patients with this diagnosis appear to have a favorable prognosis with a variety of treatment approaches. Systemic chemotherapy rather than radiotherapy may avoid potential persistent epiphora due to radiation-induced lacrimal duct stenosis.

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10. Pe’er JI, Stefansyzyn M, Hidayat AA. Nongenti-
and serial follow-up, as the patient was asymptomatic with stage I disease. A trial of topical 0.5% cyclosporin A drops (prepared in artificial tears), 4 times daily, resulted in dramatic improvement of conjunctival hyperemia and complete resolution of the lower fornical nodules within 2 weeks (Figure 3). The patient is currently receiving maintenance therapy with cyclosporin drops, once per day, in each eye.

Comment. Cyclosporin is an immunomodulator with a selective inhibitory effect on CD4+ T-lymphocyte proliferation via inhibition of interleukin 2 receptor expression. Although the pathogenesis of sarcoidosis is not fully understood, T-lymphocyte–mediated hypersensitivity appears to play a central role, and corticosteroids remain the mainstay of therapy. Although no controlled trial data exist, uncontrolled case reports or small case series demonstrate favorable outcomes of oral cyclosporin therapy in refractory pulmonary sarcoidosis, neurosarcoidosis, and vision-threatening sarcoid-associated uveitis.

Topical administration of cyclosporin has been highly effective in the treatment of various cell-mediated anterior segment inflammatory conditions. In our patient, topical cyclosporin therapy was preferred, owing to the patient’s history of increased intraocular pressures with topical steroid use. Dramatic improvement of symptoms and signs occurring within a short time suggests that sarcoid conjunctivitis may represent another indication for cyclosporin eyedrops.

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2. Obenauf CD, Shaw HE, Sydnor CF, Klinthworth GK. Sarcoidosis and its ophthalmic mani-
Orbital Inflammatory Disease After Pamidronate Treatment for Metastatic Prostate Cancer

Pamidronate sodium is a bisphosphonate drug used to inhibit bone resorption in the treatment of the hypercalcemia of malignancy, Paget disease of bone, and osteolytic bone metastases. It is administered as a slow intravenous infusion and is excreted renally. Although its mechanism of action is incompletely understood, it inhibits osteoclastic activity in vitro and binds directly to hydroxyapatite within the bone matrix.

The most common adverse effects of pamidronate infusion are nausea and anorexia. Ocular adverse effects are rare but include conjunctivitis, anterior uveitis, episcleritis, and scleritis. One case of orbital inflammation occurring 6 days after pamidronate treatment has been reported. Most of these patients had Paget disease of bone, which generally requires higher and more frequent doses of the drug.

We describe 2 patients who developed orbital inflammation after treatment with pamidronate for bone-involving metastases and discuss the implications both for the drug’s mechanism of action and for the pathogenesis of this disease.

Report of Cases. Case 1. A 63-year-old man was diagnosed as having advanced prostate cancer in November 1997. Tumor metastases were found in the thoracic spine and ribs, and the patient underwent external beam radiotherapy. In October 1999, 6 days after receiving his first infusion of pamidronate, he had a sudden onset of left orbital pain and then developed diplopia with upgaze. At examination, his corrected visual acuity was 20/20 OU. Confrontational visual field measurements were full to finger counting. Pupils were equal and round without a relative afferent pupillary defect. Posisis and proptosis were absent. Elevation of the left eye was mildly restricted, and a 3–prism dioptr left hypotropia was measured in upgaze. Upper and lower eyelid edema, conjunctival injection, and mild chemosis were present in the left eye. No anterior segment or vitreous inflammation was observed. The results of a dilated fundus examination were normal. Magnetic resonance imaging of the brain and orbits with gadolinium contrast showed no evidence of a metastatic lesion. The patient was treated with oral prednisone (80 mg/d), experienced prompt resolution of his symptoms, and received no further doses of pamidronate.

Case 2. A 64-year-old man was treated for prostate cancer with a radical prostatectomy in 1991 followed by treatment with leuprolide acetate and flutamide. In the spring of 2002, he was diagnosed as having osteopenia and received his first infusion of pamidronate in July 2002. Within 24 hours, he experienced lower extremity myalgia and arthralgia. The next day he noted retrobulbar pain, initially in the left eye but progressing to involve the right eye. He then developed bilateral periorbital swelling. A clinical diagnosis of orbital inflammation was made, and computed tomography of the orbits with iodinated contrast revealed no gross abnormalities. Oral prednisone (80 mg/d) was prescribed, and the symptoms rapidly abated. The patient was seen at a referral visit 3 weeks later, by which time his prednisone dose had been tapered to 30 mg/d. He was pain free, and his examination results were normal. Review of his computed tomographic scan results confirmed the absence of mass orbital lesions. The patient was instructed to continue his prednisone taper and forego further treatment with pamidronate.

Comment. In early clinical trials of pamidronate and in postmarketing reviews, ocular adverse effects including conjunctivitis, anterior uveitis, episcleritis, and scleritis were infrequently noted within 1 to 6 days of administration. Orbital inflammation has been reported in a patient who received pamidronate 24 hours previously for Paget disease of bone. In this case, initial antibiotic therapy for presumed infectious orbital cellulitis produced no response, and significant visual deterioration ensued. Subsequent use of systemic corticosteroids allowed a prompt and complete recovery.

Animal studies performed prior to human clinical trials showed ocular adverse effects including conjunctivitis and episcleral congestion in rabbits after daily intravenous treatment for 6 months with 30 mg/kg of pamidronate sodium, a dose more than 100-fold greater than that used therapeutically. The symptoms remitted if treatment was withheld for several weeks or if the dose was reduced by 75%. There are no reports of posterior segment or orbital inflammatory disease in any of the animal models studied.

Although it has been suggested that the secretion of pamidronate into tears may cause conjunctivitis, the mechanism by which inflammation affects other ocular structures remains unknown. Treatment with bisphosphonates is known to trigger the release of cytokines interleukin 1 and interleukin 6 along with other acute-phase proteins. No specific localization of these factors to the eye or orbit has been reported. A few patients in previous case reports of orbital inflammatory disease had transient fever prior to the onset of symptoms, but most affected patients did not. In patients with Paget disease of bone, pamidronate treatment is given for longer periods at higher doses and may heighten sensitivity to the drug. It has been proposed that patients with other diseases, particularly malignancies, are less likely to develop autoimmune-related adverse effects owing to a general down-regulation of cytokine production. Harboring a malignancy is considered a relatively immunocompromised state, which might be protective for ocular inflammatory disease. Both of our pa-