

Cystoid Macular Edema as a Manifestation of Sarcoidosis

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Case History

A 40-year old systemically healthy male presented for a few months of blurry vision in his left eye. The patient had no prior eye conditions other than near-sightedness corrected with spectacles. There was no prior history of blurry vision, ocular inflammation, injuries, or surgeries. The patient reported no significant medical history or regular medication use, allergies or family history. He worked with a local railroad company and denied any new sexual partners, illicit drug use or travel outside of the United States. Review of systems was negative for fevers, rashes, joint pain, dysuria, but significant for occasional dyspnea associated with chest tightness.

Examination revealed near normal visual acuity of 20/25 in each eye with mild anterior uveitis in both eyes, optic nerve edema and cystoid macular edema in the left eye. Optical Coherence Tomography (OCT) confirmed absence of retinal edema in the right eye (Figure 1) and cystoid macular edema in the left eye (Figure 2). Work-up including laboratory studies revealed mild elevation of the angiotensin converting enzyme level (ACE) as well as reticular densities on the chest plain film (Figure 3). After infectious etiologies including tuberculosis and syphilis were ruled out, the patient was started on topical steroid and non-steroidal eye drops without significant resolution of the cystoid macular edema or subjective visual improvement. The patient started a tapering course of oral prednisone in addition to his steroid and non-steroidal eye drops and referred to the Medical Retina clinic for additional evaluation and management.

Ocular photographs (Figures 4 and 5) were taken along with retinal angiography. The study confirmed the retinal vascular leakage in the left eye (Figure 6), but also revealed optic nerve edema in the asymptomatic right eye (Figure 7). As there had not been improvement with the topical steroid eye drops and oral prednisone, a regional triamcinolone steroid injection was administered around the left eye with improvement in the retinal edema and visual symptoms (Figure 8). The same treatment was administered to the right eye and the patient was able to taper off oral prednisone and reduce the frequency of steroid and non-steroidal eye drops to daily maintenance.

Discussion

Introduction

Sarcoidosis is characterized by non-caseating granulomatous inflammation in multiple organ systems, most commonly the lungs and skin. The precise etiology of the condition is unknown, but an aberrant cellular immune response has been postulated to be primarily responsible for the granuloma formation, with numerous environmental and infectious triggers proposed [1,2]. The T-lymphocyte appears to be the predominant cellular player in sarcoidosis, with an abnormal ratio of T-helper to T-suppressor cells in organ granulomas. This T-helper cell imbalance may lead to excessive B-cell stimulation and secondary hypergammaglobulinemia [2].

Ocular features

Ocular findings have been reported to occur in 25% to 50% [1,3] of patients with sarcoidosis. Ocular inflammation may be the initial

manifestation of sarcoidosis or co-exist with systemic inflammation and typically occurs early in the disease course [3].

Recent epidemiologic data have shown a higher prevalence as well as earlier age of presentation of ocular sarcoidosis among African Americans compared to white Americans [1,4]. Anterior uveitis (iritis) is the most common ocular manifestation of ocular sarcoidosis, occurring in up to 60% of patients with sarcoidosis. This feature typically causes eye pain, redness, and blurry vision. Conjunctival lesions can be seen in up to 40% of patients with sarcoidosis [5,6]. Less common, but more vision threatening posterior ocular inflammatory findings include vitritis, optic nerve edema, macular edema, and retinal vasculitis (with the venules affected more often than the arterioles) [1]. Peripheral chorioretinal lesions in the retinal periphery may also be seen and must be distinguished from active peripheral multifocal choroiditis [2,7]. Sarcoidosis may also affect the periocular structures including the lacrimal gland and parotid gland and cause facial nerve palsies.

Diagnosis

There is no definitive serologic or radiographic study to identify the granulomatous changes of sarcoidosis. The combination of

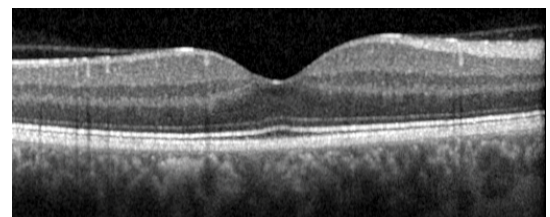


Figure 1: Optical Coherence Tomography (OCT) of the macula in the right eye with normal contour.

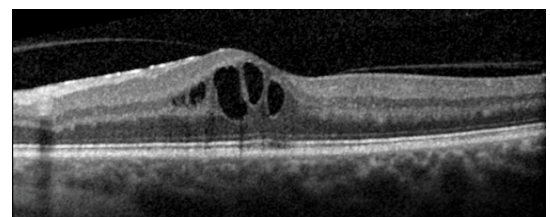


Figure 2: Optical Coherence Tomography (OCT) of the macula of the left eye showing cystoid edema.

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Figure 3: Anterior-posterior chest plain radiograph showing multiple reticular densities scattered throughout both lung fields with focal densities localized around the hilar region bilaterally.



Figure 4: Fundus photo of the right eye showing generally normal appearance to the optic nerve and vessels.



Figure 5: Fundus photo of the left eye showing generally normal appearing optic nerve and blood vessels with a granular appearance near the fovea.

elevated serum Angiotensin Converting Enzyme (ACE), elevated serum calcium, along with pulmonary and hilar findings are, however, very suggestive of sarcoidosis. Elevated ACE levels are a non-specific finding and can also be seen in other granulomatous diseases including tuberculosis and leprosy as well as primary biliary cirrhosis and diabetes mellitus [1,2]. Normal to low normal ACE levels can be seen in localized or mild sarcoidosis as well as those taking ACE inhibitors for hypertension, so this should not rule out a diagnosis. Computerized Tomography (CT) of the chest may be more sensitive than chest radiography, so a normal chest film should also not rule out the diagnosis of sarcoidosis. Gallium scan abnormalities, serum lysozyme elevation and hypergammaglobulinemia have also been seen to occur in sarcoidosis, and are used in some institutions in addition to chest imaging, serum ACE, and calcium. Biopsy of lesions on the conjunctiva or via transbronchial approach can be used to confirm the non-caseating histology of these sarcoid lesions.

Screening

The role for screening sarcoidosis patients for asymptomatic ocular or periocular lesions is unclear. As detailed above, most of the ocular features of sarcoidosis tend to produce eye pain or blurry vision, and typically occur early in the course of the disease. A dilated eye examination with an Ophthalmologist seems prudent in a patient with recent diagnosis of sarcoidosis and particularly in a patient with vision symptoms with or without concurrent systemic symptoms.

Treatment

The mainstay of treatment for sarcoidosis is corticosteroids, and the disease is exquisitely responsive to these agents. Lack of response to corticosteroids should prompt consideration of other diagnostic entities including tuberculosis or other inflammatory or granulomatous conditions [7].

Sarcoid uveitis treatment is tailored to the focus of inflammation (anterior, intermediate, posterior) or pan-uveitis. Topical steroid eye drops are effective for anterior uveitis, but posterior uveitis is often incompletely responsive to steroid eye drops, particularly in younger patients who have not had cataract surgery, as the natural lens is a relative barrier for penetration of eye drops to get into the vitreous cavity or retina.



Figure 6: Fluorescein angiogram of the asymptomatic right eye revealing vascular leakage around the optic nerve.



Figure 7: Fluorescein angiogram of the left eye revealing inflammatory retinal vascular leakage around the optic nerve and fovea.

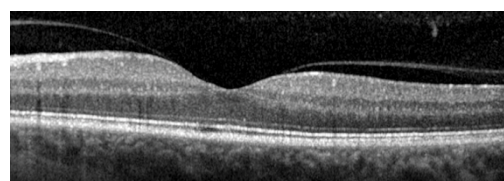


Figure 8: OCT of the left eye showing resolution of the cystoid retinal edema after periocular triamcinolone injection.

The use of regional steroid can be effective in controlling posterior uveitis while often reducing the dose of and associated toxicity of oral corticosteroids. Periocular regional steroid injections deliver a depot of steroid and are particularly effective in cases of cystoid macular edema secondary to intraocular inflammation in sarcoidosis [8]. The most significant consequences of high dose depot steroid around the eye include elevation of the intraocular pressure and earlier development of cataract. Rare complications can include inadvertent perforation of the eye, ptosis (drooping) of the upper eyelid, endophthalmitis (severe intraocular infection), and allergy to the steroid vehicle [1]. A recent large retrospective study of 900 patients identified periocular corticosteroid injections as an efficacious means of controlling intraocular inflammation in 70% of patients as well as improving visual acuity in 50% of patients. Roughly 30% of the patients receiving such treatments were found to have elevations of the intraocular pressure and 20% demonstrated increased cataract development with these treatments [9].

Methotrexate is effective as a steroid sparing agent in ocular and or systemic sarcoidosis [1]. This agent inhibits dihydrofolate reductase, an enzyme necessary for cellular mitosis, thereby affecting rapidly dividing cells including inflammatory lymphocytes. Systemic methotrexate is usually administered in a single oral dose or subcutaneous injectable dose once weekly and is often taken with folic acid to protect normal cells. Intraocular (intravitreal) methotrexate has been shown to improve ocular inflammation in posterior uveitis [10] but can cause toxicity to the cornea and must be compounded as a single use vial for ocular use is not approved in the United States. Intravitreal methotrexate has also been used for intraocular lymphoma, where it controls proliferation of malignant cells [11].

Prognosis

Most patients with sarcoidosis do not develop debilitating ocular, pulmonary, dermatologic or other organ dysfunction. Ocular anterior uveitis tends to cause flares which quickly respond to topical steroid

eye drops. Posterior uveitis associated with sarcoidosis can have a smoldering course, so prompt and aggressive treatment of inflammatory flares and cystoid macular edema can reduce the risk of permanent vision loss. Physicians treating patients with sarcoidosis should have a low threshold for referring patients to an Ophthalmologist if there is concern for ocular inflammation.

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