Foundation of the Retina Society, Cape Town, South Africa (Dr C. L. Shields); Mellon Charitable Giving from the Martha W. Rogers Charitable Trust, Philadelphia, Pennsylvania (Dr C. L. Shields); the LuEsther Mertz Retina Research Foundation, New York, New York (Dr C. L. Shields); a donation from Michael, Bruce, and Ellen Rater, New York (Drs C. L. Shields and J. A. Shields); the Eye Tumor Research Foundation, Philadelphia (Drs C. L. Shields and J. A. Shields); and the Paul Kayser International Award of Merit in Retina Research, Houston, Texas (Dr J. A. Shields).


Orbital Inflammatory Disease After Intravenous Infusion of Zoledronate for Treatment of Metastatic Renal Cell Carcinoma

Zoledronate, a bisphosphonate, is an inhibitor of osteoclastic bone resorption, indicated for treatment of osteolytic bone lesions from multiple myeloma and other solid tumors. The most common adverse effect of zoledronate is a transient flu-like syndrome. Ocular adverse effects of bisphosphonates include conjunctivitis, uveitis, episcleritis, and scleritis. Cases of orbital inflammatory disease have been reported after treatment with another bisphosphonate, pamidronate. There have been no reported cases of orbital inflammatory disease after treatment with zoledronate. We describe a case of a man developing orbital inflammation after intravenous treatment with zoledronate for bone-involving metastases from renal cell carcinoma.
Report of a Case. A 55-year-old white man with bone metastases from renal cell carcinoma developed a transient fever (temperature, ≤ 38°C) with scleral injection in both eyes, more in the left eye than the right, one day following an infusion of 4 mg of zoledronate. By day 6, he noted the onset of significant periocular pain and edema in his left eye with diplopia. Visual acuity was 20/20 OU. Visual fields were full.

Upper and lower lids were edematous with prolated chemosis, ptosis, and significant proptosis in his left eye. Extraocular movement was restricted in all left-eye gazes, greatest in the elevated gaze (Figure 1). There was no afferent pupillary defect. Mild cell and flare were present in the anterior chamber of the left eye. The fundus examination results were normal. A computed tomography scan demonstrated diffuse nonspecific inflammation with a focus involving the superior orbit surrounding the superior rectus muscle (Figure 2). We diagnosed orbital inflammatory disease in the patient.

Treatment with 60 mg of oral prednisone lead to rapid clinical resolution of symptoms (Figure 1). The prednisone treatment was tapered during 10 weeks. Monthly treatments with zoledronate were continued. There were no recurrences of orbital inflammation.

Comment. Orbital inflammation has been reported in 3 patients treated with pamidronate.2,3 In all cases, the patients experienced complete recovery after withdrawal of treatment and initiation of oral steroids. The more common ocular adverse effects (scleritis, conjunctivitis) generally resolve once the bisphosphonate is discontinued, but may recur following rechallenge.4 No rechallenge occurred in these previous reports of orbital inflammation. The close temporal relationship of the infusion of zoledronate and the occurrence of orbital inflammation in our patient agrees with prior reports of orbital inflammation following bisphosphonate therapy.2,3 The demonstration that a rechallenge does not necessarily lead to a recurrence of disease when treated with steroids implies that orbital inflammation following treatment with zoledronate may not contraindicate the continued use of this quality of life–improving medication.

Bisphosphonates activate antigenic receptor T cells, whose activation releases cytokines. This may contribute to an immunologic or toxic ocular reaction in some patients. The T-cell rise occurring after treatment with bisphosphonates is less pronounced with each.

Figure 1. Nine cardinal positions of gaze. A, At presentation, the right eye is proptotic and chemotic with decreased motility in all directions, most notably in elevation and adduction. B, At day 3 after treatment with 60 mg of oral prednisone, the proptosis and chemosis have resolved with normal motility.

Figure 2. Computed tomography scan of the orbits. A, Coronal section demonstrating diffuse edema nasally and superiorly involving the extraocular muscles and displacing the globe anteriorly and inferiorly. B, Axial section demonstrating edema with noticeable thickening of the sclera consistent with scleritis.
successive treatment. This may explain the lack of recurrence of orbital inflammation on successive treatments in our patient. Clearly, immune suppression with steroids aids in the resolution of orbital inflammation. Additional experience with rechallenge of bisphosphonate therapy following steroid treatment of orbital inflammation will help clarify the likelihood of successful retreatment.

Paul M. Phillips, MD
Steven A. Newman, MD

Correspondence: Dr Phillips, PO Box 800715, Charlottesville, VA 22908-0715 (paulphillipsmd@gmail.com).

Financial Disclosure: None reported.


Archives Web Quiz Winner

Congratulations to the winner of our August quiz, Salem Abdulkareem Basar, Riyadh, Saudi Arabia. The correct answer to our August challenge was metastatic cutaneous melanoma. For a complete discussion of this case, see the Photo Essay section in the September Archives (Khurana RN, Tran VT, Rao NA. Metastatic cutaneous melanoma involving the retina and vitreous. Arch Ophthalmol. 2007;125[9]:1296-1297).

Be sure to visit the Archives of Ophthalmology Web site (http://www.archophthalmol.com) and try your hand at our Clinical Challenge Interactive Quiz. We invite visitors to make a diagnosis based on selected information from a case report or other feature scheduled to be published in the following month’s print edition of the Archives. The first visitor to e-mail our Web editors with the correct answer will be recognized in the print journal and on our Web site and will also be able to choose one of the following books published by AMA Press: Clinical Eye Atlas, Clinical Retina, or Users’ Guides to the Medical Literature.