Zoledronic acid-induced orbital inflammation

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DESCRIPTION

A 62-year-old man was referred for left eye redness and pain from the emergency department. He had a medical history of metastatic castrate-sensitive prostate cancer, Gleason 9, with diffuse skeletal and pulmonary metastases diagnosed 1 year prior to presentation. He received androgen deprivation therapy and a course of palliative radiation to T10, ribs and right femur. He was started on chemotherapy with docetaxel, which was completed 1 month prior to presentation. He also had type 2 diabetes mellitus, dyslipidaemia and atherosclerotic disease with an infrarenal abdominal aortic aneurysm. Medications included metformin, rosuvastatin and tamsulosin. He underwent his first infusion of zoledronic acid 3 days prior to presentation to the emergency room with left eye redness, periorbital discomfort and pain with eye movements. He was also sensitive to light and had mild blurred vision. His visual acuity was found to be 20/20 in both eyes, pupils were equal and reactive to light and there was no relative afferent pupillary defect. External examination revealed mild left ptosis, significant conjunctival injection and chemosis, and a mild diffuse limitation of eye movements in all directions in the left eye (figure 1A and B). There was 2 mm of left proptosis. CT orbits with contrast was performed and he was found to have fat stranding surrounding the posterior sclera and within the orbital fat. The most likely diagnosis was zoledronic acid-associated orbital inflammation and he was treated with prednisone 1 mg/kg and his symptoms promptly resolved within a few days. He was seen in follow-up 1 week later and his ocular symptoms resolved, he had no conjunctival injection and his ocular motility was normal. Zoledronic acid was discontinued.

Orbital inflammation is an increasingly recognised condition arising from the use of bisphosphonates, such as zoledronic acid. Previously, there have been a total of 28 reports of zoledronic acid-induced orbital inflammation and 39 reports of any bisphosphonate-induced orbital inflammation.^{1–27} Indications for bisphosphonate use included osteoporosis, Paget's disease and metastatic cancer with 8, 2 and 20 cases of orbital inflammation reported for each, respectively. Hence, the association between bisphosphonate use and orbital inflammation should be recognised by those providing the medication, ophthalmologists and emergency physicians. As was the case for our patient, orbital inflammatory disease typically presents with symptoms, such as pain and pain with eye movements, redness, diplopia and blurred vision.

Figure 1 (A) External photographs at presentation showing mild left ptosis and a mild diffuse limitation of eye movements in all directions, and conjunctival injection and chemosis. (B) One week after initiating corticosteroids, the patient had complete resolution of signs and symptoms.

The mechanism of bisphosphonate-induced orbital inflammation includes activation of gamma delta T-cells that initiate an acute inflammatory response in extraocular muscles and release of acute-phase reactants and cytokines, such as interleukin-1 and interleukin-6.^{19 28} In most cases, disease presentation was within 72 hours of medication administration when given intravenously and within 2 weeks when given orally.^{1–27} All patients in previous reports were treated with corticosteroids and showed good response. In most cases, bisphosphonate use was discontinued; however, rechallenge was observed in one case and led to no recurrence.² Treatment, therefore, should consist of corticosteroids with further exploration into the need to discontinue the medication. Physicians should be aware of the association between bisphosphonates and inflammatory ocular disease.

Learning points

- ▶ There is an association between bisphosphonate use and orbital inflammation. It is important to recognise signs, such as blurred vision, pain, pain with eye movements and eye redness.
- ▶ Our study supports the use of corticosteroids to completely resolve symptoms. Physicians should then carefully consider the risks and benefits of continuing the medication further.

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Correction: *Zoledronic acid-induced orbital inflammation*

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This article was previously published with errors in authorship. Please see below changes: Dan DeAngelis and Patrick Daigle are added prior to author Jonathan Andrew Micieli. They are affiliated to the Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, Canada.

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