Atypical Infectious Nodular Scleritis

Mycobacterium tuberculosis is an uncommon cause of scleritis in the developed world. Definitive diagnosis is usually made by identification of acid-fast bacilli (AFB) using microscopy or culture techniques.1 We report a case of tuberculous scleritis in which diagnosis was made only after quantitative polymerase chain reaction (PCR) on tissue specimens.

Report of a Case. A 54-year-old woman originally from Mexico had redness and pain in her right eye for 6 months and was diagnosed with nodular scleritis. She was referred to the University of Illinois at Chicago when her symptoms did not resolve with oral prednisone. Her medical history was significant for diabetes, hypertension, hypercholesterolemia, and atrial fibrillation. Her best-corrected visual acuity was 20/80 OD and 20/25 OS. Examination revealed marked scleral injection with 2 scleral nodules superiorly in the right eye. The rest of the ocular examination was unremarkable. She was taking 10 mg/d of prednisone on presentation. Methotrexate (15 mg/wk) was added.

When workup revealed a positive Quantiferon-TB Gold test result (Cellestis Inc, Valencia, California) and calcified granulomas in bilateral hila on chest radiography and chest computed tomography, the patient was referred to the infectious disease service and began treatment with quadruple antituberculosis therapy (rifampin, isoniazid, pyrazinamide, and ethambutol hydrochloride). Methotrexate was stopped, and she self-discontinued prednisone treatment without taper. The scleritis worsened 1 week later, so prednisone treatment (30 mg/d) was restarted; the dosage was later increased (60 mg/d) owing to continued deterioration. Despite 3 months of tuberculosis therapy and treatment with oral prednisone, new nodules developed (Figure 1A). Because the infectious disease service was convinced that the scleritis did not represent infection with tuberculosis, treatment with cyclophosphamide (150 mg/d) was started but was discontinued after 10 days because of worsened scleritis. Scleral biopsy was recommended to rule out multidrug-resistant Mycobacterium, but the patient refused and sought another opinion. She continued receiving prednisone (40 mg/d) with antituberculosis therapy elsewhere.

On return 2 months later, the number of nodules had increased and biopsy was performed. Gram stains, AFB stain, and bacterial cultures had negative results. Microscopy revealed extensive scleral necrosis without classic granuloma formation (Figure 1B and C). Results for tissue Gram stain and stains for AFB (Ziehl-Nielson and Fite stains) were negative. Immunohistochemical staining results were positive for herpes simplex virus type 1. Valacyclovir hydrochloride (1 g 3 times daily) was added.

When the patient was noted to have hyphema and retinal whitening on examination 9 days after the biopsy, vitreous tap and intravitreous ganciclovir sodium and foscarnet sodium injections were performed. Results from PCR were negative for herpes simplex virus, varicella zoster virus, and cytomegalovirus.

She became noncompliant with medications and anticoagulation clinic visits, and she presented to the emergency room in diabetic ketoacidosis with emesis, an extremely high international normalized ratio (INR), and bleeding from her right eye. Vision was no light perception with scleral rupture superonasally and extrusion of intraocular contents (Figure 2A). Once the patient was medically stabilized, enucleation was performed. Histopathologic analysis revealed extensive necrotizing scleral and uveal inflammation. Results from histochemical stains for AFB and cultures were negative (Figure 2B). Results from microbiological testing of bronchoalveolar lavage were negative.

Specimens were sent to the Ocular Pathology Laboratory, Doheny Eye Institute, Los Angeles, California, for realtime PCR, which revealed M tuberculosis genome. There
were 702 copies of mycobacteria in four 20-µm histologic sections (44.9 fg of \textit{M tuberculosis} DNA/1 µg of total DNA). The method and primers used have been previously described.²

\textbf{Comment.} Ocular involvement with tuberculosis is rare.³ In this case, diagnosis was based on positive PCR results following negative results on multiple cultures and stains for AFB on tissue sections and body fluids. Histopathologic analysis may not always offer adequate sensitivity, especially when bacteria are few. This report exemplifies the importance of quantitative PCR in such cases. A confounding factor in this case was tissue immunoreactivity to herpes simplex virus type 1 antibody. Although the antibodies used have a high sensitivity, variable specificity and false-positive reactions may occur.⁴

This case also highlights the difficulty in treating multidrug-resistant tuberculosis scleritis, which is more likely to have a dismal prognosis as has scleritis secondary to drug-resistant atypical mycobacteria.⁵

\textbf{Choroidal Melanoma Occurring in a Nonhuman Primate}

A 7-year-old female cynomolgus monkey (\textit{Macaca fascicularis}) was obtained in January 2006. Results of the prearrival screening tests for tuberculosis and simian retrovirus were negative. Mild hepatomegaly and moderate dental tartar were present on physical examination on arrival. Minimal hypochromic, normocytic anemia, neutropenia, and lymphocytosis were found on clinicopathological examination. The serum chemistry data, including levels of hepatic enzymes, were unremarkable.

A prestudy ocular examination was performed in May 2006. Results of the external and anterior segment examinations of both eyes were unremarkable. The dilated examination showed a healthy retina in the right eye and an elevated choroidal mass involving the macula with some intrinsic peripheral pigmentation in the left eye (Figure 1A). Fluorescein angiography showed an intrinsic circulation within the mass with areas of hyperfluorescence (Figure 1B). Optical coherence tomography revealed a choroidal mass with high reflectivity and adjacent subretinal and intraretinal fluid (Figure 1C). B-scan ultrasonography showed acoustic hollowness with medium internal reflectivity. There was excavation of the underlying sclera (Figure 1D). The differential diagnosis included primary intraocular tumor or metastatic spread of a systemic malignant neoplasm as well as rare peripheral nerve sheath tumors such as schwannoma; however, the clinical presentation suggested a choroidal melanoma. The animal was euthanized 2 years after initial presentation, and a necropsy was done with enucleation. No significant change was noticed in the tumor on imaging prior to euthanasia. No other abnormalities were observed. The eye was fixed in Davidson solution prior to its transfer to 70% ethanol.

The histopathological examination of the eye showed a dumbbell-shaped mass arising from the choroid, penetrating the Bruch membrane, and involving the overlying retinal pigment epithelium.
Correction

Error in Text. In the Letters: Research Letters article titled “Atypical Infectious Nodular Scleritis” by Kesen et al, published in the August 2009 issue of the Archives (2009; 127[8]:1079-1080), an error occurred in lines 12 through 16 of the third paragraph on page 1079. The text should have read, “Despite 3 months of tuberculosis therapy and treatment with oral prednisone, new nodules developed (Figure 1A). Because the infectious disease service was convinced that the scleritis did not represent infection with tuberculosis, treatment with cyclophosphamide (150 mg/d) was started but was discontinued after 10 days because of worsened scleritis.” This article was corrected online for typographical errors on August 10, 2009.