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CASE REPORT

Orbital myositis induced by alendronate: A case report

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Abstract

Background and purpose: Bisphosphonates are widely used, notably for osteoporosis treatment. Their common side effects are well known. However, they can trigger less common effects such as orbital inflammation. Here, the case is reported of an orbital myositis triggered by alendronate.

Methods: This is a case report at an academic medical center. An orbital magnetic resonance imaging scan, a thoraco-abdominal computed tomography scan and blood sample analyses were performed.

Results: A 66-year-old woman treated by alendronate for her osteoporosis was investigated. She developed an orbital myositis after the first intake. Neurological examination revealed a painful diplopia with decreased downward and adduction movements of the right eye and edema of the upper eyelid. Orbital magnetic resonance imaging showed an orbital myositis of the right eye. No other cause of orbital myositis was found than the alendronate intake. After alendronate arrest and a short course of prednisone, the symptoms resolved.

Conclusion: This case highlights that alendronate can cause an orbital myositis whose early diagnosis is of major importance because it is a treatable side effect.

KEYWORDS
alendronate, bisphosphonates, orbital inflammation, orbital myositis

CASE DESCRIPTION

A 66-year-old woman received an alendronate treatment for postmenopausal osteoporosis. The day after the first intake, she developed binocular diplopia, right orbital pain in eye movements and right upper eyelid edema, which gradually resolved after 4 days. After the second intake, the symptoms reoffended in the same eye, and then persisted and worsened. The patient had no systemic symptoms. The clinical examination showed decreased downward and adduction movements of the right eye and edema of the upper eyelid.

Orbital magnetic resonance imaging (MRI) revealed a swelling of the right eye medial rectus and superior oblique muscles with hyperintensity in T2 and T2 FAT SAT (spectral fat suppression) sequences, and contrast enhancement of muscles. These abnormalities were in keeping with a myositis (Figure 1). The rest of the investigations (thoraco-abdominal computed tomography scan and blood sample analyses) excluded infectious, immunological and paraneoplastic diseases. The diagnosis of alendronate-induced orbital myositis was made, based on a close temporal relationship between administration of alendronate and symptom onset, and the absence of another identified cause of orbital myositis.

Alendronate was stopped and oral prednisone 1 mg/kg/day was initiated. Symptoms disappeared within 2 days. Prednisone was then tapered off, without recurrence of symptoms. The total course of

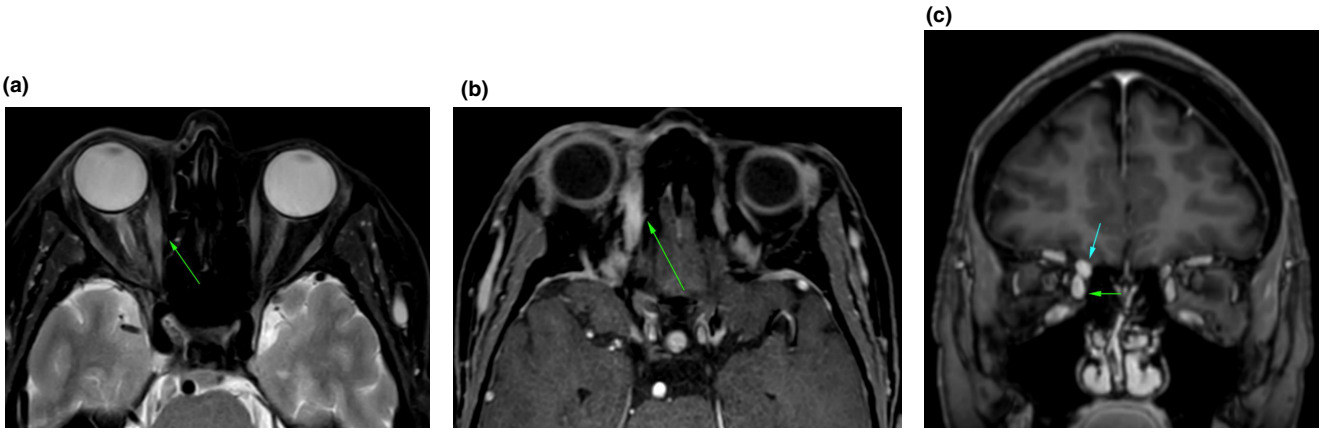

FIGURE 1 (a) An asymmetric enlargement and a slight hypersignal of the right medial rectus muscle (green arrow) are seen in this axial T2 sequence. (b) A bright enhancing of the right medial rectus muscle (green arrow) is seen on this axial T1 sequence, after gadolinium injection. (c) An asymmetrical enhancement of the right medial rectus muscle (green arrow) and of the right superior oblique muscle (blue arrow) are seen in this coronal T1 sequence, after gadolinium injection.

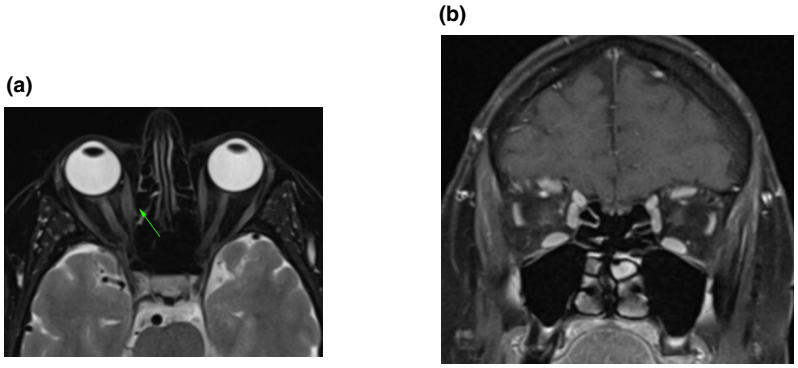

FIGURE 2 (a) After 6 weeks of treatment, in this axial T2 sequence, the right medial rectus muscle (green arrow) has symmetrical intensity on both sides, even though it is still slightly enlarged on the right side. (b) After 6 weeks of treatment, in this coronal T1 sequence after gadolinium injection, a perfect symmetrical aspect and enhancement of the right medial rectus muscle and of the right superior oblique muscle are seen on both sides.

prednisone was short and lasted 4 weeks. At the end of treatment, a new MRI showed near disappearance of the previously seen lesions (Figure 2).

DISCUSSION

Orbital myositis symptoms are a painful binocular diplopia often associated with periocular edema and erythema, conjunctival injection or chemosis. Orbital MRI is the diagnostic examination of choice, showing an enhancing enlargement of the muscle belly, often with involvement of the muscle tendon.[1]

Orbital myositis most often occurs as an idiopathic acute form in young adult females, usually responding to a course of corticosteroids.[1, 2] Rarely, orbital myositis is of dysimmune, infectious or paraneoplastic origin. It can also be an adverse effect of a medication. Thyroid-associated orbitopathy, inflammatory bowel disease and immunoglobulin G4 related ophthalmic disease are the most common dysimmune causes. Rarely, orbital myositis has been reported in sarcoidosis, lupus, giant-cell myocarditis, psoriasis, relapsing polychondritis, post streptococcal pharyngitis, rheumatoid arthritis, eosinophilic granulomatosis with polyangiitis (GPA), Behçet disease, GPA, psoriasis, Sjögren syndrome, dermatomyositis, HLA B27 spondyloarthrosis and scleroderma.[1] Moreover, orbital myositis can also be caused by infectious diseases such as herpes zoster ophthalmicus, Lyme disease, Whipple disease, varicella zoster virus, Coxsackie virus or cysticercosis.[1] Paraneoplastic orbital myositis has been described in the setting of breast carcinoma, seminoma, lung carcinoma, upper stomach carcinoma, high-grade non-Hodgkin lymphoma and paraganglioma.[1] Finally, orbital myositis can be triggered by immunotherapeutic drugs, bisphosphonates, statins, alpha 2b interferon, ribavirin, anti-flu vaccine.[1]

Bisphosphonates are widely used osteoclastic bone resorption inhibitors. The old generation of non-aminobisphosphonates (clodronate and etidronate) was replaced by the new and more efficient generation of aminobisphosphonates (alendronate, ibandronate, pamidronate, risedronate and zoledronate).[2–4] Common side effects of both bisphosphonate types are renal toxicity, hypocalcemia,

nausea, osteonecrosis of the jaw and atypical femur fractures. However, only aminobisphosphonates have proinflammatory effects. They activate monocytes, macrophages and T-cells to release proinflammatory cytokines and mediators initiating a proinflammatory cascade. This has been reported to cause an acute phase reaction in about one-third of patients receiving intravenous zoledronate. Patients may experience fever, chills, musculoskeletal pain and gastrointestinal symptoms.[2, 4] Inflammatory side effects of bisphosphonates involving eyes and periocular structures have been described, including uveitis, conjunctivitis, scleritis, cranial nerve palsy, ptosis, periocular edema and retrobulbar optic neuritis. The exact incidence of bisphosphonate-induced orbital inflammation is not known but is quite rare.[2] Physiopathology is not completely understood. Orbital fibroblasts may have a greater inflammatory response to inflammatory stimulation than other types of fibroblasts, leading to orbital inflammation.[4] In our patient, after the first alendronate intake, the symptoms disappeared in a few days. But, after the second intake, they persisted, and so the presence of different kinds of pathophysiological processes might be suspected in our case.

Twenty-nine bisphosphonate-induced orbital inflammation cases have been reported since 1999. Amongst them, eight were orbital myositis which were mostly unilateral (4/29 bilateral). The average age was 66,6 years and 58.6% were female. Inflammation occurred within 1–28 days (mean 3 days) following the drug intake. Zoledronate was the most common precipitant. This may be simply the reflection of its greater use. Only four cases of orbital inflammation were attributed to alendronate, with two orbital myositis. This smaller number is probably explained by alendronate pharmacokinetics properties (low oral bioavailability and quick clearing).[3, 4] The management of bisphosphonate-induced orbital inflammation consists in discontinuation of the biphosphonate and administration of a course of high dose systemic corticosteroids.[5] Patients usually have a rapid and complete recovery.[1, 2, 4]

A new case of alendronate-induced orbital myositis is reported. Even if bisphosphonate-associated orbital myositis is rare, clinicians should be aware of it because of the frequent use of bisphosphonates. The diagnosis should be considered in any patient developing acute orbital inflammation within days to weeks following bisphosphonate intake, in the absence of other identified cause. A full recovery is expected with prompt diagnosis and proper management, consisting in bisphosphonate discontinuation and corticosteroid therapy.

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CONFLICT OF INTEREST STATEMENT

None.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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