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DIAGNOSIS IN ONCOLOGY

Giant-Cell Tumor of the Tendon Sheath in the Upper Cervical Spine

Introduction

Giant-cell tumor of the tendon sheath (GCTTS) is part of the group of synovial tumors that can affect joints, bursas, and tendon sheaths.[1,2] It is rare for GCTTS to involve the spine. When present, it is more common in the lower cervical spine. In the literature, there are only four cases described in the upper cervical spine.[2-5] In this report, we describe a rare case of GCTTS in the upper cervical spine, which was treated with en-bloc marginal resection.

Case Report

A 31-year-old patient, previously asymptomatic, underwent computed tomography (CT) of the cranium for investigation of a complicated otitis media. The imaging examination revealed a tumor of the upper cervical spine. The lesion was located in the region of the intervertebral foramina between C1 and C2, on the right side, with a mass of soft tissue in the epidural and foraminal regions involving the root of C2. There were no signs of bone destruction on cervical angiotomography of the spine, which revealed proximity to the tumor and vertebral artery (Fig 1; [A] computed angiotomography with paramedian right sagittal reconstruction showing the lesion and the vertebral artery; [B and C] axial slices demonstrating the involvement of the C1-C2 foramen and the relationship with the right vertebral artery). Tomographies of the chest, abdomen, and pelvis; bone scintigraphy with technetium; and cervical spine magnetic resonance imaging (MRI) examinations were performed, and no other neoplastic lesions were found (Fig 2; axial cervical spine MRI with gadolinium showing [A] lesion at C1-C2, involving right C2 nerve root, and [B] lesion around the lamina of C2).

The patient underwent a percutaneous biopsy guided by CT. Little material could be obtained, and the anatomopathologic result, although inconclusive, was suggestive of malignant neoplasm.

Three months after identification of the neoplasia, the patient began to experience intense, progressive pain in the upper cervical region, with right occipital and hemicranial pain. Because of the lack of a conclusive anatomopathologic result and the presence of symptoms related to tumor growth, surgical treatment was indicated, aimed at en-bloc resection of the tumor.

The surgical procedure was performed through a posterior approach to the upper cervical spine. A fibroelastic mass was identified in the foraminal region between C1 and C2, involving the laminae of C1 and C2, without evident signs of bone involvement at surgery (Fig 3; operative view of the lesion, between the C1 arch and the C2 lamina, at right). A right hemilaminectomy of C1 and C2 was performed to remove the tumor. The root of C2, on the right, was ligated, and the tumor was resected en bloc. At the end of the procedure, an accidental lesion of the right vertebral artery was identified. The artery was ligated, without any functional complications in the postoperative period.

The anatomopathologic examination showed a tumor weighing 5 g, with a volume of 2.2 × 2.0 × 1.5 cm and marginal margins. The

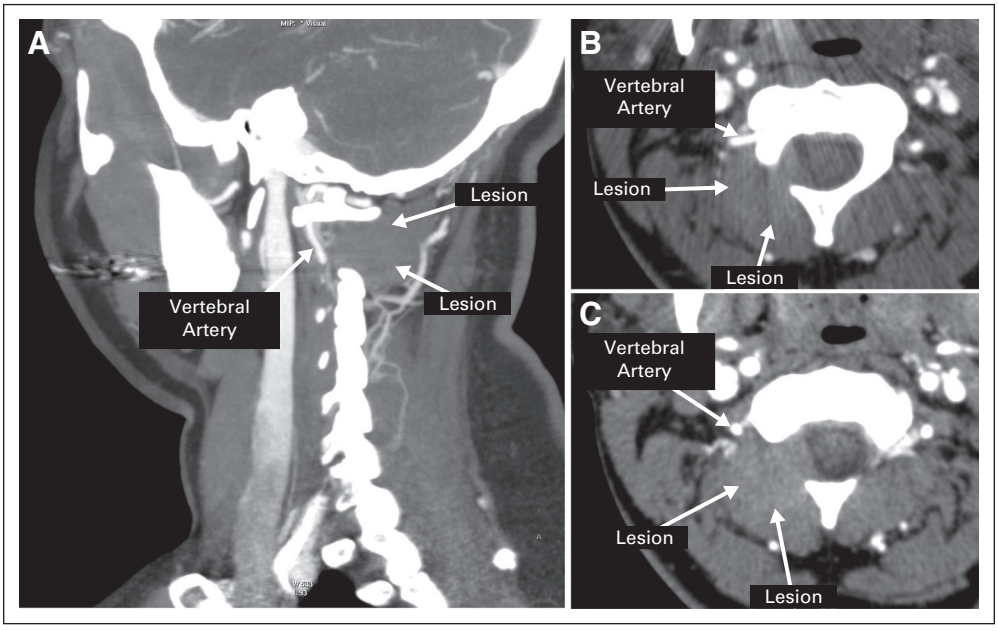

Fig 1.

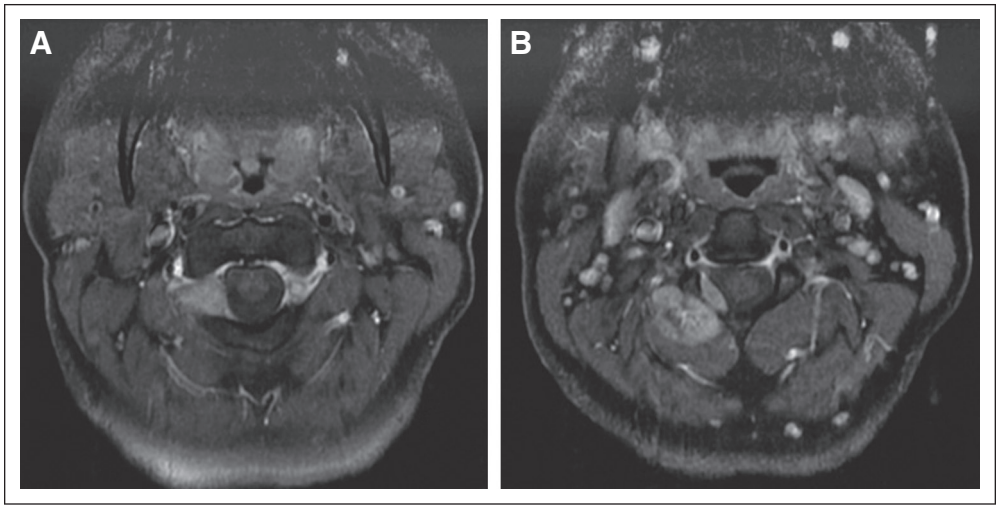

Fig 2.

result of the immunohistochemical examination (Table 1) was compatible with localized GCTTS (Fig 4; nodular fragment of tissue, measuring 2.2 × 2.0 × 1.5 cm after ressection).

The patient continued without postoperative complications, and the headaches disappeared. After 18 months of follow-up, she presented with mild, intermittent cervical pain and a reduction of approximately 30% in the cervical rotation range of movement. The control MRI at that time showed no signs of tumor recurrence (Fig 5; control magnetic resonance imaging, showing no signs of tumor recurrence; white arrow indicates absence of flux in right vertebral artery).

Discussion

GCTTS is also known as pigmented villonodular synovitis. It can be divided into two forms: localized and diffuse. The diffuse form is generally found in the large joints, like the knee or hip. The localized form is more common, and it more often occurs in the hands, feet, and knees.[1]

Approximately 50 cases of GCTTS of the spine are described in the literature. Approximately half of all cases occur in the lower cervical region, followed by the lumbar and thoracic spine.[3,6,7] The upper cervical region is a rare site for the occurrence of GCTTS, and only four cases have been described to date.[2-5]

Because of its rarity, GCTTS of the axial skeleton is often not included in the differential diagnoses for lesions of the upper cervical spine. There is often an extension of the tumor into the epidural space; therefore, the differential diagnosis in imaging examinations includes benign diseases, such as schwannomas and meningiomas, and malignant diseases, like metastases.[8-10]

The pathogenic mechanisms of GCTTS are still unknown. They are characterized by a proliferation of mononuclear, often circumscribed, cells. There are also variable numbers of multinucleated osteoclast and inflammatory cells, with fibrous, hyalinized stroma. Cytogenetic studies show numeric and clonal chromosome changes, suggesting a neoplastic cytogenetic mechanism.[11,12] GCTTS express high levels of colony-stimulating factor 1 receptor (CSF1R).[12] West et al[12] determined that the *CSF1* gene, which encodes the ligand of CSF1R, is translocated in only 2% to 16% of tumor cells, suggesting that only few GCTTS cells are neoplastic. Most cells in the tumor

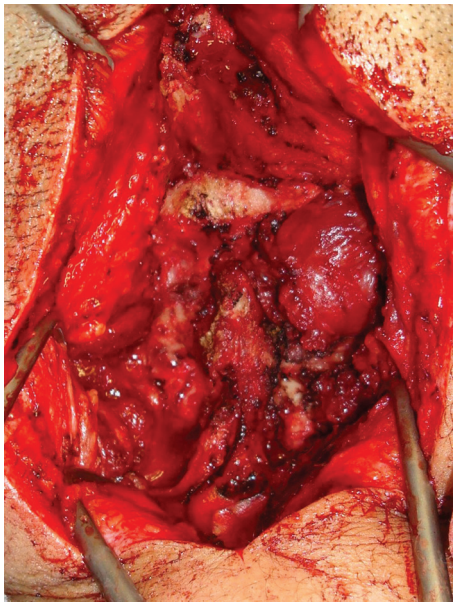

Fig 3.

Table 1. Immunohistochemistry Results

Antigen	Result
KI-67	Positive (low index)
EMA	Negative
Vimentine	Positive
CD68	Positive
CD34	Negative
Protein S100	Negative
Desmine	Negative

Abbreviation: EMA, epithelial membrane antigen.

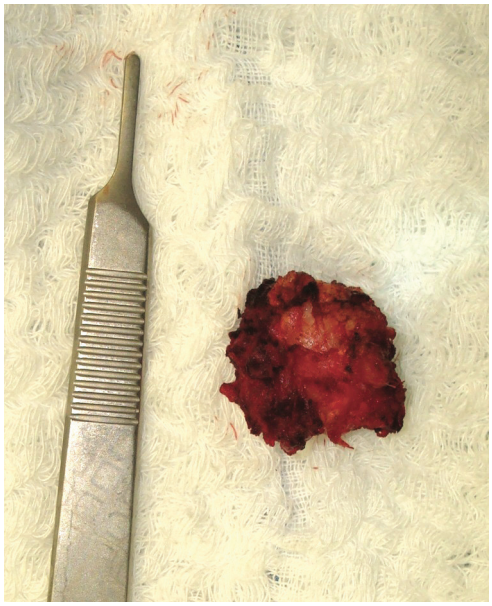

Fig 4.

would be reactive and recruited by the increased production of CSF1 by the neoplastic cells.[12]

Immunohistochemical and electronic microscopic findings show that proliferating cells have characteristics of synovial cells and fibroblasts as well as hystiocytes. Recently, the immunohistochemical marker clusterin, which is normally expressed in normal synoviocytes, was also shown to be positive in GCTTS, in both diffuse and localized forms.[13] This characteristic demonstrates that neoplastic cells have synovial differentiation.

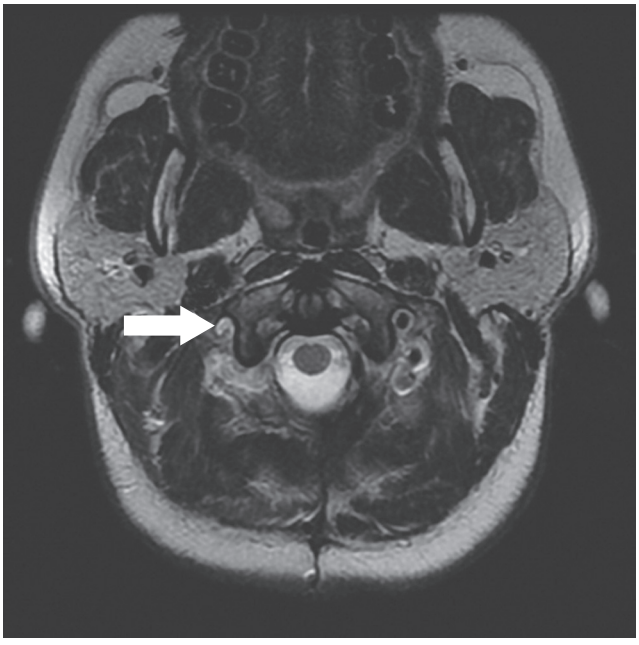

Fig 5.

The high cellularity of this lesion, along with the presence of frequent mitoses, can lead to incorrect interpretation of a sarcoma. The differential diagnosis in the pathologic anatomy includes epithelioid sarcoma and malignant fibrous hystiocytoma, which present necrosis and anaplasia. Pigmented villonodular synovitis located in the joint is histologically similar.[13] However, it has papillary projections and pseudoglandular spaces covered by synovial cells as well as hemosiderin.

It was once thought that GCTTS was more common in women,[3] but in fact, it is equally distributed between sexes.[3,6] It can occur in from age 7 to 81 years; there have been a high number of patient cases between the third and fifth decades of life.[3,6,14]

In the vertebral column, the most common description of the origin of the tumor is the synovial membrane of the facet joints,[3] but it can also originate in bursas.[2] It is not always possible to correctly identify the origin of the lesion. In our patient, the lesion probably originated in the facet joint between C1 and C2, and tumor growth was predominantly extra-articular.

GCTTS of the spine can be asymptomatic or may be associated with axial pain, radicular pain, or neurologic deficit, depending on the size and location of the tumor.[3] In the case described here, the patient's symptoms were related to compression of the C2 nerve root on the right side.

In imaging examinations, GCTTS may have a variable appearance. In a CT scan, the lesion may demonstrate hyperattenuation resulting from hemosiderin content.[7] The matrix of the tumor is rarely calcified.[10] Sometimes, it occurs as a tumor in the soft tissue and, other times, as a destructive bone lesion with pressure erosion, and sclerotic margins of the posterior elements of the vertebra, associated with a nodular soft tissue mass.[10] In our patient, the lesion caused a widening of the foraminal space between C1 and C2 with bone remodeling as a result of the growth of soft tissue mass.

In an MRI, the lesion is isointense to the muscle in T1-weighted images. Areas of low or intermediary signal can be found because of the presence of hemosiderin, which is accentuated in echo gradient sequences in T2-weighted images.[10,15] However, it can demonstrate variable appearance depending on mass composition, which may have variable content of hemosiderin, liquid, lipids, fibrous tissue, and hemorrhage.[10] The small number of described GCTTS cases occurring in the spine, along with the variable character of the MRI, makes differential diagnosis of the tumor difficult.[10] In our patient, the GCTTS diagnosis was not considered among the diagnostic possibilities during evaluation of the imaging examinations.

The recommended treatment for GCTTS, because of its aggressive nature, is complete resection whenever possible.[16-18] In the spine, the estimated rate of local recurrence is 18%,[6] which is comparable to that of GCTTS of the apendicular skeleton.[19] Our patient has been undergoing follow-up for 18 months, without any signs of local relapse in imaging examinations after marginal en-bloc resection.

Recently, the use of imatinib was described for treating tenosynovial sheath giant-cell tumor in patients with recurrent or irresecable lesions.[20,21] Cassier et al[22] performed an international multicentric retrospective study to evaluate the use of imatinib in 16 patients with GCTTS. One patient (6%) had a complete response, two (13%) had partial responses, and in eight (50%), the disease stabilized. It seems that the use of imatinib is promising for patients with recurrent and inoperable lesions, although this should be confirmed by prospective

clinical studies. The inhibition of tumoral growth may be mediated by imatinib activity against CSF1R.[22,23]

Despite the rarity of the disease, GCTTS should be considered during differential diagnosis of lesions of the axial skeleton located close to the intervertebral foramen. Knowledge of the existence of this tumor is important, because the radiologic characteristics can simulate other neoplastic diseases of the spine.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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