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## Uveitis Due to Bisphosphonates: A Rare Side Effect?\*



### Uveítis por bisfosfonatos: ¿un raro efecto secundario?

To the Editor,

The use of bisphosphonates has increased in recent years, especially for the treatment of osteoporosis. This circumstance, together with the fact that these treatments are lengthy, has resulted in the development of adverse effects: osteonecrosis of the maxilla, bone and muscle pain, atrial fibrillation, atypical fractures or ocular inflammatory disorders. The latter include conjunctivitis, uveitis (most frequently, anterior uveitis)<sup>1</sup> and episcleritis.<sup>2</sup>

We report the case of a 51-year-old woman with a history of hypothyroidism, tension headache, polymyalgia rheumatica and a posteriori clinical suspicion of temporal arteritis with a negative biopsy, worsening polyarthralgia and back pain. Treatment consisted of an intermittent prednisone regimen with doses ranging between 1 and 2.5 mg/kg/day. She underwent a lateral radiograph of the spine, which focused on thoracic vertebra T8 and lumbar vertebra L2 and, as there was reasonable clinical suspicion of vertebral fracture (back pain of recent onset and height loss of 2 cm in a postmenopausal woman who had received several regimens of glucocorticoids at doses higher than 7.5 mg/kg/day), treatment with ibandronic acid was begun. Approximately 4 months after the initiation of treatment, she presented with ocular discomfort consisting of pain and conjunctival erythema, and was referred to the ophthalmology department, where she was diagnosed with anterior uveitis. Oral glucocorticoid therapy was discontinued and treatment with eye drops containing dexamethasone was begun. The patient was then referred to the rheumatology department, where an autoimmune origin of her condition was ruled out and treatment with bisphosphonates was discontinued, whereas the ophthalmological treatment was maintained. In subsequent visits, a progressive improvement of the anterior uveitis was observed and she chose not to continue with follow-up.

There have been several reports of ocular inflammatory events in patients taking oral bisphosphonates, suggesting that these ocular effects are underdiagnosed.<sup>3</sup> Only 1 epidemiological study has examined the risk of scleritis and uveitis associated with the use of oral bisphosphonates: a 1-year follow-up of a cohort of United States veterans. The relative risk of scleritis and uveitis was 1.23 higher among the users of bisphosphonates, but this finding was not statistically significant. Only 9 cases were recorded among the participants taking these drugs for the first time.<sup>1</sup>

The majority of the cases of scleritis and uveitis developed after use of the bisphosphonate was begun and resolved when it was

discontinued,<sup>3</sup> although reports of recurrent uveitis after renewed treatment with pamidronate corroborate the causal relationship, indicating that the use of bisphosphonates, as a class, may increase the risk of uveitis.<sup>4</sup>

Anterior uveitis is usually bilateral and can be associated with fever and flu-like symptoms; it can be mild or severe, and recurs if the use of topical glucocorticoids is reduced. Scleritis may resolve with topical ocular medication, with no need to discontinue bisphosphonate therapy.<sup>5</sup>

Regarding the pathophysiology, inflammatory mediators are thought to play a major role in provoking a mechanism for induction of the inflammatory response,<sup>3</sup> although, in reality, the mechanism is still not clear.

The risk of developing ocular disorders associated with the use bisphosphonates is very low. Patients receiving this treatment should undergo an ophthalmological examination if they note a persistent loss of vision or ocular pain,<sup>3</sup> as both uveitis and scleritis require immediate treatment to prevent additional complications such as cataracts, glaucoma, macular edema and scleral perforation.<sup>3</sup> Clinicians should inform their patients of the signs and symptoms of scleritis and uveitis in order that these diseases be detected and treated rapidly. Patients taking oral bisphosphonates should be aware of these signs and symptoms so that they can be evaluated immediately by an ophthalmologist.

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