Bilateral Acute Anterior Uveitis and Conjunctivitis following Intravenous Zoledronic Acid

Samrat Chatterjee1, Deepshikha Agrawal1

Abstract

The ocular side-effects of bisphosphonates have the potential to escalate with their widespread use. We report a patient of osteoporosis who was treated with zoledronic acid infusion. He developed ocular pain, redness, watering, photophobia and swelling of both the eyes. He was diagnosed with acute anterior uveitis and conjunctivitis and treated with topical 1% prednisolone acetate and 1% atropine sulphate. The signs of inflammation abated by one week and the steroids were tapered over the next six weeks. There were no further recurrences. Patients must be educated about the ocular side-effects of bisphosphonate therapy, monitored closely after intravenous infusion and advised to seek ophthalmic consultation promptly if any ocular symptoms or signs develop.

Introduction

Bisphosphonates are widely used in the treatment of hypercalcemia and osteoporosis. They have been reported to cause adverse ocular inflammation like conjunctivitis,1 episcleritis/scleritis,2 anterior uveitis,1-4 orbital inflammation,2 and optic neuritis or other cranial nerve palsies.2 These manifestations are part of an acute phase reaction mediated by peripheral blood γδ T cells which cause release of pro-inflammatory cytokines like interleukin-6 and tumor necrosis factor.5 However the low incidence of such complications4,5 means that a physician or an ophthalmologist may infrequently encounter such an event. Thereby these patients pose a diagnostic and therapeutic challenge. We report a patient with bilateral conjunctivitis and anterior uveitis following treatment with zoledronic acid, a potent bisphosphonate, for osteoporosis secondary to prostate malignancy.

Case Report

A 70-year old man had been diagnosed to have high risk adenocarcinoma of the prostate in 2012. He underwent bilateral orchiectomy and radiotherapy at a distant tertiary cancer treatment facility. In December 2015, he was diagnosed with osteoporosis when he complained of low back ache and was advised yearly zoledronic acid. The first dose was given at the time of diagnosis as an infusion of 4 mg in 100 ml of normal saline. Following administration of the drug he was discharged the same day. Next day during his return journey, he experienced flu-like symptoms and mild pain in both the eyes which progressed in quick succession to swelling, redness, watering and blurring of vision. At presentation two days later, his flu-like symptoms had subsided but he was in pain and anxious. His vision in both the eyes was 20/64, N12 and this was not improving with refraction. The ocular movements were full and pupillary reaction normal. The lids of both the eyes were edematous with diffuse conjunctival injection and chemosis (Figures 1A and B). There was no inflammation but fresh keratic precipitates were observed on the corneal endothelium in both the eyes. There was anterior chamber reaction in the right eye and fibrinous reaction in the anterior chamber without hypopyon in the left eye (Figures 1C and D). There was early nuclear sclerosis in lens of both the eyes with brown iris pigments on...
the surface. Intra-ocular pressure was 18 mm Hg in both eyes. The fundus examination was normal without any vitreous cells.

A diagnosis of acute non-granulomatous anterior uveitis with conjunctivitis in both the eyes was made. He was treated with topical 1% prednisolone acetate two hourly and 1% atropine sulphate three times daily. After a week the symptoms had subsided and his best corrected visual acuity improved to 20/20, N6 in both the eyes. The inflammation in the conjunctiva and anterior chamber had subsided (Figure 2). The topical steroid was tapered over six weeks and the atropine discontinued. There were no further recurrences.

Discussion

The incidence of uveitis following intravenous zoledronic acid is faster compared to oral administration, the former occurring within the first week, with a median of three days, while in the latter it is delayed by several days to months.3 In our patient the onset was within two days after infusion similar to what is seen in an acute phase reaction.5,6 Our patient had been discharged the same day of receiving the infusion and as the journey there was a delay in his seeking medical advice, resulting in significant worsening of conjunctivitis and uveitis.

The conjunctivitis and uveitis caused by bisphosphonate are nonspecific and the uveitis may be unilateral or bilateral and range from mild to severe with tendency to form posterior synechiae.1,3 The presence of pigments on the lens surface in our patients indicate the onset of posterior synechiae formation (Figures 2C and D). As both these entities present without characteristic features, etiological diagnosis depends on a carefully elicited drug history.

Bisphosphonate induced uveitis is treated with topical corticosteroids and cycloplegic drugs.1,3,4,6 Oral bisphosphonates need to be discontinued. Due to contrarian reports in literature it is unclear at present whether re-treatment with the same or an alternate bisphosphonate, would result in recurrence of ocular side-effects. Fraunfelder et al reported the recurrence of scleritis in the same eye of five patients, who were re-treated with the bisphosphonate pamidronate,2 while Patel et al did not observe any recurrence in three patients re-challenged with multiple infusions of zoledronic acid 18 months apart without any prophylactic topical corticosteroid.6

Patients treated with intravenous formulations need close observation during the first week. Treatment is usually uneventful with topical corticosteroids and cycloplegics although there are differing opinions about re-treatment with bisphosphonates in patients who experience ocular adverse effects.

Conclusion

Ophthalmologists need to be sensitized to bisphosphonate induced uveitis as the drug is extensively prescribed. The diagnosis of bisphosphonate induced uveitis requires careful history taking. The physician needs to inform patients on bisphosphonates about ocular adverse effects and seek ophthalmic consultation promptly.

References