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Clinical challenges

A pox upon your house

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(In keeping with the format of a clinical pathologic conference, the abstract and key words appear at the end of the article.)

1. Case Report

An 81-year-old white man presented with a 3-day history of acute left-sided eye pain, left-sided temporal pain, headache, and intermittent dizziness. The eye pain directly followed an episode of low-grade fever that had resolved, and he had been empirically treated with doxycycline. Past medical history was significant for childhood chickenpox, herpes zoster vaccine, atrial fibrillation, hyperlipidemia, coronary artery disease, and skin cancer involving the right lower lid with no history of perineural tumor spread. His medications were warfarin, furosemide, simvastatin, and fenofibrate.

His visual acuity was 20/20 OU. The pupils were equal and reactive to light with no relative afferent pupillary defect. Ocular motility was full. Slit-lamp biomicroscopy showed mild conjunctival injection with chemosis OS, but was normal OD. There was no evidence of uveitis. Intraocular pressures were initially normal. Dilated fundus examination was normal. Serum erythrocyte sedimentation rate and C-reactive protein were normal. The patient was started on oral prednisone. A temporal artery biopsy showed "segmental loss of internal elastic lamina and media fibrosis without giant cell or eosinophil infiltration." Prior to the temporal artery biopsy, he was noted to have new onset anterior uveitis, and the intraocular pressure was now 40 mm Hg OS and remained normal OD. Intraocular pressures normalized following latanoprost and dorzolamide hydrochloride–timolol maleate. He then developed a central nontraumatic corneal epithelial defect, thought to be neurotrophic because of decreased corneal reflexes and sensation OS, that was treated with punctal occlusion.

What would you do now?

What is the differential diagnosis?

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2. Comments

2.1. *Comments by Lynn Gordon, MD*

At the time of disease onset, this 81-year-old man presented with a constellation of pertinent symptoms including fever, eye pain, new onset headache, temporal pain, and dizziness. There was significant and appropriate concern for giant cell arteritis (GCA), despite a normal erythrocyte sedimentation rate and C-reactive protein, and the patient was started on corticosteroids, pending temporal artery biopsy. Additional symptoms that might have further validated the tentative diagnosis include weight loss, jaw or tongue claudication, and/or transient visual blurring, which were not commented on in the history. Additionally the platelet count, often elevated in this disease, was not provided. The pathology of the biopsy specimen was not pathognomonic for GCA.

The sudden onset of anterior uveitis with a high intraocular pressure (IOP), however, is not consistent with GCA and thus warrants additional evaluation for an underlying disease process that might be responsible for the constellation of signs and symptoms. The combination of uveitis and a neurotrophic cornea would invoke a possible herpetic etiology. Complete characterization of the uveitis, such as degree of anterior chamber reaction, type of keratitic precipitates, presence of synechiae, and thorough retinal and pars plana evaluation might help in developing a differential diagnosis. Acute unilateral uveitis with high IOP may be seen in glaucomatocyclitic crisis and in association with viral infections such as herpes simplex virus, varicella zoster virus (VZV), cytomegalovirus, and rubella.[6]

Therapeutically, one would aggressively treat the uveitis with topical steroids and pressure-lowering agents. Use of systemic acyclovir should be considered for potential herpetic ocular infection. Both antigens and DNA of the herpes viruses have been found in the anterior chambers of patients with this type of uveitis, but this testing is not done routinely. The visual prognosis for patients with herpes virus–associated anterior uveitis is generally good, and thus a diagnostic aqueous study is not indicated unless there is a poor response or systemic associations. At this point, the only other diagnostic test that one might consider would be magnetic resonance imaging (MRI) to evaluate the patient with otherwise unexplained dizziness, headache, and eye pain.

3. Case Report (Continued)

The patient continued to experience left eye pain. Visual acuity was 20/40 OU. Intraocular pressures were 20 mm Hg OD and 36 mm Hg OS despite topical treatment. Slit-lamp biomicroscopy indicated residual corneal edema, irregular corneal epithelium, diffuse conjunctival injection, and a new iris transillumination defect OS; the examination was normal OD. Pupils measured 5 × 4 mm with an irregular oval shape OS, but was normal OD. No neovascularization of the iris was detected OU. MRI of the brain indicated only small vessel ischemic disease bilaterally. Serological tests for herpes zoster were negative for IgM, but positive for IgG (titer 1:128).

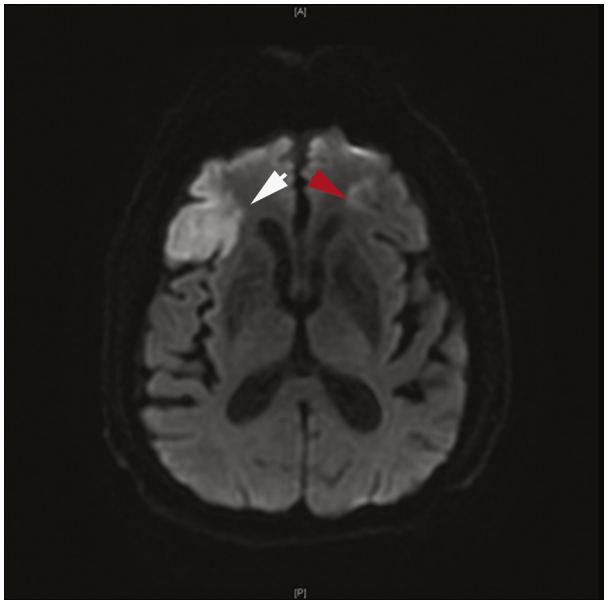

Fig. 1 – Axial diffusion-weighted MRI of the brain taken July 2011 indicated a 3.5-cm infarction in the right frontal lobe (*white arrow, left*) and ischemic change in the left frontal-parietal region (*dark arrow, right*). Minor evidence of ischemia was seen bilaterally in the insula, pons, cerebellum, and occipital cortices.

A month later the patient began to experience recurrent conjunctivitis OS without pain. He then developed new acute symptoms of confusion, memory loss, slurred speech, nausea, and vomiting. Repeat cranial MRI now showed a 3.5-cm infarction in the right frontal lobe with restricted diffusion on diffusion weighted imaging and older ischemic changes in the left frontal-parietal region (Fig. 1). Ischemic change was also seen bilaterally in the insula, pons, cerebellum, and occipital cortices. Lumbar puncture showed an elevated white cell count (157 cells; 92% lymphocytes, 6% monocytes) and an elevated protein (122 mg/dL).

What should be done now?

4. Comments (Continued)

4.1. *Comments by Dr. Gordon*

The clinical course of this patient dramatically changed with the onset of an acute neurologic syndrome. The transillumination defects seen on slit-lamp evaluation provide further support for a viral etiology for the uveitis. Viruses are the primary etiology for infections of the central nervous system, and the gold standard for diagnosis is polymerase chain reaction (PCR) of the cerebrospinal fluid. New multiplex PCR techniques are being validated as having high sensitivities and specificities for a variety of causative viral agents in order to initiate prompt and appropriate therapy.[2,7] It was appropriate for this patient to undergo MRI followed by cerebrospinal fluid (CSF) evaluation and PCR for viral etiologies of this disease. Notably, MRI imaging may be reported as normal in up to 80% of individuals with VZV-associated central