Minocycline for the Treatment of Ocular and Ocular Adnexal Sarcoidosis

Sarcoidosis is a chronic systemic inflammatory disorder characterized by noncaseating granulomas. Although almost any organ can be affected, common sites of involvement include the skin, lungs, lymph node, eye, and ocular adnexa. Corticosteroids have remained the first-line therapy since their introduction in the 1950s.1 However, because of the significant adverse effects associated with chronic corticosteroid use, treatment is typically reserved for those with severe visceral involvement or refractory ocular and ocular adnexal involvement.

A number of steroid-sparing agents have been used with varying success in the treatment of chronic sarcoidosis. Bachelez et al2 reported clinical response in 10 of 12 patients with cutaneous sarcoidosis treated with minocycline. We describe herein the first reported case of ocular, ocular adnexal, and systemic sarcoidosis treated with minocycline.

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Report of a Case. A 41-year-old white woman was referred with a 3-week history of swelling involving the medial canthus, parotid gland, and lacrimal gland area bilaterally. Medical history was positive for morbid obesity, seasonal allergies, depression, spinal stenosis, and psoriasis. Medications included cetirizine, escitalopram oxalate, furosemide, celecoxib, zaleplon, and allergy shots. Until 8 months prior to our initial examination, the patient was receiving methotrexate for psoriasis. Review of systems was positive for back and joint pain, xerostomia, daytime somnolence, and snoring.

On examination, visual acuity was 20/20 OU and visual fields were full to confrontation. Pupils were equal and reactive with no relative afferent pupillary defect and extraocular movements were full in both eyes. External examination disclosed mildly tender, indurated nodular fullness involving the subcutaneous tissues of the medial canthus and in the lacrimal gland bilaterally (Figure 1A and B). Conjunctival nodules were present (Figure 2A). Posterior segment examination was unremarkable.

Computed tomographic scan of the orbit disclosed symmetric bilateral enlargement of the lacrimal and parotid glands (Figure 3A). Angiotensin converting enzyme level was 49 U/L (normal, <46 U/L).

Incisional biopsy of the right lacrimal gland and subcutaneous medial canthal masses and fine-needle aspiration biopsy of the parotid gland revealed noncaseating granulomas consistent with sarcoidosis (Figure 4A and B). Grocott methenamine-silver stain for fungi and auramine/rhodamine stain mycobacteria were negative.

Pulmonary evaluation, including polysomnography, revealed obstructive sleep apnea. Computed tomographic scan of the lungs showed patchy infiltrates at both lung bases but no apparent hilar adenopathy; these findings were not considered typical for pulmonary sarcoidosis. A right renal lesion was noted on an abdominal computed tomodigraphic scan (Figure 3C), and excisional biopsy disclosed features consistent with sarcoidosis (Figure 4C). Prednisone therapy was considered at this time but was deferred in view of concern regarding adverse effects given the patient’s medical comorbidities.

Two weeks following initial pulmonary evaluation, the patient visited the emergency department with acute dyspnea, new subcutaneous nodules in the chin and perioral area, and worsening papular eruptions on the upper torso (Figure 5A). Chest computed tomodigraphic scan disclosed a new nodule in the middle lobe of the right lung (Figure 3B). Skin biopsy disclosed dermal and pannicular granulomatous inflammation, which was suggestive of sarcoidosis (Figure 4D). Minocycline 100 mg by mouth twice daily was
started. Within 3 months, the cutaneous, lacrimal gland, and pulmonary lesions showed marked improvement (Figure 1C and D, Figure 2B, and Figure 4B). Dilated funduscopic examination revealed bilateral choroidal granulomas (Figure 6). Angiotensin converting enzyme level at this time was 89 U/L.

Seven months after the initiation of minocycline, the cutaneous, conjunctival, and choroidal lesions had regressed with normalization of the angiotensin converting enzyme level (25 U/L) and chest x-ray findings. The patient continued to do well while receiving minocycline 11 months after starting treatment.

Comment. Given the morbidity associated with long-term corticosteroid use, steroid-sparing agents have been used with increasing frequency in patients with refractory disease or those requiring long-term corticosteroid administration. In an observational study, Bachelez et al² treated 12 patients with biopsy-proven cutaneous sarcoidosis with minocycline 200 mg daily over a median 12-month period. With a median follow-up of 26 months, the authors noted complete and partial response to treatment in 8 and 2 patients, respectively. The mean time to reach maximal response was 3.2 months. Of the 8 patients who had a complete response, minocycline was able to be withdrawn in 7, 3 of whom experienced recurrent lesions and received further treatment with doxycycline 200 mg daily. Complete remission was maintained for a mean of 15.3 months. Regression of pulmonary infiltrates and mediastinal lymphadenopathy was noted in the 2 patients with concurrent pulmonary involvement.

The anti-inflammatory properties of tetracyclines have been demonstrated by in vitro studies and corroborated by clinical trials. Tetracycline has been shown to suppress neutrophil migration and chemotaxis,³ and minocycline was shown to inhibit T-lymphocyte activation and proliferation.⁴ Both minocycline and doxycycline have been shown to obviate granuloma formation in vitro.⁵ In 2 small, double-blind prospective clinical trials of rheumatoid arthritis, minocycline was shown to affect a significant clinical improvement compared with placebo⁶ and hydroxychloroquine.⁷ Minocycline has also been demonstrated to have some clinical effectiveness in early diffuse scleroderma.⁸

The antimicrobial properties of tetracyclines may play a role in its
efficacy in treating sarcoidosis. In a study of 15 patients with sarcoidosis, ribosomal RNA fragments of Propionibacterium acnes and Mycobacterium tuberculosis were isolated from the lymph nodes of 12 and 3 patients, respectively. In a collaborative multinational follow-up study, ribosomal RNA fragments of either P acnes or P granulosum was detected in 106 of 108 patients (98%).

The patient in this report demonstrated a complete and recurrence-free response of the lacrimal gland and choroidal lesions as well as parotid granulomas and pulmonary infiltrates after 3 months of minocycline therapy. To date, the patient has tolerated minocycline with minimal adverse reactions limited to hyperpigmentation in the area of the regressed cutaneous lesions. Hyperpigmentation is a well-known adverse effect of minocycline, is thought to be dose-responsive, and resolves with discontinuation of the

Figure 4. Surgical photograph demonstrates an enlarged and inflamed lacrimal gland (A). Light photomicrographs demonstrate lacrimal gland infiltrated with noncaseating granulomas and obliteration of the glandular architecture (B) (original magnification ×400, hematoxylin-eosin), noncaseating granulomas in the kidney (C) (original magnification ×200, hematoxylin-eosin), and skin lesion (D) (original magnification ×40, hematoxylin-eosin).

Figure 5. Clinical photographs show an erythematous tender subcutaneous nodule on the anterior torso measuring approximately 1 cm (A) with resolution and secondary hyperpigmentation 6 months after minocycline therapy (B).
Other significant systemic adverse reactions include renal toxicity, hepatotoxicity, hemolytic anemia, Stevens-Johnson syndrome, and elevated intracranial pressure. To our knowledge, this case represents the first case of ocular and ocular adnexal sarcoid treated with minocycline.

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Figure 6. Fundus color photograph of the right eye shows prominent whitish choroidal granulomas (A) with diminution following treatment (B).

Paclitaxel Maculopathy

Cystoid macular edema (CME) is thought to result from disruption of the normal blood-retinal barrier. Leakage from paravascular capillaries is demonstrated on fluorescein angiograms in a classic petalloid pattern in typical CME.

Expansion of the intracellular fluid space may also lead to CME. Accumulation of fluid in the intracellular space may lead to CME without evidence of leakage on fluorescein angiograms. We report a case in which CME was secondary to paclitaxel (Taxol; Bristol-Myers Squibb Co, New York, NY) use without evidence of leakage at angiography.

Report of a Case. A 63-year-old woman reported gradual decreased vision in both eyes. The patient’s medical history was significant for metastatic breast carcinoma with previous radiation therapy to the brain. Her chemotherapeutic regimen consisted of trastuzumab (Herceptin; Genentech Inc, South San Francisco, Calif) and paclitaxel (175 mg/m² for 10 months). At the initial ophthalmologic examination, the best-corrected visual acuity was 20/80 OU. Anterior segment examination yielded normal findings. Dilated fundus examination revealed no evidence of vitreitis. Cystoid macular edema was clinically noted in both eyes. Fluorescein angiograms exhibited normal filling of the choroidal and retinal vessels and an intact parfoveal capillary net. Late frames of the angiograms did not show any significant leakage. Optical coherence tomography scans of both eyes revealed CME with a foveal thickness greater than 500 µm (Figure). Findings from the examination were consistent with CME in both eyes without any evidence of fluorescein leakage. Niacin maculopathy, Goldmann-Favre syndrome, and congenital X-linked retinoschisis were ruled out on the basis of history and clinical examination. Literature review yielded 1 case report of CME without fluorescein...