Bilateral Anterior Uveitis following Zoledronic Acid therapy in Breast Cancer: a Case Report

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Keywords
Oncology; Medical Ophthalmology; Allergy

Introduction
Bisphosphonates are commonly used in the treatment of osteoporosis and metastatic bone disease. Their mechanism of action involves the inhibition of the osteoclast activity leading to the reduction of bone resorption [1]. Their activity reduces the incidence of skeletal complications, such as fractures, pains, and hypercalcemia. Nowadays among the different bisphosphonates Zoledronate is largely used because of its relative higher potency and short infusion time [2]. Zoledronate is usually well tolerated; well known side effects of zoledronate include, fatigue, fever, myalgia or arthralgia, nausea, bone pains, and elevation in serum creatinine [3]. Retrospective studies have reported an association between long-term bisphosphonate therapy and osteonecrosis of the jaw [4]. Ocular adverse events have been reported with nitrogen-containing bisphosphonates [5-7] with unclear underlying mechanisms. No ocular factors or predispositions are known. The inflammations could be explained with the release of elevated levels of cytokines, including tumor necrosis factor and interleukin-6 [8].

Case report
A 59-year-old woman with a carcinoma of the right breast and metastatic bone disease showed bilateral anterior uveitis following the first administration of zoledronic acid. She was diagnosed to have a right stage pT3 pN3 M0, hormone-positive, Her 2 negative breast cancer, in 2012. She was treated at first with lumpectomy, adjuvant chemotherapy with cyclophosphamide, epirubicin, 5-FU for 3 cycles every 3 weeks followed by docetaxel for 3 cycles every 3 weeks and subsequently with radical right mastectomy, hormonal adjuvant therapy with letrozole and local adjuvant radiotherapy. Due to progressive bone disease the patient was scheduled to have in fulvestrant 500 mg every 28 days and zoledronic acid (4 mg in 100 ml normal saline over 15 minute every 28 days). The patient did well throughout the injection and overnight. Three days after the infusion of zoledronic acid she developed ocular pain, decreased visual activity, edema of the lids and conjunctival hyperemia. Four days later an ophthalmological examination revealed bilateral acute uveitis of moderate severity, anterior segment flare was present, cells were present (Tyndall +++) . The intraocular pressure was 14 mmHg in the right eye and 17 mmHg in the left eye. The patient was treated with topical prednisone every six hours for six days and atropine eye drops, she recovered completely in two weeks.

Discussion
Bisphosphonates, in particular zoledronic acid, are widely used in malignant hypercalcemia or for the treatment of bone metastases, but mostly in osteoporosis and Page’s disease. Uveitis should be considered more and more as a possible
complication in the first course of zoledronic acid. Patients and physicians should be instructed to immediately refer eye complications, such as pain, inflammatory signs, or visual disorders, in order to perform an ophthalmologic examination and to start a specific therapy. The great dilemma is how to continue the treatment after an episode of uveitis. In most reported cases zoledronate was stopped; in one case uveitis associated with clodronate relapsed after the treatment with the same drug was re-challenged [9]. In another case; the therapy with Biphosphonates was replaced by a different drug of the same class with reduced inflammatory effects and that brought to the resolution of the problem, suggesting the development of immunological tolerance [10]. With this rationale, after the full recovery, bisphosphonate therapy was replaced with denosumab. After the first course and subsequent cycles neither uveitis nor other ocular toxicities of any kind were observed.

Acknowledgements
The staff at Oculistic Department, Pescia Hospital, participating in the care of the patient is gratefully acknowledged.

Conflicts of interest
No conflicts of interest
Funding
The study received no funding.

Ethical approval
The case has been presented based on hospital medical records and written by the physicians participating in the treatment of the patient. Therefore, no ethical committee approval was required.

Consent
An informed consent was obtained from the patient.

Guarantor
Barbara Salvadori and Alfredo Falcone are nominated as the guarantors and have full access to the data.

References


