Acute unilateral anterior uveitis and scleritis following a single infusion of zoledronate for metastatic breast cancer

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Clinical record

We report the case of a 54-year-old woman who presented with a painful and swollen left eye 3 days after receiving zoledronate.

The patient had been diagnosed with locally advanced breast cancer 3 years earlier. This was managed with four cycles of neoadjuvant chemotherapy (with adriamycin and cyclophosphamide) followed by breast-conserving surgery and axillary dissection. Histological sections from the surgical specimen revealed a 10 mm grade 3 infiltrating ductal carcinoma that was negative for both oestrogen and progesterone receptors. Eight out of 10 axillary lymph nodes were positive for malignancy. The patient went on to receive four cycles of adjuvant chemotherapy (paclitaxel) and postoperative radiotherapy.

The patient remained well until a month before presentation, when she developed right hip pain. An x-ray and bone scan showed a suspicious bone lesion within the ischium on the contralateral side to the pain. A computed tomography scan of the chest, abdomen and brain revealed a 1.5 cm right upper lobe lung lesion as well as multiple brain lesions. A biopsy of the lung lesion confirmed the presence of adenocarcinoma consistent with metastatic breast cancer.

She commenced oral dexamethasone treatment 4 mg three times daily and, because of the symptoms associated with bone metastases, also received a 4 mg intravenous dose of zoledronate. Three days later, she was reviewed by her local ophthalmologist when she presented with an acutely swollen and painful left eye with associated blurring of vision. On the basis of a moderate cellular infiltrate in the anterior chamber, she was diagnosed with acute iritis and commenced on homatropine 2% three times daily as well as ocular dexamethasone hourly.

Two days later, the patient noted increasing pain in the eye, worsening blurring of vision and onset of photophobia. She was reviewed by the ophthalmology department at the hospital where she was undergoing whole brain radiotherapy. She was noted to have reduced visual acuity in the left eye, an injected conjunctiva, a hazy and oedematous cornea, and cells in the anterior chamber. Fundoscopy was unremarkable. A diagnosis of acute anterior uveitis and anterior diffuse scleritis was made. She was continued on homatropine drops but the dexamethasone drops were changed to 2-hourly prednisolone acetate/phenylephrine hydrochloride drops.

The patient was reviewed regularly in the ophthalmology clinic over the following 2 weeks. At the time of discharge from the clinic, her visual acuity had improved and the anterior chamber was clear of cells. She had ceased homatropine treatment and was on a weaning dose of ocular steroids. Three months later, she had ceased ocular steroid therapy and her vision had returned to normal. She received no further doses of bisphosphonate after the first administration. ◆

Bisphosphonates are indicated for treatment of a number of conditions, including osteoporosis, Paget's disease, hypercalcaemia associated with malignancy, and bone metastases. Their mechanism of action is via inhibition of osteoclast activity, leading to reduced bone resorption. Common side effects of bisphosphonate treatment are dysphagia, heartburn and oesophagitis.

Lessons from practice

- Bisphosphonates are used to treat a number of clinical conditions, including osteoporosis, Paget's disease, hypercalcaemia of malignancy, and bone metastases.
- Various ocular complications of bisphosphonate use have been reported, including conjunctivitis, scleritis, iritis and uveitis.
- These complications are rare and are readily treatable. Management usually involves cessation of the bisphosphonate and treatment with an ocular topical mydriatic drug and steroids. ◆

Since the early 1990s, there have been a number of case reports documenting various ocular complications of bisphosphonate use, including conjunctivitis, scleritis, iritis and uveitis.[1-9] In most cases, ocular symptoms began within 72 hours of administration of the bisphosphonate, and symptoms generally improved after local therapy and cessation of the drug. Usually it is the nitrogen-containing bisphosphonates that have been implicated (alendronate, pamidronate, zoledronate, risedronate), but in one report uveitis was associated with a non-nitrogen-containing bisphosphonate (clodronate).[5] The mechanism of the inflammation is unclear, but it is known that the nitrogen-containing bisphosphonates cause elevated levels of pro-inflammatory cytokines, including tumour necrosis factor α and interleukin-6.[10] The factors that predispose some patients to develop ocular symptoms are not known. Management of patients with ocular complications of bisphosphonate use includes treatment with an ocular topical mydriatic drug and a steroid. In most of the cases described in these case reports, the bisphosphonate treatment was stopped, and, in one case, ocular symptoms recurred on rechallenge with the drug.[5] In another case, in which the original bisphosphonate was replaced by a different drug of the same class, eye inflammation was reduced and eventually resolved with continued use, suggesting the development of immunological tolerance.[11]

Between 1997 and April 2004, there were nearly 6 million Pharmaceutical Benefits Scheme prescriptions filled in Australia for bisphosphonates.[12] This figure underestimates overall use, as it does not capture bisphosphonates administered to hospital inpatients. Bisphosphonates are an extremely useful class of drugs, and the point of our case report is not to advocate lesser use, but to highlight the importance of early recognition of potentially sight-threatening ocular conditions, as they are readily treatable.

Competing interests

None identified.

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