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CASE REPORT

Bisphosphonate-associated jaw osteonecrosis. Clinical case presentation

Osteonecrosis mandibular asociada a bifosfonatos. Presentación de caso clínico

Rocío Gloria Fernández López,* Águeda M Arellano Flores,§
Sayra Nayelli Velázquez Serrano||

ABSTRACT

The aim of the present paper was to present the association between mandibular osteonecrosis and use of bisphosphonates for therapeutic purposes. Bisphosphonates are drugs used for the treatment of primary and secondary bone disorders. They are mainly used for local and general osteoporosis treatment, metabolic bone diseases, soft tissue calcification as well as hypercalcemia occurrence, among others. They can also act as antineoplastic agents through the inhibition of activation of cancer-linked proteins. In recent years, bisphosphonates have been used to prevent post-menopausae osteoporosis, since they enhance mineral density increase in bone and therefore contribute to a decrease in fractures. The clinical case here presented is that of a 61 year old female patient with previous history of breast cancer and ongoing 3 year bisphosphonate intake. The patient presented asymptomatic, spontaneous bone exposition. Surgical and medical handlings of the case are presented, as well as its evolution.

Key words: Bisphospohonates, jaw osteonecrosis.

RESUMEN

El objetivo del trabajo es presentar la asociación de la osteonecrosis mandibular y el uso de bifosfonatos con fines terapéuticos. Los bifosfonatos son fármacos utilizados en el manejo de los desórdenes primarios y secundarios del hueso. Principalmente en la osteoporosis tanto local como general, enfermedades metabólicas óseas, calcificación de tejidos blandos y estados de hipercalcemia, entre otras. Asimismo también pueden actuar como antineoplásicos al inhibir la activación de proteínas vinculadas al cáncer. En los últimos años se ha incrementado su uso para la prevención de osteoporosis postmenopáusica, gracias a que favorece el incremento en la densidad de minerales en huesos, lo que ha permitido la disminución de fracturas. Se presenta un caso clínico de paciente femenina de 61 años de edad con el antecedente de cáncer de mama, ingesta de bifosfonato desde hace 3 años, la cual presentó exposición ósea espontánea, asintomática. Se muestra su manejo medicoquirúrgico y su evolución.

Palabras clave: Bifosfonatos, osteonecrosis maxilar.

INTRODUCTION

Bisphosphonates are drugs used in the treatment of bone metastasic and osteolytic lesions, multiple myeloma, malignant hypercalcemia, Paget's disease and even in osteoporosis conditions.[1-8] Fleish[7] defines these drugs as being synthetic analogues, resistant to pyrophosphate enzymes; they inhibit bone mineralization of the latter, bond to hydroxyapatite crystals and are degraded by alkaline phosphatases. They act in the following fashion: they inhibit bone exchange and resorption, osteoclastic proton pump for hydroxyapatite dissolution and the components of the cholesterol biosynthesis line. They also decrease activation and production of osteoclasts, increasing apoptosis.[1-3,7,8]

MycekM[2] mentions there are three bisphosphonate generations related to their chemical structure, potency and effectiveness:

First Generation: they contain lateral chains (medronate, clodronate, etidronate) or a chlorophenyl group (tiludronate).

Second Generation: they contain a nitrogen group in the lateral chain (alendronate and pamidronate). Its potency is 10 to 100 times higher than that of the first generation.

* Teacher, Oral Surgery Department, National School of Dentistry, National University of Mexico (UNAM).
§ Subject Teacher, Oral Surgery Department, National School of Dentistry, National University of Mexico (UNAM).
|| Graduate Student, Orthodontics Department, National School of Dentistry, National University of Mexico (UNAM).

Third Generation: they contain a nitrogen atom with a heterocyclic ring (risedronate and coledronate). They are 10,000 times more potent than those of the first generation.[1-3,7-10]

Bisphosphonate –associated osteonecrosis of the jaws (OJ) is evident with bone exposition in the oral cavity, when it endures for over 8 weeks in patients under bisphosphonate treatment with no previous history of radiotherapy. History of the condition generally begins with an alveolitis, which progresses to osteomyelitis with bone sequestrations.

Ruggiero and Marx consider there are three stages of evolution:

Stage 1. Bone exposition. Necrotic bone. Asymptomatic. Free of infection.

Stage 2. Bone exposition. Necrotic bone. Pain and infection.

2 a. No progression.

2 b. Progression without reaching stage 3.

Stage 3. Bone exposition. Necrotic bone. Pain and infection and one or more of the following signs: pathological fracture, extra-oral fistulae.[3]

To this day, there are still no well designed studies to address bisphosphonate-associated osteonecrosis treatments. Nevertheless, there are certain measures that, when adopted, can help to prevent or control the condition.

Treatment of osteonecrosis depends on the stage of the disease.

Stage 1

1. Quantification in mm of exposition size.

2. Suggestion of bisphosphonate treatment suspension.

3. Mouth rinsing with 0.12% chlorhexidine, three times a day for 15 days.

Stage 2

Stage 1. Antibiotics therapy. NSAIDs

First indication: amoxicillin / clavulanic acid every 12 hours for 15 days.

Stage 3

Stage 1, stage 2 and sequestrectomy.

In cases when evolution is negative: A new conservative surgical event must be programmed under local anesthesia. In cases when no improvement is achieved, block resection is recommended.[2,11,12]

CLINICAL CASE

61 year old patient attended the Oral Surgery Seminar of the National School of Dentistry, National University of Mexico (UNAM) for assessment and treatment of a two month evolution, asymptomatic lesion. The lesion measured approximately 10 x 6 mm and was located in the lingual side of the right lower molar region (*Figure 1*).

The patient informed of breast cancer history, taking place 5 years before. Bisphosphonates were prescribed and ingested. (alendronate, oral ingestion), 10 mg, 30 minutes before breakfast, during 3 years.

The patient denied any surgical, allergic, trauma or infectious history. She also denied having been subjected to any treatment before the onset of radiotherapy. The orthopantomography (*Figure 2*) and periapical x-ray (*Figure 3*) revealed absence of changes in bone, dental or periodontal structures, or presence of any pre-existent lesions.

Laboratory studies, CBC and coagulation times were found to be within normal parameters.

Clinical diagnosis was the following: spontaneous osteonecrosis associated to bisphosphonate use. Treatment consisted on suspension of bisphosphonate intake, non invasive sequestrectomy under local anesthesia, antibiotics therapy, NSAIDs (amoxicillin-clavulanate and nimesulide) (437.5 mg-62.5 mg 50 mg), (two capsules every 12 hours for 15 days), chlorhexidine mouth wash (0.12% three times a day for 15 days).

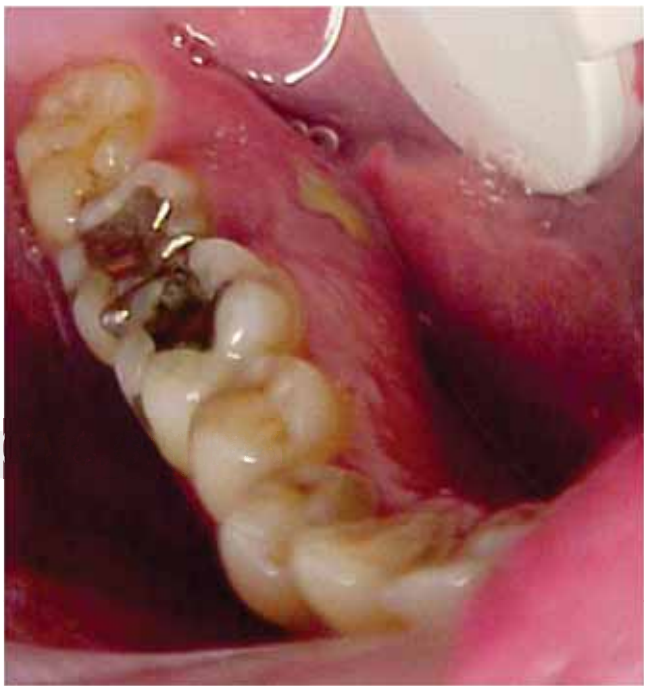

Figure 1. Spontaneous trabecular bone exposition, lingual aspect of the lower jaw.

The histopathological study revealed necrotic bone plates, bacterial colonies, severe and diffused mixed inflammatory infiltrate, parakeratinized stratified squamous epithelium with intercellular edema and leukocyte migration (*Figure 4*).

DISCUSSION

Marx mentions the fact that bisphosphonate associated osteonecrosis of the jaws is present in 78% of cases; it occurs spontaneously in 14%, and in 8% is due to infections.[3] In the present case, osteonecrosis was considered to have appeared spontaneously, since no previous signs of infection, trauma or periodontal disease could be found.

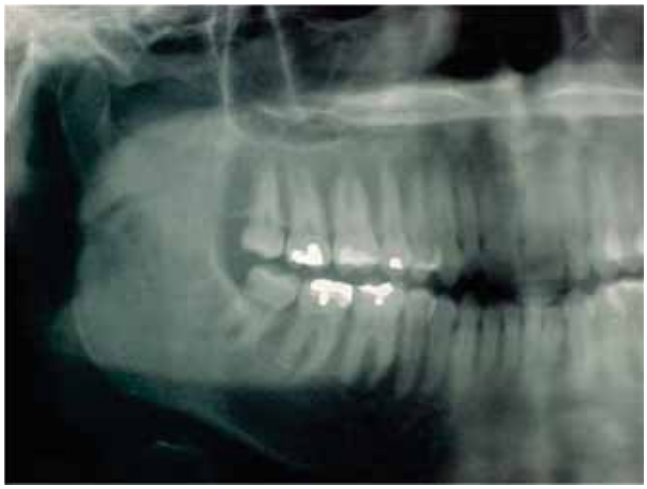

Figure 2. Orthopantomography.

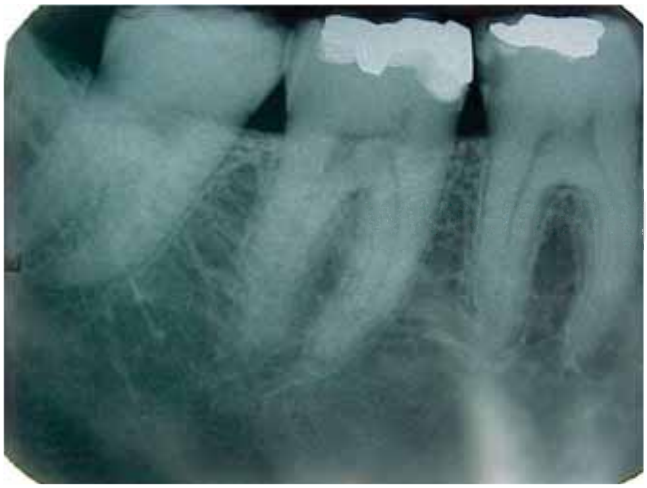

Figure 3. Periapical projection.

This condition appears more frequently in the lower jaw (63-80%). This might be due to the fact that the lower jaw experiences lesser irrigation when compared to the upper jaw. In our case, the site was the lower jaw, this is in agreement with frequency reported in scientific literature.

Oral drug administration is low risk when compared with IV administration.[8,10] Our patient ingested drugs orally. Asael mentions the fact that once bisphosphonates are ingested, negative effects persist even after treatment is discontinued. This is due to the fact that these drugs can remain in the bone tissues for months or even up to 10 years.[13]

CONCLUSIONS

Patients ingesting bisphosphonates must be advised of risks incurred when extracting teeth. This procedure can elicit serious complications among which we can count ulcerations in the lining of the mouth, infections, jaw fractures and osteonecrosis.

During the first 6 months of bisphosphonate intake, bone appears to be healthy and well able to regenerate. At this point, essential invasive procedures are not contra-indicated.

The clinical operator must diagnose presence of alveolar or periodontal sources of infection and then proceed to treatment and prevention. He must also prevent possible existence of prosthetic trauma, especially trauma located in the lower jaw area; he

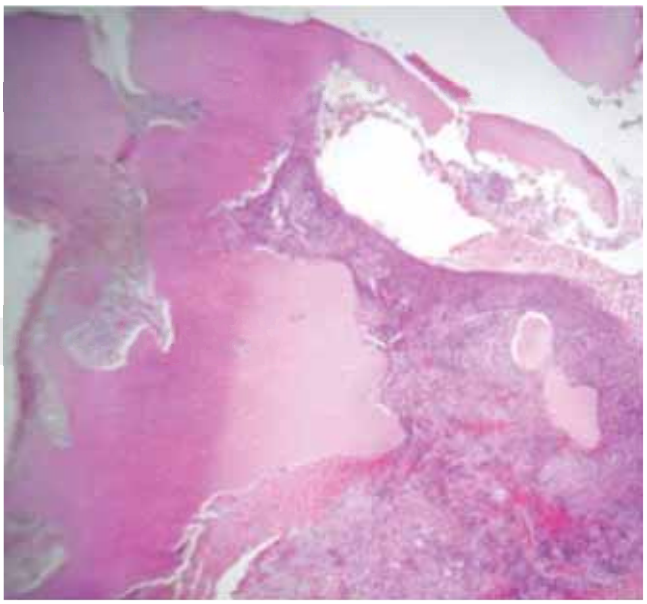

Figure 4. Histopathological study.

must also assess exostosis or bone prominences which could be considered risk factors in patients wearing removable prostheses.

After IV treatment, any oral surgery must be avoided at least during a period no lesser than 10 years.

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Mailing address:
Rocío Gloria Fernández López
E-mail: oshilina@hotmail.com