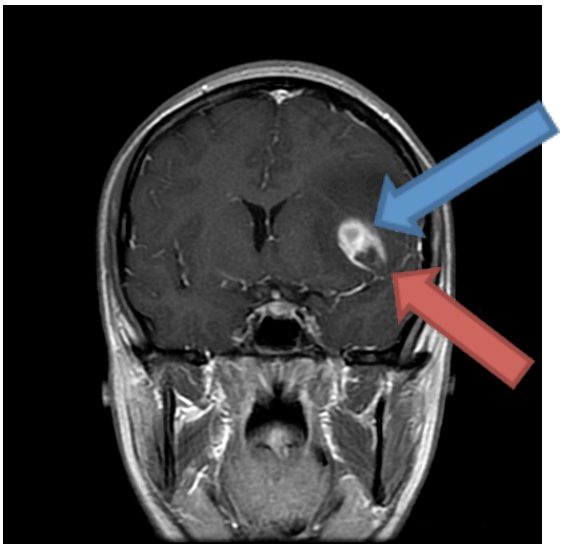

Figure 5. Repeat coronal MRI with the blue arrow pointing to the original lesion and the red arrow pointing to the new lesion.

The patient continued to have headaches and six days after admission, she became increasingly confused and developed right upper extremity weakness in addition to left facial drooping. A

repeat MRI (Figure 5) demonstrated a new area of enhancement and diffusion restriction inferolaterally to the original lesion as well as increased vasogenic edema. The following day, she underwent a CT-guided biopsy of the original lesion with cultures. The tissue culture grew *Micrococcus luteus/lylae.* After the procedure, IV dexamethasone was added to her antibiotics to reduce brain tissue swelling. She continued this treatment regime for two additional weeks as her neurological symptoms began to subside. The patient was then discharged home for the remaining five weeks of IV antibiotics. During this time frame, her facial palsy resolved and she regained strength in her right upper extremity. Her headaches also improved.

During her admission, it was discovered that she had a past medical history significant for migraine headaches since the age of twelve and recurrent episodes of epistaxis. It was also revealed that her mother had hereditary hemorrhagic telangiectasia (HHT). There was a high level of suspicion for HHT due to family history and recent events, so studies of the chest to search for pulmonary arteriovenous malformations (PAVMs) as well as a transcranial Doppler study were performed. Numerous PAVMs were found in the patient's left upper lobe as well as in her right middle lobe (Figure 6). The transcranial Doppler study with agitated saline also demonstrated an arteriovenous shunt in the middle cerebral artery. The patient met 3 of the 4 diagnostic Curacao criteria for HHT[1] (Table 1) and it was concluded that her undiagnosed HHT had predisposed her to this brain abscess.

The patient completed her IV antibiotic course and follow up MRI studies demonstrated that the brain abscess had resolved. The majority of the PAVMs seen on arteriogram have since been obliterated.

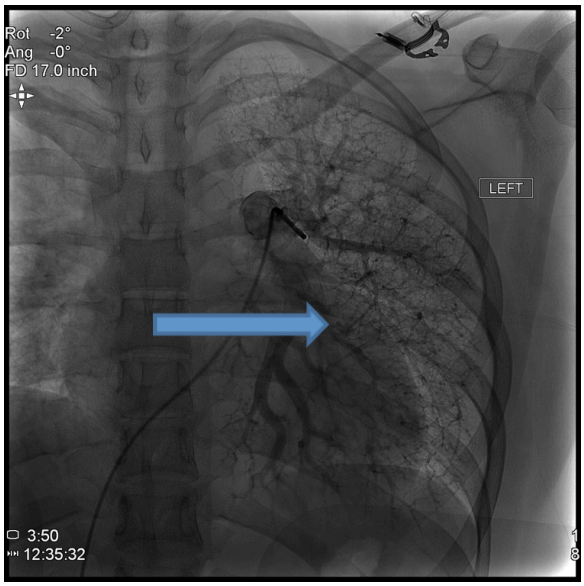

Figure 6. Pulmonary arteriogram demonstrating a dominant arteriovenous malformation in the inferior aspect of the upper lobe (arrow) along with numerous smaller malformations.

Curacao Criteria for HHT

1. **Recurrent Epistaxis**
2. **Telangiectasias**
3. **Visceral Manifestations**
4. **Affected 1st degree relative**

3-4 criteria met: definitive HHT

2 criteria met: suspected HHT

1 criteria met: unlikely to be HHT

Table 1. Curacao Criteria for the diagnosis of HHT

DISCUSSION

Epidemiology and Pathophysiology

HHT is an autosomal dominant inherited disorder that affects 1 in 10,000 people with no preference for either sex.[2] It is most common in the Caucasian population and is 97% penetrant.[2] Almost 30% of patients do not have a family history of the disease.[2] The genes affected by this disorder both code for Transforming Growth Factor-β receptors: *ENG* on chromosome 9q34.1 and *ACVRL-1* (activin A receptor type II-like 1) on chromosome 12q13.13.[3] These genes are crucial in the development of vascular endothelial cells during angiogenesis and either mutation will manifest in the same manner.

Clinical Manifestations

The syndrome is defined by telangiectasias, or dilated post-capillary venules, of the skin, mucous membranes and internal organs. Cutaneous telangiectasias typically occur on the face, hands, and lips. When telangiectasias occur in the nasal mucosa, they may cause spontaneous recurrent epistaxis which is the first symptom for more than 90% of patients.[4,5] More than 50% of patients with HHT will manifest with this symptom before the age of twenty.[1] The bleeding can be so severe that 10-30% of patients will require blood transfusions over the course of their lifetime. In roughly 40% of patients, the gastrointestinal system is involved and can also be the source of significant blood loss.[3,6]

The diagnostic Curacao criteria[1] (Table 1) require three of the following four findings: recurrent epistaxis, cutaneous telangiectasias, visceral organ involvement (i.e., arteriovenous malformations that may bleed) and an affected first-degree relative. Few patients, however, manifest enough signs and symptoms within the first three decades of life to meet the criteria, and therefore, it is recommended that asymptomatic children of HHT patients be genetically screened for the disease.[1]

Neurological manifestations

In a healthy patient, the lung capillary beds function to filter the blood before it is pumped to the brain, but pulmonary vascular malformations (PAVMs) found in HHT patients compromise this protection system.[7] Large PAVMs can result in paradoxical micro-emboli entering cerebral circulation and subsequent ischemic brain injury (i.e., stroke). Abscess formation can be caused by direct seeding of pathogenic bacteria into the brain parenchyma or secondarily after an anoxic brain injury creates an environment suitable for bacteria growth. About 1% of HHT patients can develop cerebral abscess or septic meningitis, which is significantly higher than the general population.[7] For the reasons noted above, PAVMs are a significant source of morbidity and mortality in HHT patients[7] and they can also lead to high-output cardiac failure in later life.[2]

Brain abscesses are usually of poly-microbial origin; only the slow growing members of the *Micrococcus* genus were isolated in this case because empiric antimicrobial therapy had already begun by the time of the biopsy.[8,9] It is important to note that brain abscesses do not commonly present with the typical cardinal signs of infection: fever, leukocytosis, or positive blood cultures.[10]

The neurological symptoms of brain abscesses are due in large part to the mass effect of the lesion on surrounding structures. Consequently, the symptoms can include a wide spectrum of neurologic symptoms such as aphasia, seizures, and headaches depending on the location of the lesion. HHT patients can also develop cerebral vascular malformations (CAVMs), which can manifest as various neurological symptoms. Approximately one-quarter of HHT patients

will have a CAVM in their lifetime and there is a 0.5% bleeding risk per year.[1] The treatment of choice for arteriovenous malformations remains embolization of the feeding blood vessels.[11]

LEARNING POINTS

- The differential diagnosis for a pediatric patient without any known risk factors who develops a brain abscess should include HHT.
- Brain abscesses are typically poly-microbial in nature and do not present with the usual signs of infection, such as fever, leukocytosis, or positive blood cultures.

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