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## Case Report

# Zoledronic acid induced uveitis in multiple myeloma - A case report

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### ABSTRACT

This is the case report of a 67-year-old lady who was diagnosed to have Multiple Myeloma and was given injection Zoledronic acid and developed Anterior Uveitis in both eyes. Uveitis was cured completely with topical steroids and she did not have any recurrence, even though injection Zoledronic acid was continued for one year. This shows that even if the patient develops ocular inflammation with the first dose, the treatment can be continued with monitoring after discussing the risks and benefits with the patient, since the patient can develop tolerance with each infusion.

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## 1. Introduction

Multiple myeloma is a plasma cell disorder representing approximately 10%–13% of hematological cancers. Bisphosphonates prevent, reduce, and delay multiple myeloma related skeletal complications.<sup>1</sup> The present case report is that of a patient who developed uveitis following bisphosphonate use and later developed tolerance to the drug.

## 2. Case Report

A 67-year-old lady who was diagnosed to have Multiple Myeloma was started on chemotherapy with Bortezomib, Lenalidomide and Dexamethasone and was given injection Zoledronic acid 4mg intravenous infusion. She started having pain and redness in both eyes on the next day. There was no significant past history of any systemic or ocular illness. On examination, best corrected visual acuity was 6/6 in both eyes. She had medium sized keratic precipitates, fibrinous reaction in the anterior chamber and posterior synechiae in both eyes. Fundus examination was normal.

She was diagnosed to have Acute Nongranulomatous Anterior Uveitis in both eyes and was treated with topical steroids and cycloplegics. She was prescribed Difluprednate 0.05% eye drops 4 times daily for one week in both eyes which was tapered and stopped over six weeks. Homatropine 2% eye drops was given three times daily for two weeks in both eyes. Uveitis was cured completely. Injection Zoledronic acid 4 mg intravenous infusion was continued with the patient's consent every month for one year. She did not have any recurrence of uveitis. She did not develop any systemic side effects of Zoledronic acid. She had two episodes of mild episcleritis, which was treated with nonsteroidal anti inflammatory eye drops (Ketorolac 0.4% eye drops, four times daily for one week).

## 3. Discussion

The cause of Uveitis in this patient was presumed to be caused by Zoledronic acid.

Cases of ocular inflammation in patients taking bisphosphonates have been reported since the early 1990s.<sup>1</sup> Cases have involved both nitrogen and non-nitrogen-containing bisphosphonates (including alendronate, etidronate, risedronate, clodronate,

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pamidronate, and zoledronic acid). Ocular complications have been reported only rarely with zoledronic acid.<sup>2–4</sup> The side effects reported are conjunctivitis, scleritis, episcleritis, iritis, keratitis, uveitis and orbital inflammation as major side effects, and eye dryness and red eye, edema and ptosis as minor side effects.

Etmnan et al<sup>5</sup> has found that first-time users of bisphosphonates are at an increased risk of scleritis and uveitis. They found that uveitis occurred in 0.29% of people using bisphosphonates for the first time. Patel et al<sup>6</sup> found that eight of 1001 subjects receiving zoledronate (0.8%) exhibited mild to severe Acute Anterior Uveitis within seven days of treatment.

Our patient developed uveitis on the next day after receiving injection Zoledronic acid for the first time.

It has been suggested that the secretion of bisphosphonates into tears may cause conjunctivitis; however, bisphosphonates also trigger the release of cytokines, interleukin 1, and interleukin 6, along with other acute-phase proteins mediating ocular inflammation.<sup>7</sup>

Zoledronate rechallenge has been reported previously, suggesting that with continued dosing patients can develop tolerance, so that the inflammatory reaction decreases in intensity.<sup>8</sup> This explains why our patient did not have recurrence of uveitis even after continuing injection Zoledronic acid every month and why she developed few episodes of ocular inflammation in the form of mild episcleritis.

The ocular complications which have been reported with bortezomib use are blepharitis, meibomitis and chalazion<sup>9–11</sup> and with lenalidomide, cytomegalo virus retinitis.<sup>12</sup>

The diagnosis of medication-induced-uveitis by Zoledronic acid was given in our case by the nature and time correlated event described in the literature and by the exclusion of other origins. Prompt responsiveness to the treatment and complete resolution of the inflammation resulted, further arguing for confirming the diagnosis.

According to the guidelines suggested by Fraunfelder et al<sup>13</sup> for uveitis associated with bisphosphonate use, the drug may need to be discontinued only in some instances for the uveitis to resolve.

So, the possibility of ocular inflammation in patients receiving bisphosphonates should be kept in mind and all patients receiving bisphosphonates who develop ocular signs and symptoms should be promptly seen by an ophthalmologist. Even if the patient develops ocular inflammation with the first dose, the treatment can be continued with monitoring after discussing the risks and

benefits with the patient, since the patient can develop tolerance with each infusion.

#### 4. Source of Funding

None.

#### 5. Conflict of Interest

The authors declare no conflict of interest.

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