

Chondroid Tenosynovial Giant Cell Tumor of the Temporomandibular Joint: A Rare Case Report

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Tenosynovial giant cell tumor of diffuse type (TGCT-d) or pigmented villonodular synovitis (PVNS) is a locally aggressive lesion that mostly affects the joints of long bones. Chondroid tenosynovial giant cell tumor (CTGCT) or PVNS with chondroid metaplasia is a rare distinct subset of synovial tumors that has a predilection for the TMJ. We report a rare case of CTGCT in the TMJ, initially misdiagnosed as temporomandibular disorder (TMD). A 51-year-old woman was referred to the surgeon with the chief complaint of TMJ pain for 5 years and a past history of an unsuccessful TMD treatment. Extraoral examination revealed discrete preauricular swelling and restricted mandibular range of motion. Panoramic radiograph and computerized tomography showed destruction of the mandibular fossa and condyle. Histologically, the tumor was composed by large mononuclear cells with prominent eosinophilic cytoplasm and grooved nuclei, small histiocytoid cells, osteoclast-like multinucleated cells, brown pigmentation and areas of chondroid metaplasia. Morphological and immunohistochemical characteristics lead to the final diagnosis of CTGCT. The rarity of CTGCT could be attributed to the lack of recognition of this lesion, with cases diagnosed as chondroblastomas, synovial chondromatosis and chondrosarcoma. The patient received immediate reconstruction and recurrence was found 22 months after initial intervention. TGCT-d and CTGCT of the TMJ can present similar symptoms to TMD, but clinicians must distinguish both lesions by complete examination, imaging and, when necessary, histopathologic evaluation.

Introduction

Tenosynovial giant cell tumor of diffuse type (TGCT-d) or pigmented villonodular synovitis (PVNS) is a rare locally aggressive lesion of the synovium with features of both inflammatory disorder and neoplasm, that affects predominantly the knee and hip of patients mostly between 20-40 years, with a female predominance (1,2). It may be intra or extra-articular. The most common features seen in patients with TGCT-d are pain, swelling, tenderness and limitation of motion (2). Histologically, TGCT-d is composed by synovial-like mononuclear cells, multinucleated giant cells, histiocytoid cells, foamy macrophages and other inflammatory cells, associated with pigment deposition (hemosiderin), with variable proportions of each component, with cells that are arranged in a nodular or villous architecture (3,4). Although it had been considered for a long time solely as an inflammatory process, its neoplastic origin has been demonstrated (2,5) by the presence of chromosomal translocation involving chromosome 1p13 and overexpression of the gene encoding colony-stimulating factor (CSF)-1. Only a minority of cells has the translocation and overproduces CSF-1, which attracts a secondary non-neoplastic population of histiocytes (5).

TGCT-d rarely affects the temporomandibular joint (TMJ), and only 116 cases affecting this joint were reported in the literature up to November 2016 (4,6,7). Chondroid tenosynovial giant cell tumor (CTGCT) or PVNS with chondroid metaplasia is a distinct subset of synovial tumors (8) that was first reported in 1990 (9) and has a predilection for the TMJ. Up to now, only 30 well-documented cases of CTGCT affecting TMJ have been described in the English language literature (3,4,7,8,10,11). We present herein an additional case of CTGCT, affecting TMJ, initially misdiagnosed as TMJ disorder, and discuss the differential diagnosis.

Case Report

A 51-year-old Caucasian woman was referred to the surgeon with the chief complaint of TMJ pain for 5 years and a past history of an unsuccessful TMD treatment. Extraoral examination revealed discrete preauricular swelling and restricted mandibular range of motion.

In panoramic radiograph, a destructive lesion involving the right glenoid fossa and articular tubercle could be seen (Fig. 1). Computed tomography (CT) showed temporal bone destruction in glenoid fossa and a hypodense area in the

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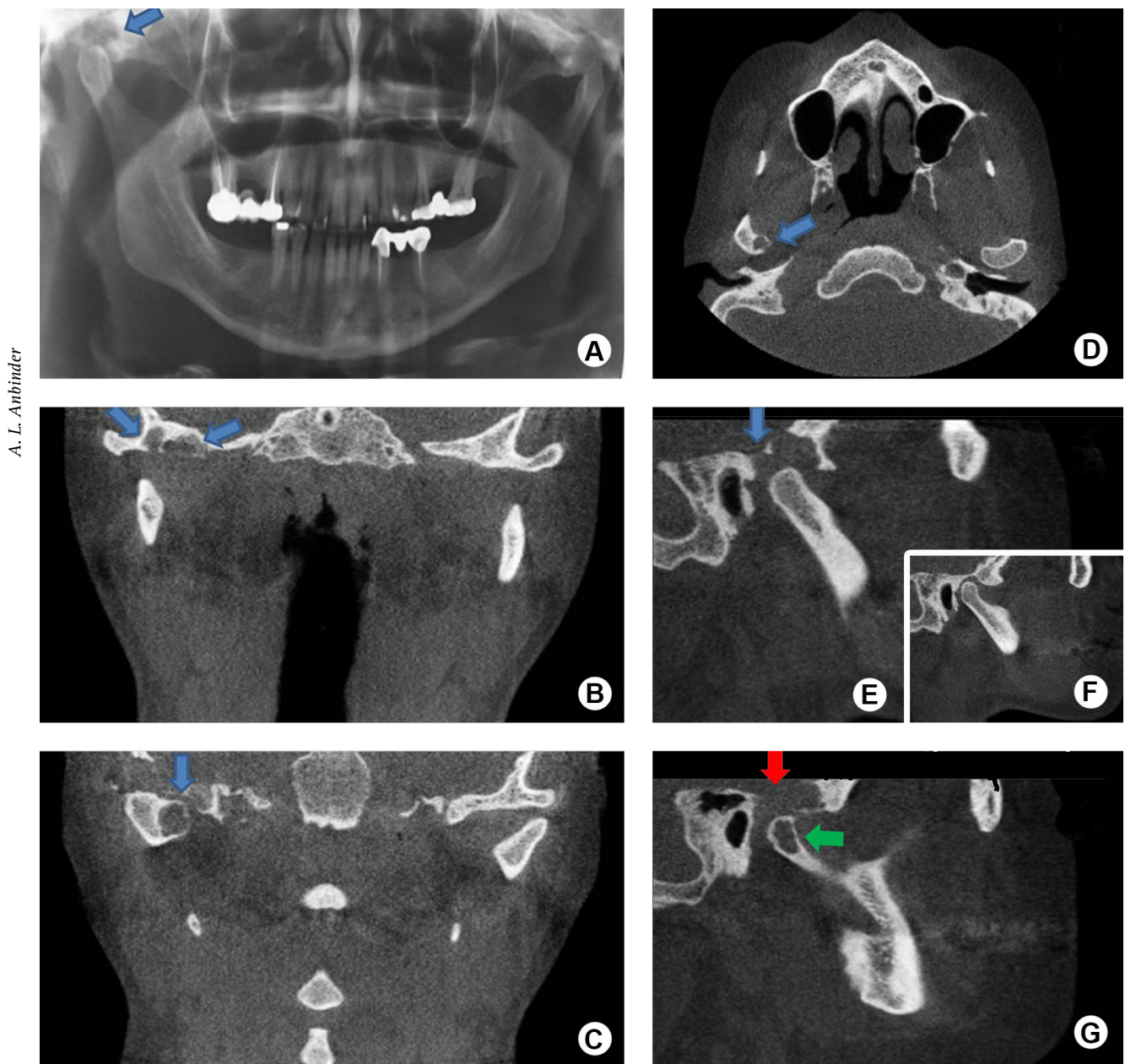
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right condyle (Fig. 1).

Clinical and imaging features of destructive growth lead to the main diagnostic hypothesis of chondrosarcoma, osteosarcoma, chondroblastoma and TGCT-d. Histologically (Fig. 2), at low magnification, the tumor was composed by cells arranged in nodules or sheets with hyaline tissue between them. At high magnification, the lesion comprised synovium-like monocytes, small histiocytoid cells, osteoclast-like multinucleated cells, brown pigmentation and areas of chondroid metaplasia. The synovium-like

monocytes showed abundant cytoplasm, eccentric and reniform nuclei and eosinophilic to amphophilic cytoplasm, that lined several cleft-like spaces. Brown pigmentation could be seen inside some cells or dispersed in the stroma. Around 40 to 50% of the lesion was composed by hyaline chondroid areas, where focal dystrophic lace-like calcification, resembling the "chicken wire" calcification of chondroblastomas could be found. Neither necrosis nor mitotic figures were identified. The differential diagnosis before immunohistochemical (IHC) analysis included



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Figure 1. Imaging aspects of the lesion. A. Panoramic radiograph showing a lesion in right glenoid fossa and articular tubercle (arrow). B. Coronal view of computerized tomography (CT) showing temporal bone destruction (arrow). C. Coronal CT showing a hypodense area in the right condyle (arrow). D. In the axial view of CT, a hypodense area in the right condyle can also be seen (arrow). E. Destruction of right glenoid fossa seen in sagittal CT, to be compared to the normal left side (F). G. In this sagittal cut, bony resorption of glenoid fossa (red arrow) and a hypodense area in the right condyle (green arrow) can be seen.

TGCT-d, chondroblastoma, chondrosarcoma and synovial chondromatosis.

Immunohistochemical stains for podoplanin (D2-40), CD68, S-100 protein and Ki-67 (Dako, Glostrup, Denmark) were performed using a streptavidin-biotin-peroxidase method. The antibodies used are listed in Table 1.

Giant cells and mononuclear cells (especially histiocyte-like) showed positive immunoreactivity for CD68.

Table 1. Antibodies used in this study

Primary antibody	Clone	Dilution
Podoplanin	D2-40	1:100
CD68	PG-M1	1:400
S-100	Rabbit anti-human (polyclonal)	1:10,000
Ki-67	MIB-1	1:100

Podoplanin (D2-40) was expressed in the synovium-like monocytes and S-100 protein staining was positive mainly in the chondrocytes of the cartilaginous metaplasia area. The lesion presented low Ki-67 labeling index (Fig. 3).

Morphological and IHC characteristics led to the final diagnosis of TGCT-d with chondroid metaplasia, also known as CTGCT. The condyle was affected by the lesion, and, after condilectomy and removal of the entire TMJ capsule and disc, the involvement of these structures could be seen histologically. The temporal bone showed areas of destruction, but during surgery, the dura mater was found to be intact. The temporal bone was treated by curettage. The patient received a patient-fitted TMJ implant (TMJ Concepts, Venture, CA, USA), composed by a mesh backing of unalloyed titanium, articular bearing of ultra-high molecular weight polyethylene (UHMWPE) and contoured mandibular body of Ti-6Al-4V ELI. Twenty-two months after the surgery, the lesion has recurred. A multilocular hypodense diffuse lesion could be seen in

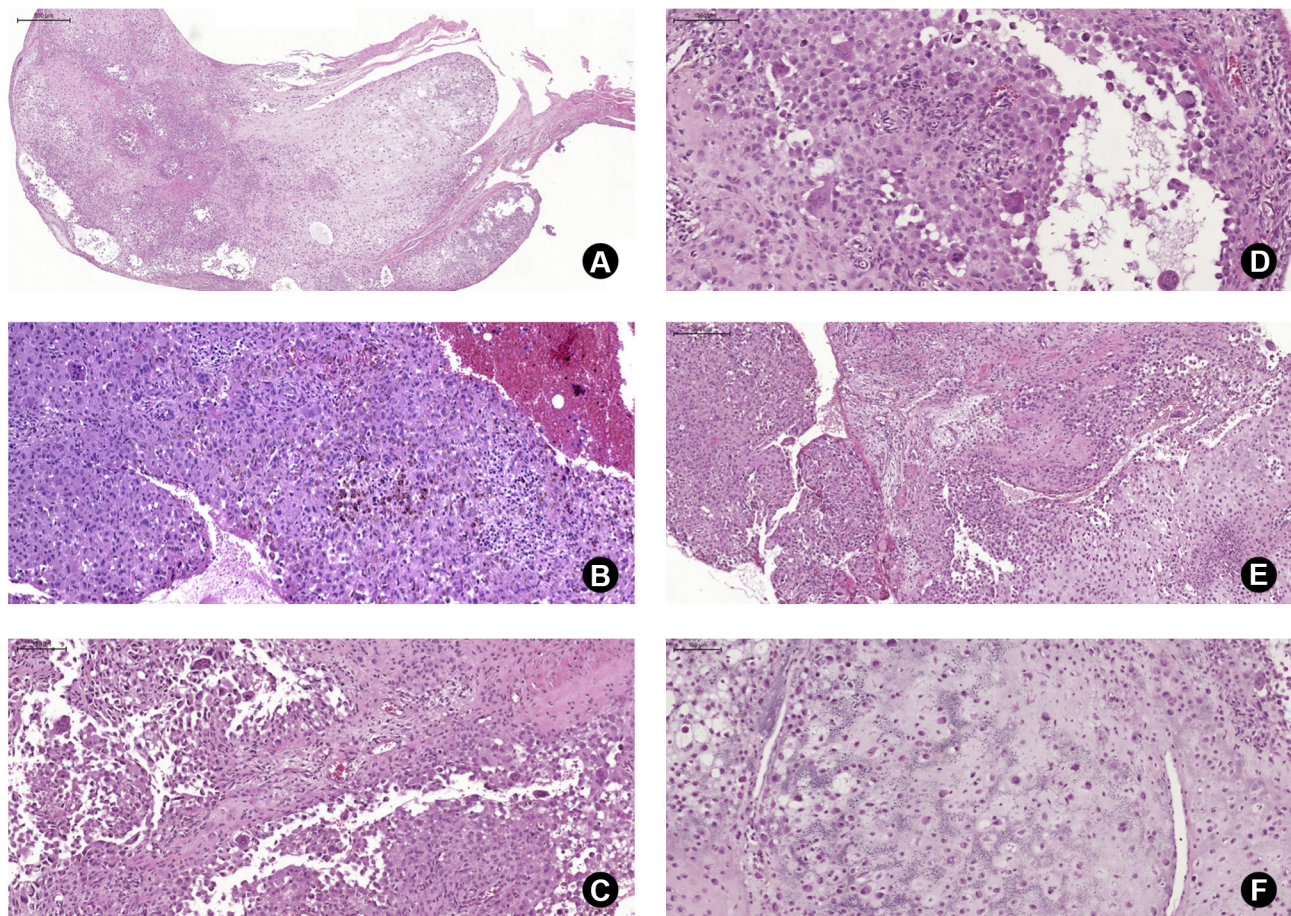


Figure 2. Histological features of the lesion. H&E staining. A: Nodule composed by sheet of cells (left) and chondroid metaplasia (right). B: Multinucleated giant cells, mononuclear cells and hemosiderin pigment. C: Multinucleated giant cells, mononuclear cells and cleft-like spaces. D: Giant cells and synovium-like cells with eccentric and reniform nuclei. Cleft-like space lined by mononuclear cells. E: Area composed by traditional TGCT-d pattern (upper left) and chondroid metaplasia (lower right). F: Chondroid matrix with "chicken wire" calcification resembling chondroblastoma.

temporal bone, over the TMJ reconstruction although the patient was asymptomatic. The new treatment planning involved complete surgical resection followed by adjuvant postoperative radiotherapy.

Discussion

TGCT-d is a rare disease, with an annual incidence estimated at 1.8 cases per million US inhabitants (12), which usually occurs in the extremities and rarely affects the TMJ. Painful or painless preauricular mass with swelling, sensation of heat, trismus and TMJ clicking are common symptoms related to TGCT-d (13). Due to non-specific clinical symptoms, the diagnosis is, many times, a parotid mass or TMD, and years may elapse until a proper diagnosis is reached (14). Although TGCT-d is a locally aggressive lesion, the development and symptoms are usually of relatively long duration (2), and in a recent review of 32 cases of TGCT-d in TMJ (4), the preoperative duration ranged from 6 to 180 months. In the present case, the patient was treated

of a misdiagnosed TMD for 5 years before the final diagnosis and treatment. The possibility of misdiagnosis on these cases should draw the attention of clinicians to consider a patient's complete examination before establishing the etiology and proper treatment, especially facing unspecific symptoms. Furthermore, TGCT-d should be included in the differential diagnosis, despite its rarity (13,15).

Panoramic radiographs, CT and magnetic resonance (MRI) are ancillary techniques useful in TGCT-d diagnosis. While panoramic radiographs are nonspecific, CT clearly defines the extent of the tumor. The most useful, however, seems to be MRI, where a nearly pathognomonic TGCT-d characteristic can be found (16,17): the blooming effect, that refers to the presence of hemosiderin as the cause of the low signal intensity in MRI (18). As hemosiderin is a magnetic material, its deposition in the lesion results in spotty or extensive low signal area within synovial masses on T1- (T1W1) and T2- weighted (T2W2) images (16). Unfortunately, MRI was not available at the time of

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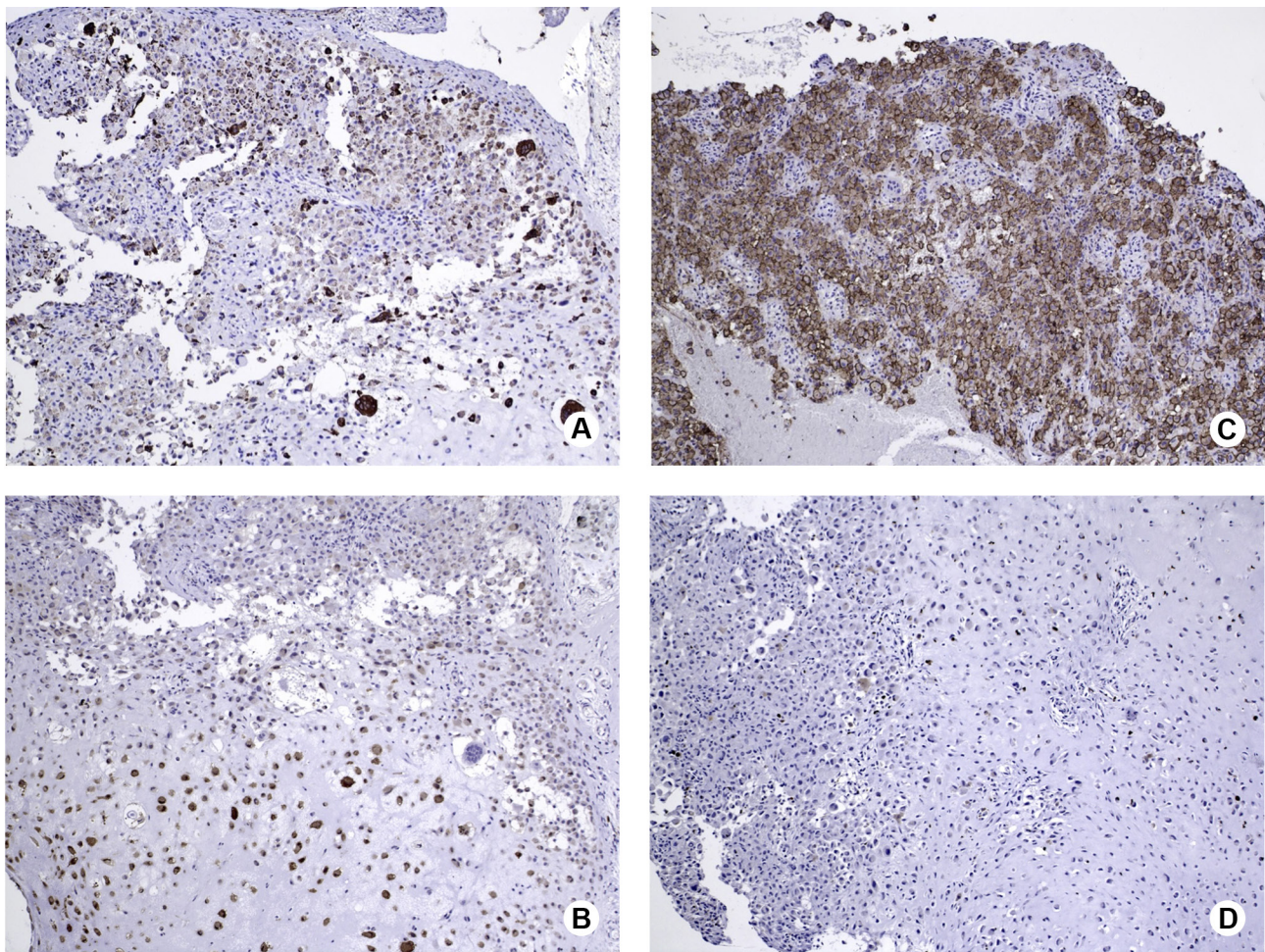


Figure 3. Immunohistochemical features of the lesion. A. Giant cells and mononuclear cells (especially histiocyte-like) showed positive immunoreactivity for CD68. B. S-100 staining was positive mainly in the chondrocytes of the cartilaginous metaplasia area. C. Podoplanin (D2-40) was expressed in the synovium-like monocytes. D. The lesion presented low Ki-67 labeling index. Original magnification $\times 200$.

diagnosis in our case.

In the literature, the main clinical differential diagnosis of TGCT-d in TMJ includes parotid tumors, rheumatoid arthritis, synovial hemangioma, synovial osteochondromatosis, chondroma, osteochondroma, gout, calcium pyrophosphate deposition disease or tophaceous pseudogout, chronic osteomyelitis, central giant cell lesion, sarcomas and metastasis (19). In the present case, the main clinical diagnostic hypotheses are chondrosarcoma, chondroblastoma and TGCT-d. All these lesions can cause long-term painful masses in TMJ of patients over 50 years old, with a destructive radiolucent/hypodense image.

CTGCT was first described 26 years ago, as a diffuse TGCT-d with a cartilaginous component (9). Since then, several other cases of CTGCT affecting TMJ were described and considered as a variant of TGCT-d (4,10,11) because of the presence of typical features of TGCT-d within the tumor. Although TGCT-d rarely affects TMJ, CTGCT has a predilection for this joint (8). The rarity of CTGCT could be attributed to the lack of recognition of this lesion, with cases diagnosed as chondroblastomas, synovial chondromatosis and chondrosarcoma. This could be explained by the varied matrix patterns mimicking other chondroid lesions and by fact that a component of conventional TGCT-d may be focal (3).

Histologically, conventional TGCT-d consists of a mononuclear component and osteoclast giant cells scattered throughout the tumor. The mononuclear component comprises small histiocytic cells and larger and round synovium-like cells with abundant eosinophilic to amphophilic cytoplasm, as well as sheets of foam cells and hemosiderin pigment (3).

Immunohistochemical studies are helpful in diagnosing TGCT-d. Small histiocytoid cells express CD163 (3,20), CD68 (10,11) and HAM56 (21) and are negative for S-100 protein (3, 10). The multinucleated giant cells express CD68 (10) and HAM56 (21), but not CD163 (20). Moreover, larger monocytoïd cells are positive to podoplanin and

clusterin, markers of synovial differentiation, and tumor cells with dendritic cytoplasm are focally positive to desmin (3,20). Although TGCT-d and CTGCT have the same immunophenotype, a nodular growth pattern predominates in cases with more extensive chondroid metaplasia instead of the villonodular pattern, common in conventional TGCT-d. The amount of chondroid matrix formation may vary from case to case, but CTGCT usually do not present foamy macrophages (3). Accordingly, in the present case, there was a nodular growth pattern and no cluster of foamy macrophages was found.

Cells in the chondroid component in CTGCT are similar to synovium-like cells, with large cytoplasm and grooved nuclei, however, they are chondroblasts that express S-100 protein (10). Besides the presence in chondroid areas, scattered dendritic S-100 positive cells, in aggregates throughout the tumor, were found in 67% of TGCT-d (21).

Because of the presence of chondroid metaplasia, the histological differential diagnosis of CTGCT includes lesions with chondroid differentiation as chondroblastoma, synovial chondromatosis, chondrosarcoma and calcium pyrophosphate deposition disease. Several histological and immunohistochemical features may help the differentiation among them (Table 2).

The gold standard treatment of TGCT-d is complete surgical resection. In case of severe primary or recurrent disease, adjunct treatment should be considered (17). Several adjuvant treatments have been cited in the literature, as external beam radiotherapy, cryosurgery, radiosynovectomy and immunotherapy (tumor necrosis factor (TNF)-alpha blockers and CSF-1 receptor-directed target therapy), with best results found, up to now, after postoperative radiotherapy (17). For TMJ lesions, dose fraction schemes include 15-25 fractions with doses ranging from 35-45 Gy (6). These patients must be followed up with CT or MRI due to the infiltrative nature of this lesion and the high recurrence rate that has been estimated between 18 and 46% for intraarticular lesions (2). In a recent review

Table 2. Important histological and immunohistochemical features of lesions included in the differential diagnosis of chondroid tenosynovial giant cell tumor

Lesion	Features
Chondroblastoma	Sheets of a single population of mononuclear cells (chondroblasts with eccentric grooved nuclei), while in CTGCT there are synovial-like monocytoïd cells and smaller histiocytoid cells. Chondroblasts are negative to synovial markers (podoplanin and clusterin) and CD68, but positive to S-100 protein
Synovial chondromatosis	Chondrocytes (S-100 positive) form clusters at the periphery of hyaline cartilage lobules. It lacks hemosiderin deposition and synovial-like monocytoïd cells hyperplasia
Chondrosarcoma	Variation in the degree of cellular atypia throughout the tumor. Cells are positive to S-100 protein and negative to synovial markers
Calcium pyrophosphate deposition disease	Polarizable crystal deposits and foreign body giant cell reaction

of 237 cases of TGCT-d, Xie et al. (1) found a recurrence rate of 20.25%, while analyzing just TMJ lesions, Zhang et al. (4) found 18.75% of recurrence.

In summary, TGCT-d can present similar clinical symptoms to a TMD, but clinicians must distinguish both lesions by complete examination, imaging and, when necessary, histopathological evaluation. Histologically, CTGCT may mimic lesions with chondroid differentiation as chondroblastoma, synovial chondromatosis, chondrosarcoma and calcium pyrophosphate deposition disease. Immunohistochemistry with the use of markers of synovial differentiation is especially helpful to final diagnosis achievement.

Resumo

Tumor de células gigantes tenossinovial do tipo difuso (TCGT-d) ou sinovite vilonodular pigmentada (SVP) é uma lesão localmente agressiva que afeta principalmente as articulações dos ossos longos. Tumor de células gigantes tenossinovial condroide (TCGTC) ou SVP com metaplasia condroide é um tipo distinto e raro de tumor sinovial que tem a predileção pela articulação temporomandibular (ATM). Nós relatamos um caso raro de TCGTC da ATM, inicialmente diagnosticado, equivocadamente, como disfunção temporomandibular (DTM). Uma mulher de 51 anos foi encaminhada ao cirurgião com a queixa principal de dor na ATM por 5 anos, e uma história de tratamento de DTM sem sucesso. O exame extrabucal revelou discreto aumento de volume preauricular e movimentação mandibular restrita. A radiografia panorâmica e a tomografia computadorizada evidenciaram destruição da fossa mandibular e côndilo. Histologicamente, o tumor era composto por células mononucleares grandes, com amplo citoplasma eosinofílico e núcleo sulcado, pequenas células histiocitoides, células multinucleadas semelhantes a osteoclastos, pigmentação acastanhada e áreas de metaplasia condroide. As características morfológicas e imuno-histoquímicas levaram ao diagnóstico final de TCGTC. A raridade desta lesão pode estar associada ao seu não reconhecimento, sendo casos diagnosticados como condroblastoma, condromatose sinovial ou condrossarcoma. A paciente recebeu reconstrução imediata e recorrência foi observada 22 meses após a intervenção inicial. TCGT-d e TCGTC da ATM podem apresentar sintomas similares à DTM, mas os clínicos devem diferenciar ambas as lesões por meio do exame clínico completo, exames de imagem e, quando necessário, avaliação histopatológica.

References

- Xie GP, Jiang N, Liang CX, Zeng JC, Chen ZY, Xu Q, et al. Pigmented villonodular synovitis: a retrospective multicenter study of 237 cases. *PLoS One* 2015;10:e0121451.
- Fletcher CD, Bridge JA, Hogendoorn PC, Mertens F. WHO Classification of Tumors of Soft Tissue and Bone. 4th ed. Lyon, France: International Agency for Research on Cancer (IARC); 2013. 468 p.
- Hoch BL, Garcia RA, Smalberger GJ. Chondroid tenosynovial giant cell tumor: a clinicopathological and immunohistochemical analysis of 5 new cases. *Int J Surg Pathol*. 2011;19:180-187.
- Zhang C, Zhu L, Wang L, Hu Y, Li J, Tian Z. Diffuse tenosynovial giant cell tumor in the temporomandibular joint area in a Chinese population: a clinicopathological analysis of 32 cases. *Int J Clin Exp Pathol* 2016;9:1105-1115.

- West RB, Rubin BP, Miller MA, Subramanian S, Kaygusuz G, Montgomery K, et al. A landscape effect in tenosynovial giant-cell tumor from activation of CSF1 expression by a translocation in a minority of tumor cells. *Proc Natl Acad Sci USA* 2006;103:690-695.
- Joshi K, Huang B, Scanga L, Buchman C, Chera BS. Postoperative radiotherapy for diffuse pigmented villonodular synovitis of the temporomandibular joint. *Am J Otolaryngol* 2015;36:106-113.
- Carlson ML, Osetinsky LM, Alon EE, Inwards CY, Lane JI, Moore EJ. Tenosynovial giant cell tumors of the temporomandibular joint and lateral skull base: Review of 11 cases. *Laryngoscope* 2017;127:2340-2346.
- Fisher M, Biddinger P, Folpe AL, McKinnon B. Chondroid tenosynovial giant cell tumor of the temporal bone. *Otol Neurotol*. 2013;34:e49-e50.
- Pignatti G, Mignani G, Bacchini P, Calderoni P, Campanacci M. Case report 590: Diffuse pigmented villonodular synovitis with a cartilaginous component. *Skeletal Radiol*. 1990;19:65-67.
- Oda Y, Izumi T, Harimaya K, Segawa Y, Ishihara S, Komune S, et al. Pigmented villonodular synovitis with chondroid metaplasia, resembling chondroblastoma of the bone: a report of three cases. *Mod Pathol*. 2007;20(5):545-51.
- Pina S, Fernandez M, Maya S, Garcia RA, Noor A, Pawha PS, et al. Recurrent temporal bone tenosynovial giant cell tumor with chondroid metaplasia: the use of imaging to assess recurrence. *Neuroradiol J* 2014;27:97-101.
- Myers BW, Masi AT. Pigmented villonodular synovitis and tenosynovitis: a clinical epidemiologic study of 166 cases and literature review. *Medicine* 1980;59:223-238.
- Liu YK, Chan JY, Chang CJ, Huang JS. Pigmented villonodular synovitis of the temporomandibular joint presenting as a middle cranial fossa tumor. *J Oral Maxillofac Surg* 2012;70:367-372.
- Tosun F, Carrau RL, Weissman J. Pigmented villonodular synovitis of the temporomandibular joint: an extensive case with skull-base involvement. *Am J Otolaryngol*. 2004;25:204-207.
- Damodar D, Chan N, Kokot N. Pigmented villonodular synovitis of the temporomandibular joint: Case report and review of the literature. *Head Neck*. 2015;37:E194-E199.
- Cheng XG, You YH, Liu W, Zhao T, Qu H. MRI features of pigmented villonodular synovitis (PVNS). *Clin Rheumatol* 2004;23:31-34.
- Verspoor FG, van der Geest IC, Vegt E, Veth RP, van der Graaf WT, Schreuder HW. Pigmented villonodular synovitis: current concepts about diagnosis and management. *Future Oncol*. 2013;9:1515-1531.
- Murphey MD, Rhee JH, Lewis RB, Fanburg-Smith JC, Flemming DJ, Walker EA. Pigmented villonodular synovitis: radiologic-pathologic correlation. *Radiographics*. 2008;28:1493-1518.
- Romañach MJ, Brasileiro BF, León JE, Alves DB, de Almeida OP, Vargas PA. Pigmented villonodular synovitis of the temporomandibular joint: case report and review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2011;111:e17-e28.
- Boland JM, Folpe AL, Hornick JL, Grogg KL. Clusterin is expressed in normal synoviocytes and in tenosynovial giant cell tumors of localized and diffuse types: diagnostic and histogenetic implications. *Am J Surg Pathol* 2009;33:1225-1229.
- O'Connell JX, Fanburg JC, Rosenberg AE. Giant cell tumor of tendon sheath and pigmented villonodular synovitis: immunophenotype suggests a synovial cell origin. *Hum Pathol* 1995;26:771-775.

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