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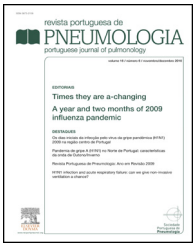

CASE REPORT

Bisphosphonate-associated osteonecrosis of the jaws in lung cancer patients☆

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KEYWORDS
Bisphosphonate-associated osteonecrosis of the jaw;
Lung cancer;
Risk factors;
Therapy

Abstract Osteonecrosis of the jaw (ONJ) can occur as a complication of bisphosphonate therapy. This condition has been described in cancer patients and its development has been associated with prolonged exposure to high doses of bisphosphonates. Bad dental hygiene, a history of prosthesis or dental extraction, chemotherapy, corticosteroids, and radiation therapy of the head and neck are reported risk factors. In the initial stages it may be asymptomatic, but the patient subsequently develops severe pain and progressive exposed bone. The authors describe three cases of ONJ in lung cancer patients after prolonged exposure to bisphosphonates and there were known risk factors. ONJ can seriously affect the quality of life of cancer patients. An early diagnosis may reduce or avoid the consequences of progressive bone lesion.

PALAVRAS-CHAVE
Osteonecrose da mandíbula associada aos bifosfonatos;
Cancro do pulmão;
Fatores de risco;
Tratamento

Osteonecrose da mandíbula associada aos bifosfonatos em doentes com cancro do pulmão

Resumo A osteonecrose da mandíbula (ONM) pode surgir como complicação do tratamento com bifosfonatos. Esta patologia tem sido descrita em doentes com cancro e o seu desenvolvimento associado a exposição prolongada a altas doses de bifosfonatos. Má higiene dentária, história de uso de próteses ou extração dentária, quimioterapia, corticosteroides e radioterapia da cabeça e pescoço são fatores de risco reportados. Nas fases iniciais pode ser assintomática, contudo, o doente posteriormente desenvolve dor significativa e exposição óssea progressiva. Os autores descrevem 3 casos de ONM em doentes com cancro do pulmão após exposição prolongada a bifosfonatos e na presença de fatores de risco conhecidos. A ONM pode atingir seriamente

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a qualidade de vida dos doentes com cancro. O diagnóstico precoce poderá reduzir ou mesmo evitar as consequências da lesão óssea progressiva.

Introduction

Bone metastization in patients with lung cancer is a frequent finding at presentation or during disease progression. Bisphosphonate therapy has demonstrated efficacy in this setting.[1–5]

Since the first reports in 2003, an association between bisphosphonates and osteonecrosis of the jaw (ONJ) has been described.[6–11] The pathophysiologic mechanism underlying ONJ still needs to be clarified, but it seems to involve impaired blood supply and secondary microorganism spread.[12–14]

ONJ occurs mainly in patients with prolonged exposure to high doses of IV bisphosphonates when risk factors are present. [6–11] In cancer patients the development of ONJ associated with bisphosphonates is most commonly seen in multiple myeloma and breast, prostate, and lung cancers.[15–17]

In the initial stages of ONJ the patient may be asymptomatic, but subsequently develops severe pain and progressive exposed bone.[18,19]

Case reports

Case 1

A 49-year-old man with stage *IV* lung adenocarcinoma (M1 lung, brain, and bone) diagnosed in May 2010 was submitted to two lines of chemotherapy, brain radiotherapy (30 Gy, 12 fractions), and 12 treatments with intravenous (IV) zolendronic acid 4 mg, every 3/3 weeks. During the course of the disease, chronic corticotherapy was prescribed. He had a previous history of tooth extraction with poor healing two months before starting bisphosphonates.

In March 2011, after 10 months of exposure to IV zolendronic acid, the patient experienced trismus with pain and soft-tissue swelling in the right jaw. At that time he was taking erlotinib 150 mg/day as a third-line treatment. Computed tomography (CT) of the face showed a marked change in the bone trabeculation of the right jaw, and orthopantomography confirmed alterations consistent with osteonecrosis (Fig. 1).

He was initially treated with multiple courses of antibiotics and analgesics, but because he maintained progressive bone exposure with associated bleeding, surgical treatment was proposed. In January 2012, he underwent maxillofacial surgery eight months after discontinuation of zolendronate. Long-term evaluation confirmed good recovery. The histopathological examination of bone tissue revealed no signs of metastasis.

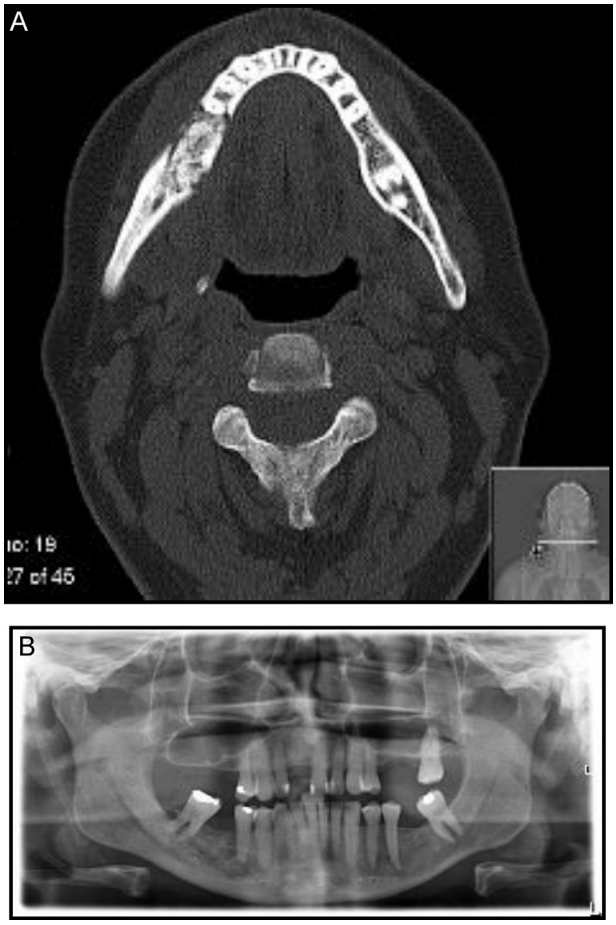

Figure 1 (A) Face CT: marked change in the bone trabeculation of the body of the jaw to the right, about 3.5 cm long and (B) orthopantomography showing changes on right jaw.

Case 2

A 59-year-old man with stage *IV* non-small cell lung carcinoma (M1 bone) diagnosed in January 2008 received two lines of chemotherapy, thoracic radiotherapy (30 Gy, 12 fractions), 35 treatments with IV pamidronate 90 mg, and subsequently oral ibandronic acid 50 mg/day. Pulse corticosteroids in association with chemotherapy were also prescribed.

The patient had a history of denture that traumatized the alveolar ridge and bad dental hygiene. In November 2010, he experienced pain associated with bone exposure at the site of trauma. Face CT and orthopantomography confirmed the diagnosis. At that time, the patient was taking pemetrexed and had been treated for 26 months with IV pamidronate