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Aneurysmal Bone Cyst of the Atlas: Treatment with Denosumab and Case Report

Quiste óseo aneurismático del atlas: Tratamiento con denosumab y reporte de caso

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Abstract

We present a case of aneurysmal bone cyst (ABC) of infrequent location and aggressive behavior in a 28-year-old male patient, in which surgical resection is controversial due to the risk of iatrogenicity and eventual recurrence. Treatment with denosumab has been recently proposed as an alternative for the management of unresectable or recurrent ABCs; however, the available literature is sparse. We report our experience with one case and analyze the available literature.

Keywords

- aneurysmal bone cyst
- denosumab
- spine
- atlas

Resumen

Presentamos un caso de quiste óseo aneurismático (QOA) de ubicación infrecuente y comportamiento agresivo en un paciente masculino de 28 años, en que la resección quirúrgica es controversial por el riesgo de iatrogenia y eventual recurrencia. El tratamiento con denosumab ha sido recientemente propuesto como una alternativa para el manejo de QOAs irresecables o recurrentes; sin embargo, la literatura disponible es escasa. Reportamos nuestra experiencia en un caso y analizamos la bibliografía disponible.

Palabras clave

- quiste óseo aneurismático
- denosumab
- columna vertebral
- atlas

Introduction

Aneurysmal bone cysts (ABCs) are biologically benign bone tumors. Their incidence rate is low (0.14 to 0.32 per 100 thousand individuals), and they are more frequent in the first 2 decades of life. Primary ABCs represent 70% of the cases, whereas secondary ABCs correspond to the remaining 30% of these lesions, and they can accompany other bone conditions, including giant cell tumors (GCTs), osteosarcomas, and fibrodysplasia.[1]

Aneurysmal bone cysts usually produce mass effects, inflammation, pain, and bone destruction; in some particularly aggressive cases, they may cause pathological fractures. These tumors often compromise the metaphyses of long bones, especially the distal femur and proximal tibia. Spinal presentations account for 10% to 30% of the total cases of ABC,

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and they can result in neurological deficits. Cervical cases represent 11% to 41% of these spinal presentations. The incidence of atlas involvement is lower than 10%, and this is an extremely infrequent location.[2,3]

Conventional radiography enables an initial assessment. It shows a radiolucent cystic lesion, preferably in a metaphyseal location, sometimes expanding to the cortical area. A magnetic resonance imaging (MRI) scan with contrast reveals cystic cavities with fluid-fluid levels, highly suggestive of ABC; however, these findings are not pathognomonic. Eventually, a preoperative computed tomography (CT) scan would enable the delimitation of these lesions if its performance is feasible. Today, the diagnosis must be confirmed through a biopsy and correlated with the imaging findings.[1]

Its natural history can be unpredictable. An ABC may exhibit a quickly destructive and expansive behavior; this is why it is often treated surgically (through curettage and graft or wide resection followed by reconstruction). Nevertheless, the complication rate ranges from 15 to 30%, and the risk of insufficient resection ranges from 10% to 44%.[3] Given the aforementioned, ABCs are a major therapeutic challenge, particularly in the spine; the scarce literature available is an additional obstacle to the decision-making process.

We herein report an ABC at the left lateral mass of the atlas. The lesion is a stage-III tumor per the Enneking classification. The therapeutic options for this ABC included surgical resection, selective embolization, sclerotherapy, or radiotherapy. Since none were feasible, we proposed an alternative treatment with denosumab.

Clinical Case

The patient is a 28-year-old man who had Hodgkin lymphoma and had undergone treatment five years before. He was referred to our unit (or orthopaedics department) due to insidious, progressive, and consistent odynophagia and left neck pain for the previous five months. The pain irradiated to the left side of the skull and shoulder, limiting mobility and disrupting sleep. In addition, the range of motion of the shoulder was limited. There was no history of weight loss, fever, or any relevant symptoms. The physical examination revealed no evident mass or enlarged lymph nodes on inspection or palpation. There was no pain in the cervical midline, and the neurological findings were within normal parameters. The most significant observation was the limited active and passive cervical ranges of motion due to the poorly-characterized and diffuse pain.

We requested a CT scan of the cervical spine, with and without a contrast medium, because of the history of cancer (►**Figure 1**). The CT showed an expansive lytic lesion in the left lateral mass of the atlas, with dense content of soft parts in its interior. In addition, we requested a CT Thorax, abdomen and pelvis, for the same reason, which ruled out other lesions. We also requested an MRI with contrast to

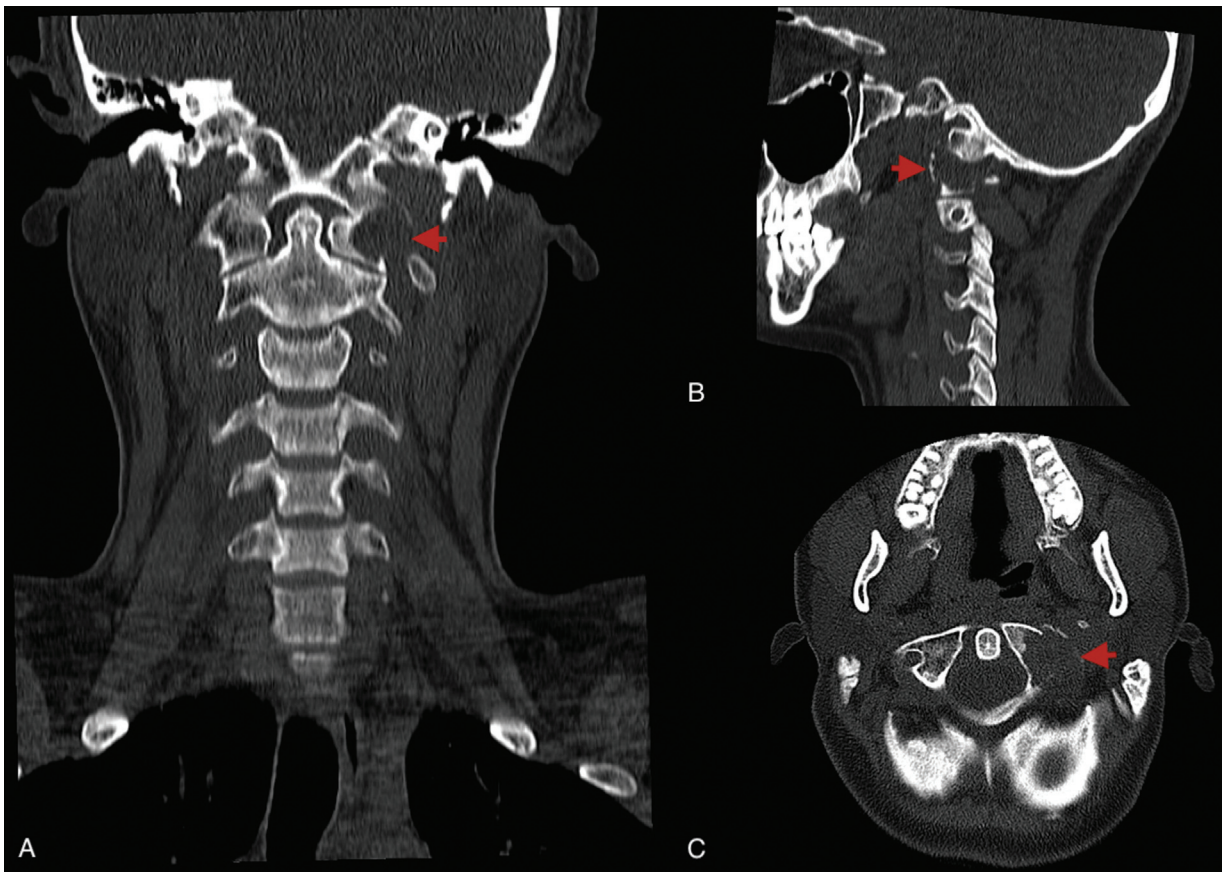

Fig. 1 Cervical computed tomography scan with no contrast. Coronal (**A**), sagittal (**B**), and axial (**C**) sections showing evidence of expansive lytic lesion at the left lateral mass of the atlas.

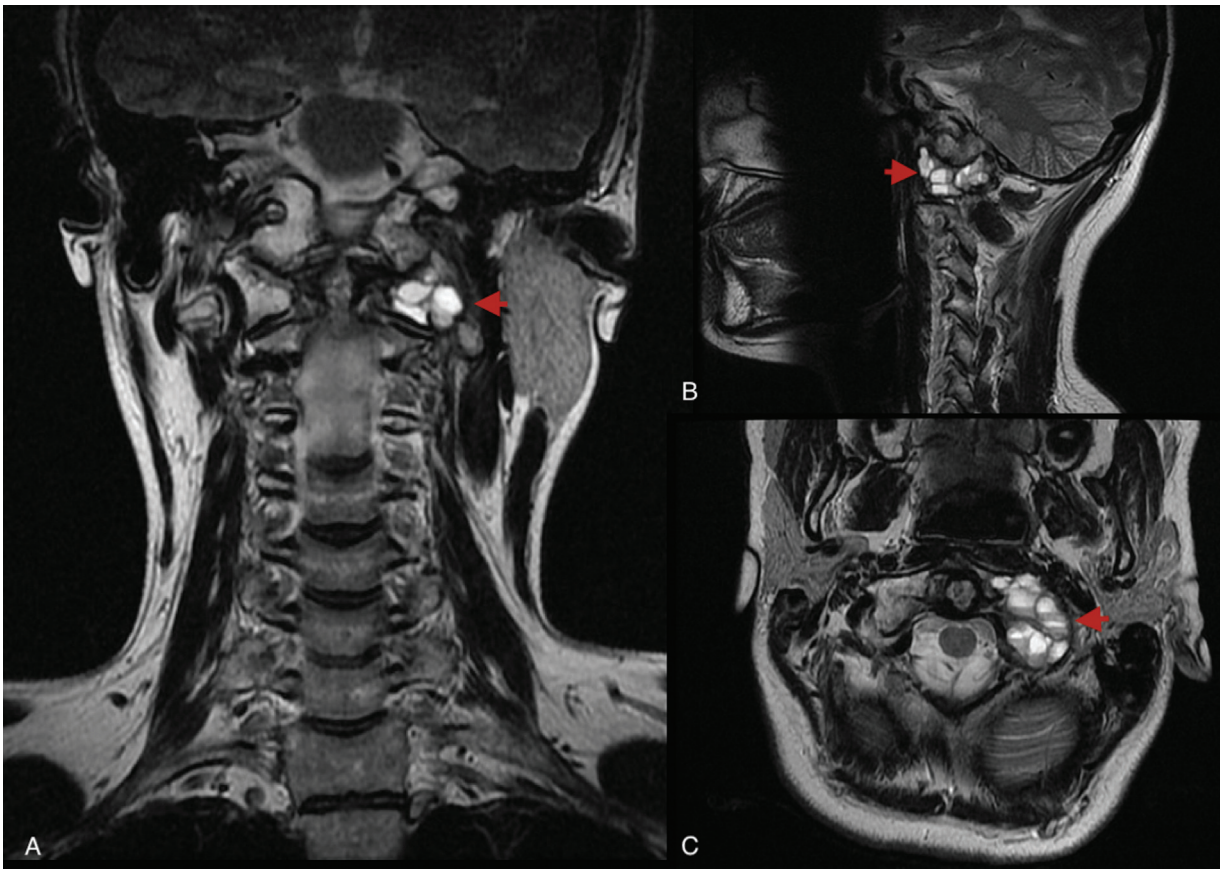

Fig. 2 Cervical T2-weighted magnetic resonance imaging scan with contrast medium. Coronal (**A**), sagittal (**B**), and axial (**C**) sections showing a lesion measuring 28 × 15 × 21 mm in the left lateral mass of the atlas, filled with multiple fluid-fluid levels.

characterize the lesion, which measured 28 × 15 × 21 mm and presented multiple fluid-fluid levels in its interior; these findings are highly suggestive of an ABC (►**Figure 2**). Next, we requested a bone scintigram, which did not show other injuries. Based on the aforementioned information, we proceeded to a CT-guided percutaneus puncture biopsy (►**Figure 3**), which confirmed our diagnostic hypothesis.

Given the rapid progression and the complex surgical approach, we proposed a treatment protocol with denosumab following a similar experience reported in the literature.[3] Before treatment, we checked the levels of calcium, phosphorus, and vitamin D; all results were within normal parameters. The dental examinations were unremarkable. Treatment started with the subcutaneous administration of denosumab 120 mg once a month for 6 months. In addition, the patient received daily oral supplementation of 1,000 mg of elemental calcium and 1,000 IU of vitamin D. Follow-up with the medical team occurred monthly. We also recommended the permanent use of a Philadelphia collar because this was a highly-unstable injury.

A cervical CT scan with no contrast medium after four months of treatment (►**Figure 4**) evidenced lesion corticalization and the absence of both tumor expansion and pathological fractures. At six months, the patient reported an evident decrease in pain. His neurological examination was unremarkable. No complications interfered with treatment

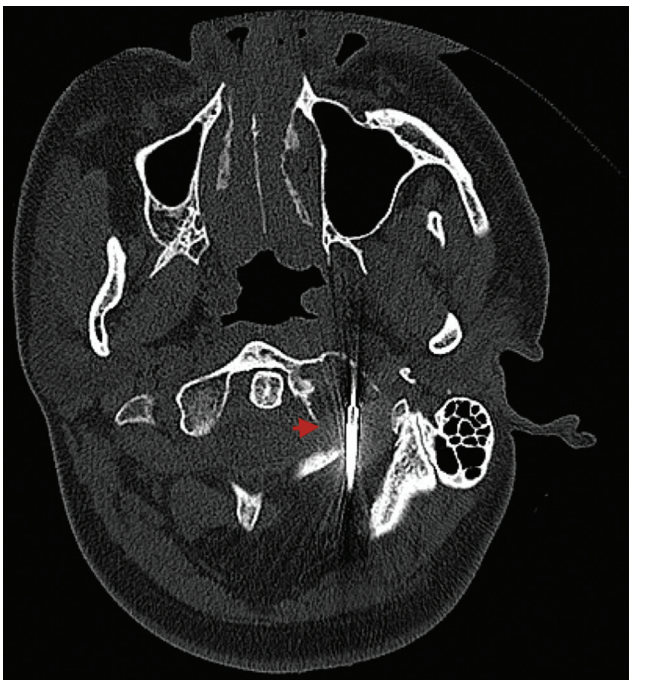

Fig. 3 Percutaneus puncture biopsy of the atlas guided by computed tomography scanner.

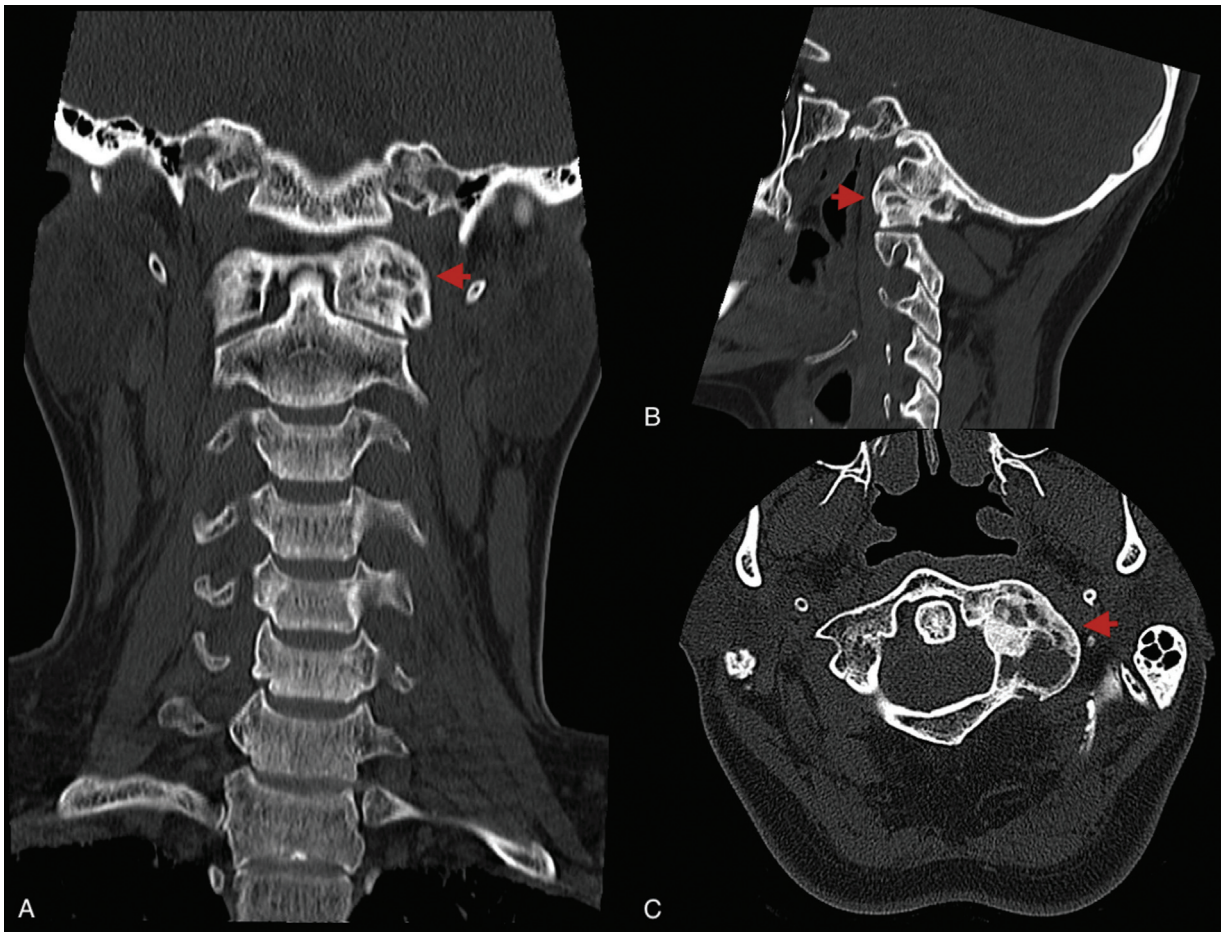

Fig. 4 Cervical computed tomography scan with no contrast four months into the treatment. Coronal (**A**), sagittal (**B**), and axial (**C**) sections showing signs of early corticalization within the lesion.

adherence, except for occasional nausea, which was well tolerated. We removed the Philadelphia collar and extended the treatment for another six months with monthly controls. At nine months, the patient was completely asymptomatic. After treatment completion, at twelve months, a CT scan revealed great corticalization of the lesion (►**Figure 5**), with no clinical or laboratory complications. Six months after treatment, we requested the last imaging study, a CT, which showed no evidence of tumor recurrence (►**Figure 6**). After one year of follow-up, the patient remains asymptomatic and with no treatment-related complications.

Discussion

Historically, ABCs have been attributed to an increase in venous bone pressure leading to small vessel dilation and subsequent bone matrix resorption. From a histological point of view, ABCs comprise cavitary lesions filled with blood and delimited by connective tissue, including fibroblasts and multinucleated giant cells. Recent studies[2,4,5] have shown the expression of the USP6 oncogene, which stops osteoblast maturation and increases the synthesis of metalloproteinases through the RANK-RANKL (Receptor activator of nuclear factor kappa beta - Receptor activator of nuclear factor kappa beta ligand) pathway; the latter is favored by the high RANK expression in multinucleated giant cells, in a behavior similar to that of GCTs.

In recent years and based on the positive experience with denosumab in GCTs, proposals have been made to extend its indication to recurrent ABCs or those with high surgical risk, because of denosumab's blocking effect on RANKL. Denosumab is usually well-tolerated and safe. However, it can trigger vomiting, fatigue, muscle pain, asymptomatic hypocalcemia, and severe rebound hypercalcemia after denosumab cessation, requiring a strict follow-up during and after treatment. Denosumab may cause other general complications, including mandibular osteonecrosis, infections, atypical fractures, and delayed growth. These complications have not been reported in ABC patients.[2,6–10]

The literature reports few cases of ABC treatment with denosumab, as pointed out by Alhumaid and Abu-Zaid,[2] who reviewed the literature available on PubMed from 1990 to 2019 using the keywords *aneurysmal bone cyst* and *denosumab*, and found a total of 12 studies and only 30 patients. When we considered this therapeutic alternative in the case herein reported, their study was the major review available. On the other hand, as far as we know, a report from Patel et al.[3] is the only one published which is similar to ours; this study was used as a reference and guided our decisions.

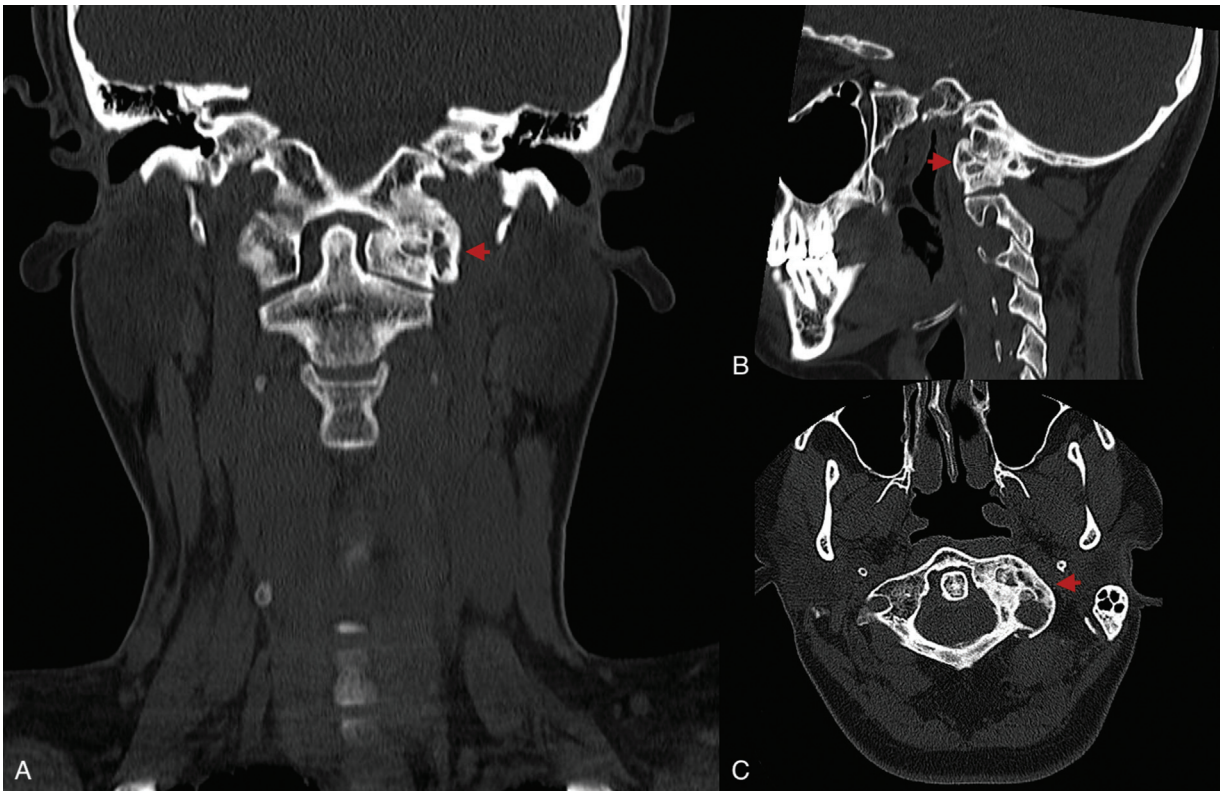

Fig. 5 Cervical computed tomography scan with no contrast twelve months into the treatment. Coronal (**A**), sagittal (**B**), and axial (**C**) sections showing significant lesion corticalization.

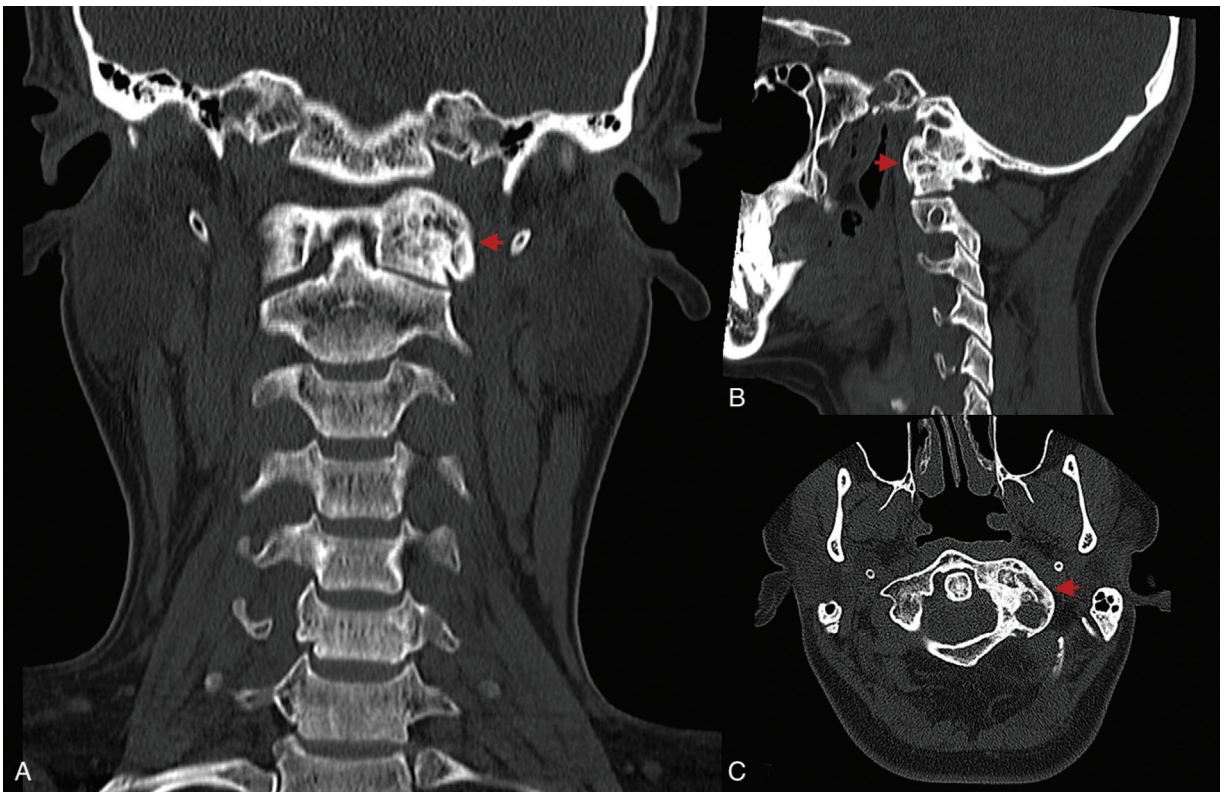

Fig. 6 Cervical computed tomography scan with no contrast six months after the treatment. Coronal (**A**), sagittal (**B**), and axial (**C**) sections showing that the lesion is virtually similar to the previous examination.

Denosumab is well established as a safe treatment. It resulted in good preliminary clinical and imaging outcomes in patients with locally advanced, recurrent, or inoperable ABCs. Its indication is very recent; until now, there is no single protocol or treatment recommendation for denosumab in ABCs, and this is why some clinical trials have extrapolated the denosumab regimen in GCTs to ABCs. However, further studies are required to establish solid conclusions.

Conflict of Interests
The authors have no conflict of interests to declare.

Level of evidence
Level of evidence: type V.

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