International Surgery Journal
Aishwaraya K et al. Int Surg J. 2025 Feb;12(2):240-242
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: https://dx.doi.org/10.18203/2349-2902.isj20250156

Case Report

A case report of zoledronic acid-induced bilateral conjunctivitis

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Received: 28 November 2024
Accepted: 14 January 2025

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ABSTRACT

Zoledronic acid is used to treat patients with osteoporosis, Paget's disease, multiple myeloma, and several bone tumors. This is to report a case of a patient with cervical spondylosis with periorbital swelling, watering, diminution of vision, and redness in both eyes after zoledronate infusion. The patient had lid edema and conjunctival congestion in both eyes. Symptoms resolved after 10 days of fluorometholone eye drops. Bilateral conjunctivitis is a rare complication of zoledronic acid. Zoledronic acid causes T-cell activation leading to the release of cytokines and inflammatory mediators. Orbital inflammation, scleritis, and acute anterior uveitis have also been reported as side effects of zoledronic acid

Keywords: Zolendronate, Conjunctivitis, Fuorometholone

INTRODUCTION

Zoledronate, also known as zoledronic acid, is a nitrogen-containing bisphosphonate. Bisphosphonates are indicated for osteoporosis, hypercalcemia of malignancy, Paget's disease of bone, multiple myeloma, and metastatic bone cancer from solid tumors.[1] Second and third-generation bisphosphonates (alendronate, risedronate, pamidronate, and zoledronic acid) have nitrogen-containing R^2 side chains. Nitrogen-containing bisphosphonates bind to and inhibit the activity of farnesyl pyrophosphate synthase, a key regulator in the mevalonic acid pathway critical to the production of cholesterol and isoprenoid lipids. Cellular apoptosis induced by nitrogen-containing bisphosphonates appears to occur only in osteoclasts. Clinical concerns associated with bisphosphonate therapy include osteonecrosis of the jaw, over-suppression of bone turnover, hypocalcemia, and severe musculoskeletal pain.[3] Oesophageal irritation and erosion can occur with oral bisphosphonate therapy. Ocular adverse effects like scleritis, conjunctivitis, acute anterior uveitis, and orbital inflammation have been reported.[4] Here, we report a case of bilateral conjunctivitis following zoledronic acid infusion.

CASE REPORT

A 60-year-old female presented with a diminution of vision, periorbital swelling, and watering in both eyes since morning. She is a known case of cervical spondylosis. She received her first zoledronic acid infusion 1 day back. The onset of symptoms was 18 hrs post-infusion. She had no history of any co-morbid disease. No previous history of ocular disease and allergy. There was no history of use of any other drug.

On examination, the patient had bilateral lid edema and conjunctival congestion (Figure 1). Her best corrected visual acuity was 6/12 in both eyes. Intra-ocular pressure was 11 and 13 mm in the right and left eye, respectively. Fundus examination was normal in both eyes. Complete blood count and serum electrolytes were unremarkable. A diagnosis of zoledronic acid-induced bilateral conjunctivitis was made, and she was started on fluorometholone eye drops four times a day. She did not receive further doses of zoledronic acid. Symptoms and signs resolved over the next 10 days, and her vision improved to 6/9 in both eyes (Figure 2).

Figure 1: Before treatment.

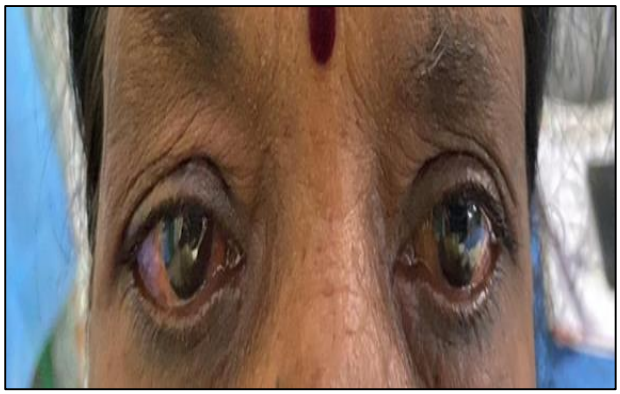

Figure 2: After treatment.

DISCUSSION

A number of ocular side effects, including conjunctivitis, scleritis, episcleritis, uveitis, orbital inflammation, and anterior ischemic optic neuropathy, have been reported from different bisphosphonates, including pamidronate, risedronate, alendronate, and etidronate.[4] Bilateral idiopathic orbital inflammatory syndrome (IOIS) has also been reported, whereas IOIS usually presents unilaterally.[5] Approximately 10% to 30% of patients experience an acute phase reaction, most commonly transient pyrexia with influenza-like symptoms. This percentage decreases with each subsequent infusion.[6]

Zoledronate has been shown to induce systemic M1macrophage polarization both in vivo and in vitro. The γδ T-cell activation through inhibition of farnesyl pyrophosphate synthase and subsequent intracellular accumulation of isopentenyl diphosphate (IPP) and dimethylallyl diphosphate (DMAPP) leads to the release of cytokines and inflammatory mediators that lead to the acute phase reaction.[2] It has been suggested that the secretion of bisphosphonates into tears may cause conjunctivitis. They also trigger the release of cytokines, interleukin 1 and interleukin 6, and other acute-phase proteins mediating ocular inflammation.[7] These cytokines can cause extraocular muscle inflammation, leading to orbital inflammation disease.[8] Zoledronic acid-induced inflammation can be unilateral or bilateral. Some patients experience symptoms like fever, 25(OH)D <30 ng/mL, and a higher risk of acute phase reaction. The ocular inflammation may even deteriorate if not treated promptly. Conjunctivitis and anterior uveitis can be treated with topical steroids in a tapering manner. If the signs and symptoms are severe or not relieved by topical steroids, systemic oral steroids can be started. Zoledronate was most reported to be associated with orbital inflammation. Bisphosphonate-induced orbital inflammation usually requires oral steroids; the close and clear chronological relationship between zoledronate administration and the onset of ocular symptoms is in line with bisphosphonate-induced ocular inflammations.

CONCLUSION

Thus, a reasonable temporal association of symptom onset and drug exposure is critical in suspecting the diagnosis. The indications for bisphosphonate therapy are increasing and span several medical subspecialty areas. Patients experiencing adverse effects need not entirely avoid the bisphosphonates. They may experience milder symptoms with further exposure. Due to the serious nature of the indications of bisphosphonates usage, the drug can be continued despite ocular adverse effects, but timely recognition of the adverse effect is significant. All physicians must understand the relationship of ocular side effects to bisphosphonate usage. Patients need to be explained regarding the possible ocular side effects and the need to consult an ophthalmologist if symptoms arise. Delayed treatment may affect the prognosis and response to treatment. Prompt diagnosis of various presentations of ocular side effects of bisphosphonates is vital for the timely administration of steroids.

ACKNOWLEDGEMENTS

Authors would like to thank to Dr. Theakarajan, Gastrosurgeon.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Aishwaraya K, Suresh K, Saravanan R, Kannan M. A case report of zoledronic acid-induced bilateral conjunctivitis. Int Surg J 2025;12:240-2.