

Zoledronic acid induced unilateral anterior uveitis

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Zoledronic acid is recommended for patients with osteoporosis. To report a case of unilateral anterior uveitis after zoledronate infusion. An osteoporotic patient presented with pain, visual loss, hyperemia, photophobia, and watering from the left eye after zoledronate infusion. Circumcorneal injection, keratic precipitates, cells, and flare suggested anterior uveitis. Her symptoms resolved completely after 20 days of prednisolone acetate with atropine eye drops. Uveitis is a rare complication of zoledronic acid with an unclear mechanism. Proinflammatory cytokines may play a role in pathogenesis. Zoledronic acid may be associated with rare but serious inflammatory ocular adverse drug reactions.

Key words: Osteoporosis, uveitis, zoledronic acid

The bisphosphonates exert multiple effects on bone mineral homeostasis, which make them useful for the treatment of hypercalcemia associated with malignancy, for Paget's disease, and for osteoporosis.^[1] They owe at least part of their clinical usefulness and toxicity to their ability to retard the formation and dissolution of hydroxyapatite crystals within and outside the skeletal system. Some of the newer bisphosphonates appear to increase bone mineral density well beyond the 2-year period predicted for a drug whose effects are limited to slowing bone resorption. With the exception of the induction of a mineralization defect by higher than approved doses of etidronate and gastric and esophageal irritation by the oral bisphosphonates, these drugs have proved to be remarkably free of adverse effects when used at the doses recommended for the treatment of osteoporosis. Esophageal irritation can be minimized by taking the drug with a full glass of water and remaining upright for 30 minutes or by using the intravenous forms of these compounds. The initial infusion of zoledronate is commonly associated with several days of a flu-like syndrome that generally does not recur with subsequent infusions.^[1] Zoledronic acid (Zoledronate) is the most potent bisphosphonate. It is generally well tolerated.

Hypocalcemia is the most common side effect of zoledronic acid. The other frequently reported adverse events include bone pain, emesis, constipation, headache, fluctuations in serum electrolyte (magnesium, calcium, and phosphorus) levels, elevation in serum creatinine, osteonecrosis of the jaw (ONJ), and transient flu-like symptoms such as nausea, myalgia, arthralgia, and low-grade fever. In English literature, serious ocular side effects after the administration of zoledronic acid have been reported in only a few articles.^[2] Here, we present a case of unilateral anterior uveitis associated with a single infusion of zoledronic acid.

Case Report

A 66-year-old woman with osteoporosis came for her first zoledronic acid infusion. Her past history was negative for any ocular disease and allergy. She had no history of any co-morbid disease. After 72 hours of the zoledronic acid injection, she developed her symptoms. She did not use any concomitant drug. She came to the eye outpatient department (OPD) 2 days post-development of her symptoms. On ocular examination, there was unilateral conjunctival suffusion. Her best-corrected visual acuity was 20/30 and 20/120 for right and left eye, respectively. Her intraocular pressure (IOP) was 12 and 7 mm Hg for right and left eye, respectively. There was circumciliary congestion in the left eye and pain during the movement of the left eyeball. Biomicroscopic anterior segment examination showed 3+ anterior segment cells with flare, the anterior chamber had fibrinous exudate, fresh keratic precipitates were observed in the whole of the cornea, but no vitreous inflammation was observed [Fig. 1]. The ocular examination of the right eye was normal. The dilated retinal examination was bilaterally normal. Laboratory evaluation including serum chemistries and complete blood count was unremarkable. A diagnosis of acute anterior uveitis secondary to zoledronic acid was made and she was treated with topical prednisolone e/d (1%) 8 times and atropine e/d 3 times after which there was a prompt resolution of all symptoms on her second follow-up visit after 7 days with only 1+ aqueous cells [Fig. 2]. She was continued on the same for five weeks on a tapering basis. She received no further doses of zoledronic acid. Her condition resolved completely in 20 days with best-corrected visual acuity of left eye recorded as 6/9.

Discussion

Till to date, a number of ocular side effects including conjunctivitis, ocular pain, scleritis, photophobia, episcleritis, blurred vision, and uveitis have been reported for different bisphosphonates including alendronate, pamidronate, etidronate, and risedronate.^[2,3] Zoledronic acid is the most widely used bisphosphonate for metastatic bone disease

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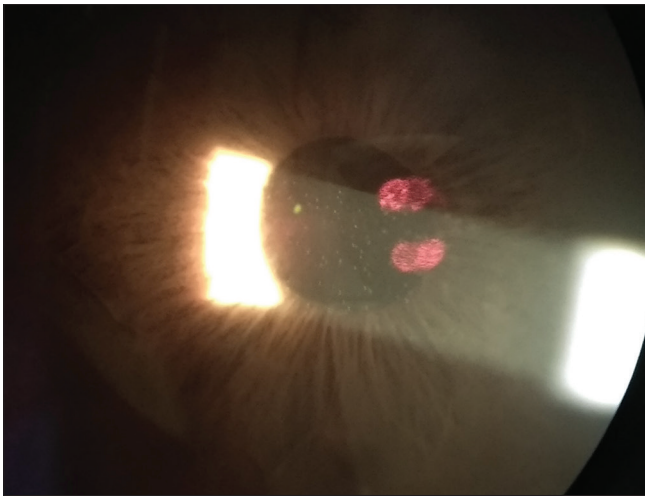


Figure 1: Day-1 - OS 3+ cells on examination with circumciliary congestion

and osteoporosis because of its relatively higher potency and short infusion time. It binds to the hydroxyapatite and accumulates in the bone, thus inhibiting osteoclast migration and maturation. Side effects of zoledronic acid are usually mild, which include a syndrome similar to flu; consisting of fever, chills, bone pain, and arthralgias. Ocular complications such as severe acute anterior uveitis, episcleritis, scleritis, and orbital inflammation requiring topical and at times even systemic steroid therapy, have been reported as a complication of pamidronate (another bisphosphonate), but only rarely with zoledronic acid.^[4,5] Non-infectious uveitis is usually initiated by an inflammatory stimulus in which cytokines play a central role. Inflammatory ocular diseases including uveitis are thought to have an imbalance among proinflammatory cytokines such as tumor necrosis factor- α (TNF- α), interferon- γ (IFN- γ), interleukin-1 (IL-1), and interleukin-6 (IL-6), which regulate the immune system to maintain the inflammatory response.^[5] Uveitis has also been characterized by a CD4(+) T-helper 1 cells-mediated inflammation with elevations in IL-2, IFN- α , and lymphotoxin, and has a distinctive cytokine pattern of IL-6, IL-8, IL-13, TNF- α , and IL-2 in aqueous humor.^[5] Four cases of open unilateral and bilateral anterior uveitis post zoledronic acid infusion have been reported.^[3,6-8] It has been suggested that secretions of bisphosphonates into tears can cause conjunctivitis and other ocular inflammations. Bisphosphonates also secrete interleukins resulting in inflammatory responses in the eye.

Conclusion

The close relationship between zoledronic acid infusion and onset of ocular signs and symptoms in our case is in accordance with bisphosphonates-related ocular inflammation. On withdrawing the bisphosphonates and starting steroids therapy on time gave a positive result. This supports drug-related etiology for this ocular process. Patient receiving bisphosphonate infusion should be explained the need to visit ophthalmologists post infusion related any eye symptom.



Figure 2: Day-7 - OS 1+ cells on examination

To the best of our knowledge, this is the first case report of zoledronate-induced unilateral uveitis being reported from the Andamans and India.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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