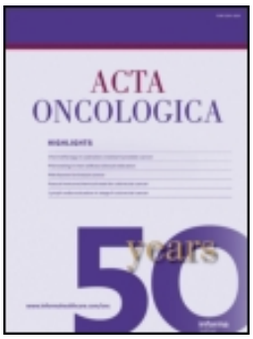

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The role of surgery in jaw bone necrosis associated with long-term use of bisphosphonates

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The role of surgery in jaw bone necrosis associated with long-term use of bisphosphonates

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In last years, several cases of osteonecrosis of the jaw (ONJ) associated with the use of bisphosphonates have been reported [1–7]. In our experience, the development of this complication in breast cancer patients seems to be higher than in other studies (frequency of about 6%) [8]. The pathogenesis of ONJ is unclear. An analogy with 'phossy jaw' has been reported, suggesting a potential alteration in the normal phosphorus and calcium metabolism in these patients [9,10]. Persistence of hypercalcemia and secondary hyperparathiroidism may eventually predispose to the development of this condition [11]. Pamidronate and zoledronic acid exert direct effects on osteoclastic activity through different mechanisms, and may induce osteoclast apoptosis [12]. The antiangiogenic effect attributed to bisphosphonates might play a role, together with microtrauma, inflammation and chronic infection [13–16].

ONJ can severely affect quality of life, and even becoming the major concern of cancer patients because of severe pain, difficulties in performing oral hygiene and in eating.

Its clinical management is controversial and no satisfactory therapy is currently available [17]. The use of hyperbaric oxygen seems to be ineffective [18]. Antibiotic therapy may be temporarily useful but does not induce clinical resolution. Temporary discontinuation of bisphosphonates may be advocated, although clinical benefit has yet not been proven. Non-surgical treatments have always been preferred: minimal debridement, cover exposed bone, protective stint [19]. In some cases of progressive disease a major surgical approach may be considered [20]. Recurrent ONJ should be taken into account when considering risks and benefits resulting from the surgical procedure [17]. Recently it has been observed that users of intravenous bisphosphonates had an increased risk of inflammatory conditions, osteomyelitis, and surgical procedures of the jaw and facial bones. The increased risk may reflect an increased risk for osteonecrosis of the jaw, even in misdiagnosed cases [21].

In this short report we describe our experience of surgery in patients with jaw bone necrosis.

The first patient is a 64 year old man affected from prostate cancer with bone, pulmonary and nodal metastasis. He received treatment with zoledronic acid from November 2004 to April 2005. In July 2005 he started to complain paresthesia in left emi-mandibular area, with no pain. Symptoms gradually worsened, with recurrent dental abscesses, treated with antibiotic therapy, and progressive pain localized

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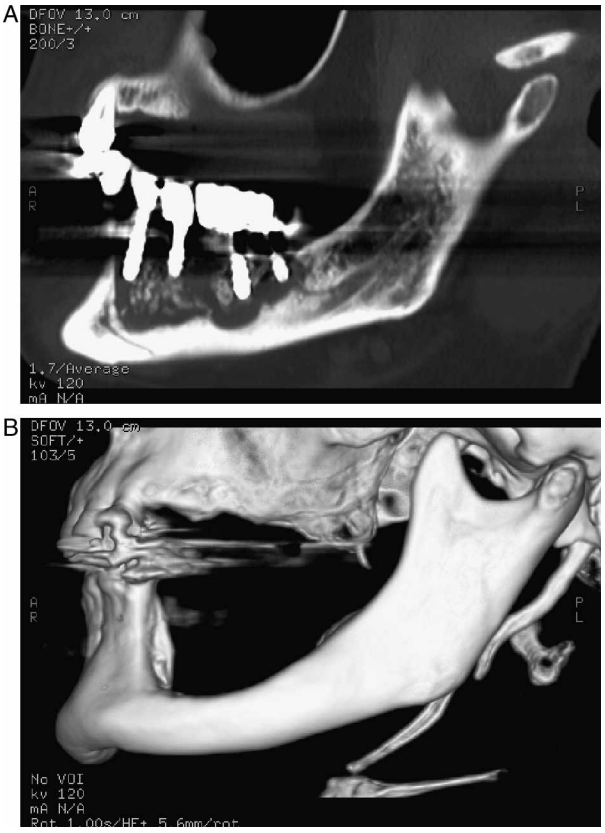

Figure 1. A. ONJ of the left hemi-mandible. CT oblique sagittal reconstruction displayed with bone window setting showing a large osteolyitic lesion with a sequestrum in the site of four dental implants, B. Follow-up CT 3D reconstruction five months after surgical resection of necrotic bone.

in the left mandible (sites of multiple dentary implants). In June 2006 a new maxillary CT scan showed a wide osteolytic area including a large sequestrum in the site of four fixtures in the left lower jaw attributable to ONJ (Figure 1a). His quality of life was severely affected by continuous pain, paresthesie and oral bleeding despite a good control of its neoplastic disease under weekly docetaxel. After multidisciplinary discussion, surgical resection of the necrotic bone sequestrum encasing the four implants was performed in general anaesthesia, with a courettage of the surgical bed to reach bleeding tissue. Histological examination confirmed the diagnosis of bone necrosis, with features of osteomyelitis. His symptoms gradually improved with resolution of pain and paresthesia. At a follow-up of 3 months, a 1 mm mucosal dyastasis was present in the retromolar trigone area, but at 5 months follow-up the surgical site was completely covered by normal mucosa (Figure 1b). The patient is still affected by occasional and transient paresthesia of the mandibular nerve, but no pain drug was necessary since after the surgery.

The other patient selected for surgery is a 58 year old woman affected from breast cancer with bone, liver, and lung metastases. She received pamidronate and zoledronic acid for around 4 years (June 2000 to May 2004). She underwent dental invasive procedure during bisphosphonate treatment. Jaw necrosis diagnosis was definitely done in September 2004 with clinical examination, and confirmed through CT scan showing an osteolytic lesion in the right mandible with sequestrum, surrounded by reactive, sclerotic bone (Figure 2a). She underwent curettage and hyperbaric therapy with no clinical benefit, and her symptoms were partially controlled by intermittent use of antibiotics. In last months, despite good control of neoplastic disease with capecitabine given at a metronomic schedule, her symptoms dramatically worsened and her quality of life was severely affected by continuous pain in the right mandible. The CT scan performed in November showed progressive jaw necrosis characterized by the presence of scattered areas of bone destruction and small islands of bone or sequestra (Figure 2b).

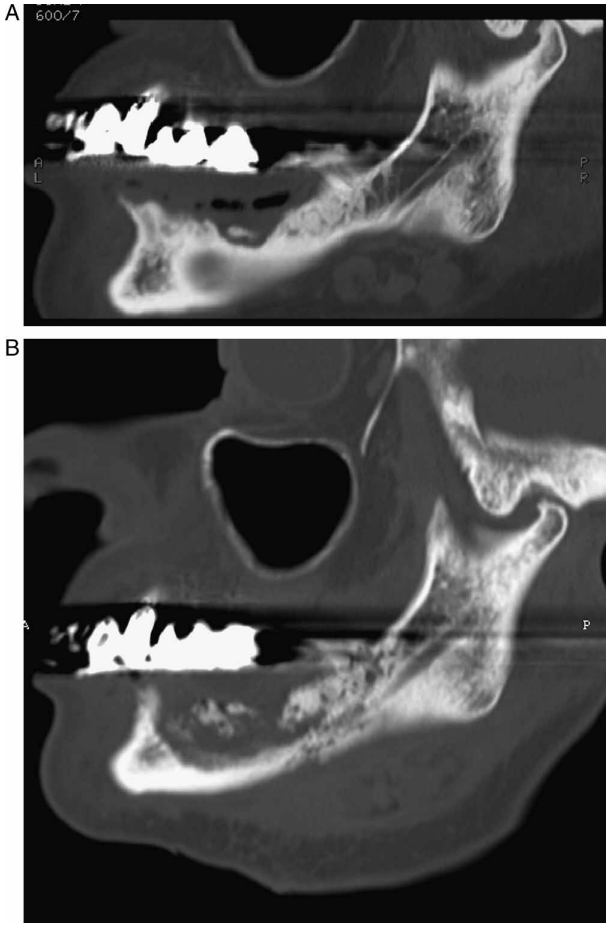

Figure 2. A. ONJ of the right hemi-mandible. First CT oblique sagittal reconstruction displayed with bone window setting showing an osteolytic lesion with a small sequestrum surrounded by sclerotic bone, B. Second CT examination reconstructed in the same plane showing progressive disease characterized by a large area of destruction with small islands of bone or sequestra.

Clinical examination showed a mass in the right lower jaw with suppurative cutaneous fistula. After an interdisciplinary discussion we decided to remove the bone sequestrum with a trans-oral approach, without interruption of the mandibular arch. During the surgery it was evident that there were no sequestrum formed and what in the CT scan seemed to be a delimited necrotic bone, was the fractured cancellous bone still inserted, but completely detached, in a shell of cortical bone. This situation forced a change to the surgical approach from the trans-oral to the submandibular and a hemimandibulectomy was performed replacing the bone with a 2 mm titanium reconstruction plate (Leibinger). Histological examination confirmed the diagnosis of bone necrosis. Follow-up at 4 months showed that the surgical field is completely closed by normal mucosa, the titanium plate is in place and there is no mobility of the fixing screws. The patient's capacity to eat improved and she stopped the morphine assumption. Otherwise in the controlateral hemimandible there was an osteomyelitis recurrence with development of paramandibular abscess with orocutaneous fistula.

In our experience, surgery seems to be feasible in selected patients, although the most adequate approach is far from being standardized. A close interdisciplinary collaboration is required to identify the best timing for the procedure, also considering the individual prognosis and the balance between risks and benefits of single cases. As evidence based therapy protocols for a remodelling of bone defect are still missing, prevention and early identification of patients at risk should be of prime concern.

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