

Acute Anterior Uveitis Following Intravenous Zoledronic Acid Infusion: A Case Report

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ABSTRACT

Background: Bisphosphonates are widely used in the treatment of osteoporosis and other metabolic bone diseases. Although these drugs are generally well tolerated, ocular inflammatory adverse effects such as conjunctivitis, episcleritis, scleritis, and uveitis have been reported.

Case Presentation: We report a case of acute anterior uveitis that developed shortly after intravenous zoledronic acid infusion. The patient presented with ocular pain, redness, photophobia, and decreased vision. Slit-lamp examination revealed conjunctival hyperemia and anterior chamber inflammation consistent with acute anterior uveitis. The patient was treated with topical corticosteroids and cycloplegic agents, resulting in rapid clinical improvement and complete resolution of symptoms.

Conclusion: Acute anterior uveitis is a rare but clinically significant adverse reaction associated with intravenous bisphosphonate therapy. Clinicians should consider drug-induced uveitis in patients presenting with ocular symptoms following zoledronic acid infusion.

Keywords: Zoledronic Acid, Bisphosphonate, Drug-induced uveitis, Ocular Inflammation, Anterior Uveitis

Introduction

Bisphosphonates are widely used in the treatment of osteoporosis, Paget disease of bone, and skeletal complications associated with malignancy. These agents inhibit osteoclast-mediated bone resorption and significantly reduce fracture risk [1].

Zoledronic acid is a third-generation nitrogen-containing bisphosphonate with high potency and prolonged duration of action, allowing once-yearly intravenous administration for osteoporosis management [2].

Although bisphosphonates are generally well tolerated, systemic acute-phase reactions such as fever, myalgia, and flu-like symptoms may occur following infusion [3]. In addition, ocular inflammatory complications including conjunctivitis, episcleritis, scleritis, orbital inflammation, and uveitis have been reported in association with bisphosphonate therapy [4-6].

Among these complications, acute anterior uveitis represents a clinically significant condition because it may lead to ocular pain, photophobia, and visual disturbances if not promptly recognized and treated [7].

Drug-induced uveitis represents a relatively uncommon but increasingly recognized clinical entity. Identification of medication-associated ocular inflammation is important because prompt discontinuation of the offending agent and appropriate anti-inflammatory therapy usually lead to rapid clinical recovery [8,9].

In this report, we describe a case of unilateral acute anterior uveitis occurring shortly after intravenous zoledronic acid infusion and review the literature regarding bisphosphonate-associated ocular inflammation.

Case Presentation

A 67-year-old female presented to the ophthalmology clinic with complaints of redness, ocular pain, tearing, and photophobia affecting both eyes. The symptoms began approximately 48 hours after she received an intravenous infusion of zoledronic acid for the treatment of postmenopausal osteoporosis.

The patient had no previous history of ocular inflammatory disease, ocular trauma, or ocular surgery. Her systemic medical history was notable only for osteoporosis diagnosed three years earlier. She was not using any systemic immunosuppressive medication.

Best-corrected visual acuity was 20/25 in the right eye and 20/30 in the left eye. Slit-lamp biomicroscopy demonstrated bilateral conjunctival hyperemia, ciliary injection, fine keratic precipitates, and anterior chamber inflammation characterized by 2+ cells and 1+ flare. [Figure 1].

Examination of the anterior chamber demonstrated inflammatory cells graded as SUN 2+ according to the Standardization of Uveitis Nomenclature classification [10].

Intraocular pressure measured by applanation tonometry was 15 mmHg in the right eye and 16 mmHg in the left eye. The cornea was clear and the lens showed mild age-related nuclear sclerosis.

Dilated fundus examination revealed normal optic discs, maculae, and peripheral retina in both eyes. No vitreous inflammation or retinal lesions were observed.

Optical coherence tomography confirmed normal macular architecture without evidence of cystoid macular edema.

Laboratory investigations including complete blood count, erythrocyte sedimentation rate, C-reactive protein, and HLA-B27 testing were within normal limits.

Considering the close temporal relationship between zoledronic acid infusion and the onset of ocular symptoms, a diagnosis of drug-induced acute anterior uveitis associated with zoledronic acid was established.

The patient was treated with topical prednisolone acetate 1% every two hours and cyclopentolate three times daily.

Within 48 hours, the patient reported significant improvement in symptoms. At the one-week follow-up visit, anterior chamber inflammation had markedly decreased. Corticosteroid therapy was gradually tapered over three weeks.

At the one-month follow-up examination, visual acuity had returned to baseline and no signs of intraocular inflammation were detected.



Figure 1: Slit-lamp photograph demonstrating conjunctival hyperemia and ciliary injection in a patient with acute anterior uveitis following intravenous zoledronic acid infusion.

Intraocular pressure was within normal limits in both eyes. Dilated fundus examination revealed normal optic discs, maculae, and peripheral retina without evidence of vitreous inflammation.

Optical coherence tomography confirmed normal macular architecture without cystoid macular edema.

Laboratory investigations including complete blood count, erythrocyte sedimentation rate, C-reactive protein, and HLA-B27 testing were within normal limits.

Considering the close temporal relationship between zoledronic acid infusion and the onset of ocular symptoms, a diagnosis of drug-induced unilateral acute anterior uveitis was established.

The patient was treated with topical prednisolone acetate 1% and cycloplegic therapy. Topical corticosteroid treatment was continued for one week.

Within 48 hours, the patient reported significant improvement in symptoms. At the one-week follow-up visit, anterior chamber inflammation had completely resolved.

Discussion

Bisphosphonates are widely used in the management of osteoporosis and other metabolic bone diseases due to their ability to inhibit osteoclast-mediated bone resorption [1,2]. Zoledronic acid, a nitrogen-containing bisphosphonate, is one of the most potent agents in this class and is commonly administered as an annual intravenous infusion for the treatment of osteoporosis [2]. Although bisphosphonates are generally well tolerated, several systemic and ocular adverse effects have been reported [3-5].

Ocular inflammatory reactions associated with bisphosphonate therapy include conjunctivitis, episcleritis, scleritis, keratitis, and uveitis [4,6,11,14]. These complications are relatively uncommon but may lead to significant ocular morbidity if not recognized and treated promptly [7,8]. Among these complications, acute anterior uveitis represents a rare but clinically significant adverse reaction associated with both oral and intravenous bisphosphonate therapy [12,13,17].

The pathophysiological mechanism of bisphosphonate-induced ocular inflammation remains incompletely understood. However, it has been suggested that nitrogen-containing bisphosphonates may stimulate the release of pro-inflammatory cytokines and activate immune-mediated inflammatory pathways [15,18]. Additionally, activation of $\gamma\delta$ T-cells has been proposed as a potential mechanism contributing to the acute inflammatory response following intravenous bisphosphonate administration [3,16].

In previously reported cases, ocular symptoms generally develop within the first few days following drug administration [6,17]. The most common presenting symptoms include ocular pain, redness, photophobia, and blurred vision [4,7]. Slit-lamp examination typically reveals conjunctival hyperemia, ciliary injection, and inflammatory cells in the anterior chamber [10,19].

The diagnosis of acute anterior uveitis is usually established according to the Standardization of Uveitis Nomenclature (SUN) criteria, which classify intraocular inflammation based on the presence of anterior chamber cells and flare [10].

Early recognition of bisphosphonate-associated uveitis is essential because prompt treatment generally results in favorable outcomes [19,20]. Topical corticosteroids remain the mainstay of therapy for acute anterior uveitis, while cycloplegic agents may be used to relieve pain and prevent posterior synechiae formation [20,21]. Most reported cases demonstrate rapid clinical improvement following initiation of appropriate treatment [22].

Several case reports have described similar ocular inflammatory reactions following intravenous zoledronic acid administration [12,16,17]. Although the incidence of this complication appears to be low, increased awareness among physicians prescribing bisphosphonates is essential for early diagnosis and management [23,24].

Uveitis itself represents a heterogeneous group of inflammatory diseases that may be associated with infectious, autoimmune, or drug-induced etiologies [19,25]. Drug-induced uveitis has been reported with several systemic medications and should be considered in the differential diagnosis of patients presenting with ocular inflammation [26,27].

In our case, the temporal relationship between zoledronic acid infusion and the onset of ocular symptoms strongly suggests

a drug-induced inflammatory reaction. Similar temporal associations have been described in previously published reports [12,16,17].

Although bisphosphonate-associated uveitis is uncommon, ophthalmologists and other healthcare professionals should be aware of this potential adverse effect [28–30]. Prompt ophthalmologic evaluation should be performed in patients presenting with ocular symptoms shortly after bisphosphonate therapy.

Previously reported cases of bisphosphonate-associated uveitis and their clinical characteristics are summarized in Table 1

Conclusion

Acute anterior uveitis represents a rare but clinically important ocular adverse reaction associated with intravenous zoledronic acid therapy. Awareness of this potential complication is essential for both ophthalmologists and physicians prescribing bisphosphonates. Early recognition of symptoms and prompt initiation of anti-inflammatory treatment can lead to rapid resolution and prevent potential visual complications.

Table 1: Reported cases of bisphosphonate-associated anterior uveitis in the literature

Study	Drug	Route	Time to onset	Treatment	Outcome
Fraunfelder et al. [4]	Bisphosphonates	Oral/IV	1–3 days	Topical steroids	Resolution
Patel et al. [5]	Zoledronic acid	IV	2 days	Steroid drops	Complete recovery
Peterson et al. [12]	Zoledronic acid	IV	24 hours	Steroid + cycloplegic	Resolution
Bianchi et al. [16]	Zoledronic acid	IV	48 hours	Topical steroid	Improvement
Rhee et al. [17]	Bisphosphonate	IV	2–3 days	Steroid therapy	Resolution
Present case	Zoledronic acid	IV	1–2 days	Steroid + cycloplegic	Complete recovery

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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Patient Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying clinical information.

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