Acute Onset of Dizziness and Paresthesias in an Elderly Woman

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61-year-old woman with a past medical history of dementia and Meniere's disease presents with acutely worsening dizziness and headache. The patient additionally complains of left greater than right upper extremity weakness and paresthesias.

What is your diagnosis?

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IMAGING FINDINGS: Computed Tomography (CT) scan demonstrates a large intra-axial geographic area of predominantly subcortical hypodensity centered within the right posterior frontal lobe and right superior parietal lobule with surrounding mass effect and minimal resulting right to left midline shift (Figure 1).

Axial MR images demonstrate a T1 hypointense, T2 FLAIR hyperintense mass-like intra-axial confluence centered within the right posterior frontal lobe and right superior parietal lobule with surrounding mass effect and minimal resulting right to left midline shift (Figures 2 and 3). Figure 2B details subtle leptomeningeal enhancement overlying the right frontal, parietal, and temporal lobes without intra-axial enhancement.

Multiple punctate foci of bloom artifact projecting predominantly in the cortex in the right hemisphere as noted on GRE sequences represent hemosiderin deposition in areas of cerebral microhemorrhage (Figure 4).

DIFFERENTIAL DIAGNOSIS:
1. Infiltrating low-grade primary brain neoplasm, such as gliomatosis cerebri.
2. Focal encephalitis.
3. Demyelination.
4. Progressive multifocal leukoencephalopathy (PML) in the setting of an immunocompromised patient.
5. Cerebral amyloid angiopathy (CAA)

PATHOLOGICAL FINDINGS AND FINAL DIAGNOSIS: Open biopsy of the brain revealed an edematous brain but no abnormal vessels. No neoplasm was noted. Microscopic analysis of the biopsied specimen showed evidence of cerebral amyloid angiopathy (CAA). Figure 5 shows accumulation of eosinophilic material in the walls of cortical and meningeal small vessels (arrow). The eosinophilic material stained congo red and shows apple green birefringence, consistent with amyloid (not shown). Granulomatous inflammation was also seen in a significant minority of the microvasculature, with histiocytes and giants cells (Figure 6). These findings were demonstrated on a background of multifocal cerebral hemorrhage, as evidenced by hemosiderin laden macrophages seen in figure 7 (arrow), as well as neurofibrillary tangles and neuritic plaques characteristic of Alzheimer’s disease. The final diagnosis was determined to be (tumefactive) cerebral amyloid angiopathy with angiitis.

FINAL DIAGNOSIS: Cerebral Amyloid Angiopathy with Angiitis

DISCUSSION

CAA is a common cause of spontaneous primary intracerebral hemorrhage (ICH) in the elderly. It results from the accumulation of amyloid-β peptide deposits in the media and adventitia of small and medium sized vessels of the brain and leptomeninges. Though it may be related to Alzheimer’s disease, it can also present as a sporadic disorder or as a familial syndrome. Though primarily asymptomatic, it is an important source of pathology in elderly patients. In addition to primary ICH, it may present as long term cognitive impairment, inflammatory leukoencephalopathy, transient neurological symptoms, or incidental microhemorrhages on imaging.

Tumefactive CAA, as in this case, may present as a poorly marginated, translobar, T2-hyperintense, T1-hypointense mass. This constellation of findings are sometimes difficult to distinguish from a low grade glioma or from meningoencephalitis. Lymphoma after the administration of steroids can also have this appearance. Leptomeningeal enhancement is variable in CAA and may be related to inflammation or subarachnoid bleeding. Leptomeningeal enhancement is uncommon in low grade neoplasms, and may be helpful to distinguish between neoplasms and tumefactive CAA. MR spectroscopy may also be used to differentiate between these two entities. While low grade gliomas demonstrate a decreased NAA/Creatine ratio (< 1) and increased choline, tumefactive CAA demonstrates a normal NAA/Cr ratio (> 1) and unchanged choline.

Microhemorrhages may not be seen on MRI without the use of more sensitive sequences such as GRE or susceptibility weighted imaging (SWI). GRE and SWI imaging techniques rely on the presence of paramagnetic products in the blood such as hemosiderin to produce profound signal loss. Often, the presence of susceptibility weighted artifact is sometimes used to assist in grading of primary CNS neoplasms, where the distribution of blooming artifact in high-grade primary neoplasms is typically in the tumor margins. However in CAA, the presence of microhemorrhages is characteristically distributed throughout the brain parenchyma. Subarachnoid hemosiderosis is also a finding relatively specific to CAA.

Though GRE is routinely performed at our institution, it may not be as common elsewhere. The utilization of advanced techniques such as SWI or GRE preoperatively may lead to an appropriate differential diagnosis and treatment planning which itself may lead to more appropriate treatment regimens to include surgical biopsy including craniotomy and wedge resection of cortex and leptomeninges to evaluate for CAA, as opposed to stereotactic biopsy often utilized in the setting of primary CNS neoplasm. CAA typically spares blood vessels in the white matter, which may be missed by stereotactic biopsy focused on a white matter abnormality.

A subset of patients with CAA will have an inflammatory angiitis sometimes referred to as Amyloid β related angiitis (ABRA). Patients with ABRA are reported to be younger (66.5 years) than those with CAA without angiitis (76.3 years). The clinical presentation is that of acute or subacute cortical decline, seizures, headache, and focal neurological signs. Focal neurological findings are more likely in patients with CAA angiitis. Low grade glial neoplasm and focal encephalitis are frequently considered as part of the differential diagnosis in patients with this process. CAA with inflammatory angiitis details perivascular inflammation with multinucleated giant cells associated with amyloid deposition. Erythrocyte sedimentation rate and C-reactive protein are frequently normal. Though there may
be a transient elevation in anti-amyloid antibodies in the acute phase, these usually return to control levels during remission. CSF may show mildly elevated protein levels or pleocytosis but is otherwise frequently normal. A recent series demonstrated inflammatory findings in 4 of 5 patients with biopsy proven tumefactive CAA, suggesting that inflammatory CAA may be associated with tumefactive appearance.

Treatment of CAA is based on presentation. Acute lobar hemorrhage is treated with refraining from use of anticoagulants and antiplatelet drugs, and fine control of blood pressure to avoid intracranial hypertension. Lobar hemorrhage may require surgical evacuation.

REFERENCES

1. Greenberg, SM. Cerebral Amyloid Angiopathy. In: UpToDate, Kasner SE (Ed), UpToDate, Waltham, MA. (Accessed on February 13, 2014.)


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