

## CHALLENGE CASES

## A Temporal Lobe Mimic and the Role of Neurodiagnostics

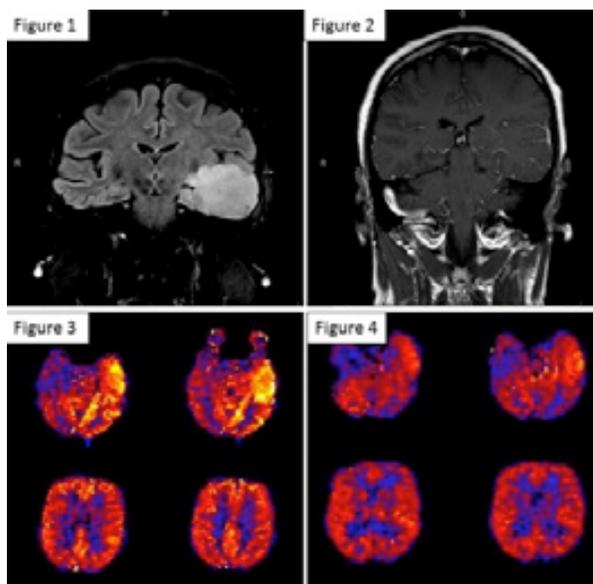
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A 60-year-old male with past medical history significant for pituitary adenoma post resection in 1980 presents to the emergency department with a one-week history of frontal headaches, auditory hallucinations, and poor memory. The headache is dull and intermittent with a gradual onset. He describes decreased hearing in his right ear and intermittently hears sirens and “far off radio voices” in this ear for the past two days.

He was hospitalized at an outside hospital for aseptic meningitis one month earlier. At that time he had become progressively confused over the course of two days. Four days prior to the confusion, he had been complaining of a headache located on the top of his head. His confusion progressively worsened to the point that he was unable to recognize familiar people, such as his wife. He also endorsed intermittent nausea and vomiting with low-grade fevers during that admission. A computerized tomography scan of the head without contrast was normal at that time. A lumbar puncture was performed and cerebrospinal fluid (CSF) showed 140 white blood cells (WBC) per microliter (normal <5/mL) with neutrophilic predominance and xanthochromia. He was admitted with initial concern of bacterial meningitis and treated with ampicillin, acyclovir, ceftriaxone, and vancomycin. All cultures were negative at the time of discharge. Per family, the patient never completely returned to his baseline functioning and continued to have confusion after discharge.

On current exam, he is encephalopathic. He states that the year is November and his birthday is the letter R. Speech is fluent and appropriate. Cranial nerves II-XII are intact. He complains of hearing “unpleasant music.” He has normal range of motion in his neck. He has normal strength and symmetric 2+ deep tendon reflexes. He has normal sensation and coordination on exam. His gait is normal.



**Figure 1:** MRI T2/FLAIR weighted image without contrast demonstrates increased signal in left temporal lobe.

**Figure 2:** MRI T1 weighted image with contrast demonstrates no parenchymal enhancement of the left temporal lobe region.

**Figure 3/4:** Perfusion Imaging (Pulsed Arterial Spin Labeling, PASL): The images on the left (Figure 3) demonstrate increased blood flow in the left temporal lobe at diagnosis that is resolving when compared to follow-up imaging (Figure 4) in clinic weeks after discharge.

CSF examination reveals protein 113 mg/dL, 2 WBC per microliter (normal <5/mL) and glucose 44 mg/dL (normal CSF glucose is 2/3 of serum glucose). CSF polymerase chain reaction (PCR) for herpes simplex virus, varicella zoster virus, Epstein-Barr virus, and cytomegalovirus are negative. Long term electroencephalogram (EEG) monitoring showed frequent sharp waves in the left temporal lobe. Levetiracetam was initiated and his auditory hallucinations resolved. The patient underwent magnetic resonance imaging of the brain (Figures 1, 2, 3, 4).

**Q1: Which diagnosis most likely explains the patient's symptoms?**

- A. Viral encephalitis
- B. Primary or secondary brain tumor
- C. Frontotemporal dementia
- D. Bacterial abscess

*The correct answer to Q1 is B.*

The patient underwent biopsy of the left temporal area and was found to have an anaplastic astrocytoma (World Health Organization (WHO) Grade III). The increased perfusion seen in PASL imaging was initially concerning for a high-grade vascular tumor, but lack of parenchymal enhancement on MRI was more suggestive of a lower grade tumor. However, occasionally higher grade tumors can lack parenchymal enhancement, as shown in this case. The resolution of increased blood flow on follow-up PASL imaging suggests that this increased blood flow was likely secondary to seizure activity around the time of the initial scan, as seizure activity can increase blood flow.

Thus, the patient's auditory hallucinations were likely secondary to seizure activity, as evident on EEG.

PASL is an imaging modality that evaluates arterial blood water by magnetically labeling it using radiofrequency pulses.<sup>1</sup> This magnetically labeled water molecule then diffuses into the brain tissue and gives a T1 decay of the label, enabling evaluation of perfusion abnormalities. Clinically, PASL imaging is being used to evaluate acute and chronic cerebrovascular disease, central nervous system neoplasms, epilepsy, neurodegenerative disorders, and neuropsychiatric diseases.<sup>5</sup>

Astrocytomas are classified as low-grade (WHO grade I or II) or high-grade (WHO grade III and IV). Low-grade astrocytomas typically have a prolonged symptom onset, while high-grade astrocytomas often present with clinical prodromes that are short in onset and rapidly progressive. Patients typically display focal neurologic symptoms that correlate to the location of the tumor and may display signs of increased intracranial pressure.<sup>2</sup> High grade astrocytomas, such as anaplastic astrocytomas, are more common in adults than in children. A majority of high-grade astrocytomas occur in the cerebral hemispheres or within the deeper midline structures, such as the midbrain and pons. High grade astrocytomas have been associated with multiple genetic abnormalities including epidermal growth factor receptor (EGFR) mutations, TP53 mutations, PTEN tumor suppressor gene mutations and mutations in DNA repair pathways.<sup>2</sup> Also, in some patients, high-grade astrocytomas can arise from low-grade astrocytomas. Diagnosis of astrocytomas typically involves imaging findings on MRI, ranging from diffuse nonenhancing lesions to focal enhancing lesions. High-grade astrocytomas usually have an altered blood brain barrier that leads to peritumoral edema that is seen as increased signal on T2/FLAIR imaging, mass effect and contrast enhancement. These tumors are infiltrative and typically spread throughout the T2 areas of abnormality and into normal brain. This makes complete resection very unlikely. Accurate diagnosis usually requires a biopsy. Studies involving dual therapy with temozolomide and radiotherapy in glioblastoma have shown survival benefits and are currently being investigated in anaplastic astrocytoma.<sup>3</sup>

Although encephalitis can cause increased signal on T2/FLAIR MRI imaging and demonstrate increased perfusion on PASL, often appearing identical to an astrocytoma on MRI, it is sometimes bilateral and is usually associated with a higher CSF white blood cell count and normal protein.

Frontotemporal dementia (FTD) lacks the focal findings seen on imaging and has a slower clinical course. The typical presentation of FTD consists of the patient having problems sustaining attention and developing personality changes.<sup>4</sup>

Personality changes can include obsessive-compulsive features, impaired judgment, emotional lability, irritability, and lack of empathy<sup>4</sup>. Patients can have semantic memory loss and signs of motor neuron disease, as there is an association with amyotrophic lateral sclerosis (ALS). Diagnosis is multifactorial, with clinical progression, neuropsychiatric testing, and imaging. Typical imaging findings of FTD include cortical volume loss in the dorsolateral prefrontal cortex and the medial temporal lobes with relative sparing of the parietal and occipital lobes.<sup>4</sup> Functional imaging, such as with fluorodeoxyglucose-positron emission tomography (FDG-PET), shows frontotemporal hypometabolism. Currently, there are no disease-modifying treatments for FTD and treatment is focused on symptomatic treatment with antidepressants and antipsychotics.

MRI findings with bacterial abscesses usually demonstrate peripheral contrast enhancement and central diffusion restriction. Also, bacterial brain abscesses usually occur in association with other risk factors, such as bacterial endocarditis, diabetes, immunosuppression, or other vascular abnormalities including congenital heart disease or hereditary hemorrhagic telangiectasia.<sup>6</sup> Lumbar punctures

are usually not very helpful with diagnosis of bacterial abscesses, as cultures are usually negative and the profile is usually nonspecific. Commonly, management includes antibiotic therapy in combination with either stereotactic aspiration or other surgical drainage.

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#### References:

1. Wolf, Ronald; Detre, John. Clinical Neuroimaging Using Arterial Spin-Labeled Perfusion MRI. *Neurotherapeutics*: 2007 Jul; 4 (3): 346-359.
2. Daroff MD, Robert; Fenichel MD, Gerald; Jankovic, Joseph MD; Mazziotta MD, PhD. Cancer and the Nervous System: Astrocytic Tumors. *Bradley's Neurology in Clinical Practice*. Ed. 6; 2012: 1163-1170.
3. Stupp, Roger; Hegi, Monika; Mason, Warren; Bent, Martin; Taphoorn, Martin JB, etc.. Effects of Radiotherapy with Concomitant and Adjuvant Temozolomide versus Radiotherapy alone on Survival in Glioblastoma in a Randomised Phase III Study: 5-year Analysis of the EORTC-NCIC trial. *The Lancet Oncology*: 2009 May; 10 (5): 459-466.
4. Rowland MD, Lewis; Pedley MD, Timothy. Frontotemporal Dementia. *Merritt's Neurology*. Ed. 12; 2010: 718.
5. Pollock MD, Jeffrey; Huan Tan; Kraft PhD, Robert; Whitlow MD PhD, Christopher; Burdette MD, Jonathan; Maldjian MD, Joseph. Arterial Spin Labeled MRI Perfusion Imaging: Clinical Applications. *Magn Reson Imaging Clin N Am*: 2009 May; 17 (2) 315-338.
6. Daroff MD, Robert; Fenichel MD, Gerald; Jankovic, Joseph MD; Mazziotta MD, PhD. Infections of the Nervous System: Brain Abscess. *Bradley's Neurology in Clinical Practice*. Ed. 6; 2012: 1262-1263