Case 10-2010: A 37-Year-Old Woman with Weakness and a Mass in the Brain

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Dr. Brian P. Walcott (Neurosurgery): A 37-year-old, right-handed woman was admitted to this hospital because of vertigo, left-sided weakness, and a mass in the brain on imaging studies.

The patient was in her usual state of health until 3 days before admission, when she suddenly had a sensation of the room spinning, associated with nausea and an unsteady gait. After approximately 4 hours, she went to the emergency department of another hospital. While in the emergency department, her symptoms worsened and numbness and weakness developed suddenly in the left arm. Subsequently, she had pain in the left thigh and involuntary movements of the left leg, which lasted for 25 minutes and resolved with the administration of intravenous lorazepam. Magnetic resonance imaging (MRI) reportedly revealed a ring-enhancing mass, measuring 8 mm by 9 mm, in the right parietal lobe of the brain. Computed tomographic (CT) scans of the chest reportedly showed an enhancing, lobulated mass in the right lower lobe of the lung, with features consistent with an arteriovenous malformation. Levetiracetam was begun, and she was admitted to that hospital; no further seizures occurred. At the patient’s request, she was transferred on the third day to this hospital and admitted to the neurosurgical service.

The patient did not have fever, chills, headache, sinus or ear pain, abdominal pain, vomiting, or diarrhea. She had a recent diagnosis of endometriosis, and an endometrial biopsy had been performed 2 weeks before admission. A dental procedure had been performed 9 days before presentation, with drainage of periodontal abscesses of the right upper quadrant. Since childhood, she had had numerous episodes of epistaxis. She had a long history of anemia and had been told she had a form of thalassemia. She worked in an office, was married, and lived with her husband and four children. She did not smoke, consume alcohol, or use illicit drugs. She had not traveled recently. She was of Italian and Irish ancestry. Her father had congenital heart disease and had a valve replacement at 45 years of age, and one brother had cardiac valvular disease. Her mother, other siblings, and children were well. No members of her immediate family were known to have similar problems.
She was allergic to sulfonamides and erythromycin. She had not taken any medications at home before this illness. Medications on admission included leviracetam.

The temperature was 36.6°C, the pulse 82 beats per minute, the blood pressure 100/66 mm Hg, and the respiratory rate 18 breaths per minute. There were no cutaneous or buccal telangiectasias. There was packing over the gingiva of the right upper quadrant but no tenderness or evidence of active infection. There was no tenderness to palpation over the sinuses or mastoids. There was no cervical lymphadenopathy. The heart sounds were normal, with no murmurs. The lungs were clear on auscultation and the abdomen was soft and nontender. On neurologic examination, the patient was alert and fully oriented. The pupils were 3.5 mm in diameter and symmetrically reactive to light exposure. The extraocular movements and visual acuity were intact, and the results of confrontation tests showed that the visual fields were normal. Sensation to light touch was decreased on the left side, with the leg affected more than the arm. Strength and deep-tendon reflexes were normal. The remainder of the detailed neurologic examination was normal.

The white-cell count was 14,500 per cubic millimeter (reference range, 4500 to 11,000) and the platelet count was normal; the hematocrit was 32.4% (reference range, 36.0 to 46.0), the hemoglobin level 10.6 g per deciliter (reference range, 12.0 to 16.0), the mean corpuscular volume 65 fl (reference range, 80 to 100), the mean corpuscular hemoglobin 21.3 pg per red cell (reference range, 26.0 to 34.0), the red-cell distribution width 19.1% (reference range, 11.5 to 14.5), and the C-reactive protein level 13.2 mg per liter (reference range for women, 11.5 to 14.5), and the C-reactive protein level 13.2 mg per liter (reference range for women, 11.5 to 14.5), and the C-reactive protein level 13.2 mg per liter (reference range for women, 11.5 to 14.5), and the C-reactive protein level 13.2 mg per liter (reference range for women, 11.5 to 14.5), and the C-reactive protein level 13.2 mg per liter (reference range for women, 11.5 to 14.5). Other routine laboratory tests, including measurement of electrolyte levels and tests of coagulation and of liver and renal function, were normal.

MRI of the brain revealed an enhancing lesion, 1.9 cm by 2.2 cm by 2.8 cm, in the right posterior cingulate gyrus, associated with surrounding T2-weighted signal hyperintensity within the left posterior frontal and parietal lobes. On diffusion-weighted sequences, there were areas of restricted diffusion within the lesion but not beyond the area of susceptibility. Proton magnetic resonance spectroscopy revealed a decrease in the N-acetyl aspartate peak, without definite evidence of a lactate doublet or a markedly elevated ratio of choline to creatinine associated with the lesion.

Later that day, a diagnostic procedure was performed.

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**Differential Diagnosis**

Dr. Fred G. Barker: May we review the imaging studies?

Dr. Kenneth R. Davis: MRI performed on arrival (Fig. 1A) revealed a heterogeneous intraaxial lesion within the right posterior cingulate gyrus on T2-weighted images. There was intrinsic signal hyperintensity on T1-weighted images, correlating with a susceptibility artifact along the medial and superior aspects of the lesion. After the administration of contrast material (Fig. 1B), the peripheral ring seen on T1-weighted sequencing was enhanced. The remainder of the brain and cranial structures appeared normal. The lesion now measured 1.9 cm by 2.2 cm by 2.8 cm, which represented marked enlargement from the initial study 30 hours earlier.

A diffusion-weighted MRI study (Fig. 1C) was also performed as part of the routine imaging protocol. The images revealed a hyperintense central area that correlated to a hypointense region of the apparent-diffusion-coefficient image (Fig. 1D); this correlation was consistent with restricted diffusion in the area of the lesion. Proton magnetic resonance spectroscopy was performed, but its use was severely limited because of a high signal-to-noise ratio. There was a decrease in the N-acetyl aspartate peak, without definite evidence of a lactate doublet or markedly elevated choline-to-creatine ratio. Perfusion-weighted MRI showed an increase in mean transit time (Fig. 1E) within the lesion, which correlated to a decrease in cerebral blood volume (Fig. 1F) in the same location. There was an increase in cerebral blood flow within the periphery of the lesion. Overall, there was a ring-enhancing intraaxial mass within the right posterior cingulate gyrus with evidence of surrounding vasogenic edema and nonspecific proton magnetic resonance spectroscopy characteristics that more than doubled in size during a period of 30 hours.

Dr. Barker: I am aware of the diagnosis in this case. Establishing the diagnosis requires consideration of the distinct but related aspects of the patient’s presentation: a long history of epistaxis, recent gingival manipulation, a recent endometrial...
biopsy, the new onset of focal neurologic symptoms, a cerebral mass that is rapidly enlarging, and the discovery of a pulmonary arteriovenous malformation.

**Brain Abscess**

Although the patient has a complex presentation, the details of her medical history help to establish a working differential diagnosis. The patient’s neurologic symptoms began on the day of her initial presentation, with a sense of disequilibrium, nausea, and suspected focal-seizure activity on her left side. This information suggests intracranial pathology involving the right cerebral cortex. The sudden and rapidly progressive nature of her symptoms, measured in hours, is typical of brain abscesses. A more rapid onset of symptoms, measured in minutes, would suggest a vascular or ischemic event, and a longer onset, measured in weeks to months, is more typical of a neoplastic process. In this young patient without a prolonged prodrome, prompt systemic and radiologic evaluation of these neurologic symptoms is required, since brain abscesses are treatable lesions. Undue delay could result in neurologic deficits.

**Figure 1. MRI Study of the Brain Showing a Heterogeneous, Ring-Enhancing Mass in the Right Posterior Cingulate Gyrus.**

A T₁-weighted image obtained after the administration of contrast material (Panel A) shows a mass with a surrounding ring of enhancement (arrow). The central region of the mass has low signal intensity, which suggests the presence of fluid. On T₂-weighted sequences obtained before the administration of contrast material (Panel B), the mass has high signal intensity centrally, a peripheral ring of signal intensity (arrow) similar to that of brain parenchyma, and an extensive contiguous surrounding area of high signal intensity. The diffusion-weighted image (Panel C) shows an area of hyperintensity in the central region of the mass (arrow). The apparent-diffusion-coefficient image (Panel D) of the same area of the lesion has a very low signal (arrow). These findings in combination indicate the restricted diffusion of water and are suggestive of the presence of a viscous fluid. Perfusion-weighted MRI scans show an increase in mean transit time within the cavity of the abscess (Panel E, arrow) and decreased cerebral blood volume in the same location (Panel F, arrow). There is increased cerebral blood flow within the periphery of the lesion, a feature consistent with reactive hyperemia.

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One of the most attention-commanding aspects of the patient’s presentation is her recent periodontal surgery. Dental procedures are well-known risk factors for the development of cerebral abscesses. She had also had an endometrial biopsy, and organisms from the vagina could have contaminated the biopsy site. Exacerbating her risk of hematogenous dissemination of bacteria was the presence of a pulmonary arteriovenous malformation. The pulmonary circulation provides an important safeguard that limits the hematogenous spread of bacteria to the systemic circulation by the filtering action of the pulmonary capillaries. In the presence of an arteriovenous malformation, bacteria have easier access to the systemic circulation through a right-to-left pulmonary vascular shunt, regardless of its size.

Additional clinical and laboratory data support the diagnosis of an infectious cause of this patient’s brain lesion. Although the patient remained afebrile, she had a persistently elevated white-cell count. Her level of C-reactive protein, an acute-phase protein with elevated levels in the serum of patients with acute inflammation, was also elevated. In patients with ring-enhancing brain lesions, an elevated C-reactive protein level is highly correlated with the presence of an infectious process and is less often seen in the presence of a brain neoplasm.

MRI provides further evidence that narrows the differential diagnosis. Many processes can present as cystic lesions with surrounding peripheral-ring enhancement, including pyogenic brain abscesses, other infections (e.g., toxoplasmosis), malignant tumors, desmizing diseases, and vascular lesions such as infarcts or hematomas. However, images in this case show a central core of restricted diffusion on diffusion-weighted sequences, a peripheral ring of contrast enhancement after the administration of gadolinium, and a thin layer of concentric low signal intensity on T2-weighted sequencing — findings consistent only in brain abscesses. Proton magnetic resonance spectroscopy, diffusion-weighted MRI, and perfusion-weighted MRI are also of value in differentiating pyogenic brain abscesses from cystic brain tumors. Increased hyperintensity and a lower relative cerebral blood volume, as seen in this case, favor the diagnosis of a brain abscess over a necrotic or cystic tumor. Finally, since this lesion had nearly doubled in size in just over 2 days, it was much more likely to be an abscess than a tumor.

### Table 1. Curaçao Criteria for the Diagnosis of Hereditary Hemorrhagic Telangiectasia

<table>
<thead>
<tr>
<th>Three of the following four criteria must be present for a definite diagnosis; two criteria make the diagnosis possible</th>
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<tr>
<td>Epistaxis</td>
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<td>Telangiectasia at characteristic sites such as the lips, oral cavity, nose, and fingers</td>
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<tr>
<td>Visceral lesions including gastrointestinal, pulmonary, hepatic, cerebral, or spinal arteriovenous malformations</td>
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<td>Family history, with a first-degree relative with hereditary hemorrhagic telangiectasia according to these criteria</td>
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* Criteria are from Shovlin et al.

Cerebral abscesses may result from contiguous spread of infection from the mastoid or frontal sinuses, from direct trauma or neurosurgical procedures, or from hematogenous spread. In this patient, imaging studies showed no evidence of contiguous spread from the oral cavity or other structures, and the likely source was hematogenous dissemination of organisms, either from the dental procedure or the endometrial biopsy. Brain abscesses are often polymicrobial, and the causative species differ depending on the source of the infection. Streptococcal species and anaerobes are frequent isolates from dental sources.

### Conclusions

The diagnosis in this case is most likely a polymicrobial brain abscess due to hematogenous spread of infection in a patient with a pulmonary arteriovenous malformation. The presence of a pulmonary arteriovenous malformation and the history of recurrent epistaxis raised the suspicion of a unifying hereditary syndrome. Hereditary hemorrhagic telangiectasia is a syndrome that results in arteriovenous malformations that affect numerous organs, including the nose (in >95% of cases), skin (in >80%), gastrointestinal tract (in 30%), lungs (in >30%), liver (in 30%), and brain (in 10%). At presentation, this patient had two of the four Curaçao criteria used to diagnose hereditary hemorrhagic telangiectasia (visceral arteriovenous malformation and epistaxis), but she did not have the other two (visible telangiectasia at characteristic sites such as the lips, oropharynx, nasal cavity, or fingers or a known family history of hereditary hemorrhagic telangiectasia) (Table 1).
venous malformation. To guide treatment, the next step should be to perform an image-guided, stereotactic needle biopsy of the lesion. A stereotactic head frame was affixed to the patient, an MRI scan was obtained, and commercially available software (Integra Radionics) was used to guide the selection of target points for the procurement of biopsy specimens. The patient was then transferred to the operating room, where she was placed in a semisitting position and given conscious sedation and a local anesthetic. We performed a burr-hole craniotomy so we could obtain a needle-biopsy specimen of the wall of the lesion, which we submitted for intraoperative pathological examination. A second target in the center of the lesion was chosen, the needle was advanced to this point, and 4 ml of purulent material was aspirated and sent for pathological and microbiologic studies. Finally, 1 mg of gentamicin was instilled locally into the cavity through the biopsy needle. The wound was closed in the standard fashion, and the patient recovered well without neurologic deficit from the procedure.

Dr. Fred G. Barker’s Diagnosis

Pyogenic, polymicrobial brain abscess, associated with a pulmonary arteriovenous malformation, suggestive of hereditary hemorrhagic telangiectasia.

Pathological Discussion

Dr. Matthew P. Froehlich: We received specimens directly from the operating room, including a specimen of brain tissue from a core needle biopsy and an aspirate consisting of gelatinous mucoid material. Examination of a smear and frozen sections (Fig. 2A) revealed acute inflammatory cells, macrophages, and necrotic debris characteristic of an acute inflammatory process. Permanent histologic sections stained with hematoxylin and eosin showed necrotic tissue with a neutrophilic infiltrate. No evidence of a malignant tumor was identified. Gram’s staining of the purulent exudate (Fig. 2B) obtained from the second target revealed the presence of abundant gram-positive cocci. A specimen with Grocott methenamine–silver nitrate staining showed no fungal organisms. These findings were diagnostic of a brain abscess of bacterial origin.

Gram’s staining of smears prepared in the microbiology laboratory revealed abundant gram-positive cocci in pairs and abundant gram-negative...
tive rods. Cultures of the contents of the abscess revealed mixed flora consisting of the aerobic *Streptococcus anginosus* group and anaerobic *Fusobacterium nucleatum*.

**DISCUSSION OF MANAGEMENT**

*Dr. Cahill:* Options for the management of brain abscesses range from medical treatment with antibiotics alone, medical treatment combined with biopsy and aspiration of the lesion, and open excision of the abscess, if it is large enough to cause neurologic symptoms from a mass effect or prove resistant to antibiotic therapy. The goal is to reduce the mass effect while providing effective control of the infection. Although antibiotic therapy is the cornerstone of treatment, it is rarely used empirically in the absence of data from cultures. Examination of a sample of the contents of the abscess enables determination of microbial species and sensitivities, allowing for targeted antibiotic therapy. Aspiration of the contents of the abscess reduces the mass effect and the burden of microorganisms and allows for direct irrigation of the abscess cavity with antibiotic solution, as was done in this case. When performed with MRI guidance, frame-based stereotactic procedures such as the one performed in this case precisely localize the abscess cavity and limit the possibility of neurologic damage, especially in areas near eloquent cortex.

After the operation, physicians with expertise in infectious diseases were consulted. The isolate of *S. anginosus* was sensitive to all tested antibiotics. On the physicians’ recommendation, broad-spectrum antibiotic treatment with intravenous vancomycin, ceftriaxone, and metronidazole was begun.

*Dr. Sanjeeva P. Kalva:* During the same admission, the patient was evaluated for treatment of the pulmonary arteriovenous malformation to avert future complications. A pulmonary angiogram (Fig. 3A) revealed two arteriovenous malformations in the right lung. The feeding arteries were selectively catheterized, and the malformations were successfully embolized with microcoils (Fig. 3B). On follow-up evaluation with CT angiography, approximately 3 months after the initial embolization, a small pulmonary arteriovenous malformation was seen adjacent to the original lesion in the right lower lobe. We recommended embolization of this new lesion, which was performed without complications.

*Dr. Brian V. Nahed* (Neurosurgery): A rash developed that was thought to be caused by ceftriaxone, and the drug was discontinued. An echocardiogram that was obtained to rule out the possibility of endocarditis showed no valvular vegetations or intracardiac shunting. The patient recovered uneventfully and was discharged on the ninth day with instructions to follow up with specialists in the divisions of infectious diseases and genetics. Treatment with intravenous vanco-
mycin and oral metronidazole was continued for 6 weeks. Because of the history of epistaxis, the patient underwent outpatient otolaryngology evaluation at another facility. She reported that the examination revealed innumerable nasal mucosal telangiectasias.

A consultant from Medical Genetics saw the patient while she was in the hospital and at follow-up.

Dr. Inderneel Sahai: At the time of presentation, the patient did not fulfill criteria for a clinical diagnosis of hereditary hemorrhagic telangiectasia, since she had only a history of epistaxis and a pulmonary arteriovenous malformation. We therefore advised genetic testing to establish a diagnosis. Most cases of hereditary hemorrhagic telangiectasia are due to mutations in one of three genes: ENG, associated with hereditary hemorrhagic telangiectasia type 1; ACVRL1, associated with hereditary hemorrhagic telangiectasia type 2; or SMAD4, associated with juvenile polyposis and hereditary hemorrhagic telangiectasia. Genetic studies, including full sequencing and deletion and duplication analyses of ACVRL1, ENG, and SMAD4 genes, revealed no mutations in this case. Likewise, approximately 20% of families who fulfill the Curaçao criteria for hereditary hemorrhagic telangiectasia do not have mutations in any of these genes. Loci on chromosomes 5 and 7 have been associated with hereditary hemorrhagic telangiectasia in two families, but the genes associated with these loci have not been identified and testing is not available.

Although the diagnosis of hereditary hemorrhagic telangiectasia could not initially be confirmed, we cautioned that the diagnosis had not been conclusively ruled out, since other clinical findings may become more apparent with age. We therefore advised that the patient follow the surveillance and precautions recommended for people with a confirmed diagnosis of hereditary hemorrhagic telangiectasia. These include periodic physical examinations, incorporating inspection for telangiectases, stool assessment for occult blood, and a complete blood count to assess for anemia. The patient already has evidence of a pulmonary arteriovenous malformation; a vascular specialist should follow up on it. Further evaluation for anemia revealed normal levels of iron and ferritin, which suggest that her anemia was not due to blood loss. However, bleeding from gastrointestinal telangiectases most commonly begins after 40 years of age and often becomes increasingly severe with age. Because of the patient’s history of epistaxis, she was advised to avoid vigorous nose blowing, cautery for nosebleeds, and anticoagulant and antiinflammatory agents. In addition, we recommended that she take prophylactic antibiotics for dental and other procedures.

Subsequent evaluation showed nasal telangiectasias, fulfilling clinical criteria for the diagnosis of hereditary hemorrhagic telangiectasia. Since hereditary hemorrhagic telangiectasia is an autosomal dominant condition, each of the patient’s children has a 50% likelihood of being affected, and her siblings are also at risk. Since she does not have an identifiable mutation, genetic testing of first-degree relatives is not indicated. However, surveillance of her children and siblings is recommended, including screening for pulmonary and cerebral arteriovenous malformations; annual evaluation for epistaxis or other bleeding, shortness of breath or decreased exercise tolerance, and headache or other neurologic symptoms; and periodic laboratory evaluation for anemia and occult blood in the stool.

Brain abscess due to infection with the Streptococcus anginosus group and Fusobacterium nucleatum.

Pulmonary arteriovenous malformation, due to hereditary hemorrhagic telangiectasia.

Anatomical Diagnoses

Brain abscess due to infection with the Streptococcus anginosus group and Fusobacterium nucleatum.

Pulmonary arteriovenous malformation, due to hereditary hemorrhagic telangiectasia.

References


4. Corson MA, Postlethwaite KP, Sey-
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