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Original Article

Diffuse tenosynovial giant cell tumor in the temporomandibular joint area in a Chinese population: a clinicopathological analysis of 32 cases

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Abstract: Objectives: To analyze the clinicopathological characteristics of diffuse tenosynovial giant cell tumor (D-TGCT) in the temporomandibular joint area in a Chinese population. Methods: A total of 32 cases of D-TGCT in the temporomandibular joint area were collected, and their clinicopathological characteristics were analyzed; follow-up was performed for all patients. Results: Among the 32 patients, the male to female ratio was 1:1.13, with an average age of 42 years. Patients experienced symptoms of joint and ear pain and headache to varying degrees. Imaging studies showed lesions centered on the temporomandibular joint. Microscopically, the tumor tissue was composed of synovium-like monocytes, small histiocytoid cells and multinucleated giant cells; 53% (17/32) of cases showed lesions migrating with the synovium and articular disc, and 44% (14/32) of cases had differing levels of cartilaginous metaplasia in the lesions. All 32 patients underwent extended surgical resection, and recurrence occurred in 11% of patients with primary disease. Conclusions: In D-TGCT of the temporomandibular joint, synovium-like monocytes show characteristics of semi-circular pigment in the cytoplasm; lesions often migrated with the synovium and articular disc. In the pathological diagnosis, clinical and imaging data should be considered together, and lesions containing giant cells near the temporomandibular joint should be differentiated.

Keywords: Diffuse tenosynovial giant cell tumor, temporomandibular joint, clinicopathological

Introduction

Tenosynovial giant cell tumor (TGCT) is a type of tumor that occurs in the synovial tissue of the joints, tendon sheath or bursa [1, 2]. According to the site and growth pattern of the tumor, TGCT can be divided into localized tenosynovial giant cell tumor (L-TGCT) and diffuse tenosynovial giant cell tumor (D-TGCT)/pigmented villonodular synovitis (PVNS). L-TGCT mainly occurs in small joints, such as the tendon sheath or synovium of the fingers and toes; D-TGCT and PVNS primarily involve large joints, including the knee, hip, ankle, elbow and shoulder. According to the site of the lesion, TGCT can be divided into the two subtypes of intra-articular and extra-articular growth [3, 4].

TGCT of the temporomandibular joint was first reported in 1973 by Lapayowker et al. [5]. Since then, a total of 73 cases have been reported in the English literature, though the majority are individual case reports [6]; These reports did not focus on the description of the histopathologic characteristics of the disease. In the literature, cases of TGCT occurring in the temporomandibular joint area are mostly classified as PVNS, which is then divided into the two major types of localized and diffuse. Localized PVNS refers to lesions that are confined to the intra-articular area, and diffuse PVNS is equivalent to D-TGCT of large joints. The literature and the 2013 version of the WHO Classification of Tumors of Soft Tissue and Bone indicates that cases of TGCT in the temporomandibular joint area are mostly D-TGCT (diffuse PVNS) [4, 6]. Because the literature consists mostly of individual case reports, the clinicopathological characteristics of D-TGCT in the temporomandibular joint area are currently poorly under-

Table 1. Antibodies used in this study

Primary antibody	Clone	Company	Dilution	Location of positive stain
Clusterin	B-5	Santa Cruz	1:100	Cytoplasm
CD68	PG-M1	DAKO	1:100	Cytoplasm
CD163	10D9	Gene company	1:100	Cytoplasm
Desmin	D33	DAKO	1:100	Cytoplasm
S-100	Polyclonal	Gene company	1:100	Nucleus

stood. The present study collected 32 cases of D-TGCT occurring in the temporomandibular joint area, which makes this the largest report on temporomandibular joint tumors. The clinicopathological characteristics and protein expression of these cases were analyzed.

Materials and methods

A total of 32 cases of D-TGCT in the temporomandibular joint area diagnosed in the Department of Oral Pathology from 2000 to 2013 were collected. All specimens were fixed in 10% neutral formalin, treated with conventional dehydration, and sectioned into 4-um slices, followed by H&E (hematoxylin-eosin) staining. The composition and characteristics of the tumor cells, cartilaginous metaplasia, bone tissue invasion, mitotic Figures/10HFP, and the relation of the tumor and the synovial tissue, as well as the surrounding tissues, were observed under a microscope. All specimens underwent staining for clusterin, CD163, CD68, Desmin, and S-100; antibody information is shown in **Table 1**. Clinical data, including gender, age, duration of symptoms, imaging findings, and surgical procedures, as well as follow-up information, were recorded for all patients.

Results

Clinical characteristics

The 32 patients included 15 males and 17 females, with a male to female ratio of 1:1.13. Patient age ranged from 16 to 65 years, with a median age of 41 years and a mean age of 42 years (**Table 2**).

Most patients had varying degrees of clinical symptoms; 75% (24/32) showed joint symptoms (**Table 2**), including restriction of mouth opening, joint snapping, and mouth-opening abnormalities. Other symptoms included joint pain, ear symptoms (pus, hearing loss), and headache. Only one patient had a painless mass. Symptom duration ranged from two months to 15 years, with an average of 30 months (**Table 2**).

The 32 patients included 29 primary cases and 3 recurrent cases, one of whom relapsed in the first year after the first surgery, and two of whom relapsed in the first 2 years after the first surgery.

Imaging characteristics

The enhanced CT showed that all patients had a tumor in the temporomandibular joint area (upper or lower articular chamber), some of which involved the temporal bone and joint recesses and/or the condyle and surrounding soft tissues. The tumors were regular or irregular, and most showed a clear boundary. Obvious enhancement was observed in the enhanced scan, and most cases were accompanied by a widening joint space. Significant condylar bone destruction was found in 40% (13/32) of patients, damage of temporal bone resorption was found in 53% (17/32) of patients, the tumor was around the condyle or mandibular ramus in 31% (10/32) of cases, the lesion was involved in the intracalvarium in 12% (4/32) of patients, and calcification in the lesion was observed in 6% (2/32) of patients (**Figure 1**).

Histopathological characteristics

The maximum tumor diameter was 2.0-6.4 cm, with an average of 3.6 cm. The surface of the tumor section was dark red, reddish brown or mixed with gray, with or without cystic change. Due to surgical resection of the condyle, the tumor was commonly around the condyle (**Figure 2**) with clear or less clear boundaries.

Under a microscope at low magnification, the tumor cells were seen to be nodular or arranged in sheets with hyaline fibrous tissue between them and no obvious capsule for the surrounding tissues; the tumors involved the surrounding soft tissue and bone. Under a microscope at high magnification, the lesion was seen to be composed of synovium-like monocytes, small histiocytoid cells, and multinucleated giant cells, with differing proportions of each cell among the cases. Scattered lymphocyte infiltration and hemosiderosis flavin deposition could be observed in the background to varying degrees. The synovium-like monocytes were in

Table 2. Clinicopathological details and follow-up information of 32 cases D-TGCTS

No	Sex	Age	MD (cm)	CM	FM	IS	Primary	JS	PD (mo.)	Radiographic	Condyle excision	Follow-up (mo)
1	F	53	4	Yes	No	Yes	Yes	Yes	24	Condyle resorption	Yes	NED (93)
2	F	38	4.1	No	No	No	Yes	Yes	36	Condyle and tomporal bone resorption	Yes	NED (84)
3	M	31	4	Yes	No	Yes	Yes	Yes	24	Tomporal bone resorption	Yes	NED (83)
4	M	65	1.5	Yes	No	Yes	Yes	Yes	12	Condyle resorption	Yes	DOOD (48)
5	M	50	2.7	Yes	No	No	Yes	Yes	24	Mass next to the TMJ	No	LR (13) *AWD (68)
6	F	50	4.7	No	Yes	No	Yes	Yes	60	Condyle sclerosis, tomporal bone resorption, invasion of intracranial	Yes	NED (64)
7	F	27	2	Yes	No	No	Yes	Yes	12	Mass next to the TMJ	No※	NED (48)
8	M	48	6.2	No	Yes	No	Yes	Yes	24	Tomporal and sphenoid bone resorption, invasion of intranial, calcification	No*	LR (7) AWD (51)
9	M	35	3.2	No	Yes	Yes	Yes	Yes	12	Tomporal bone resorption, around the condyle	No	LR (19) AWD (49)
10	M	59	2.7	Yes	No	Yes	Yes	Yes	36	Tomporal bone resorption, invasion of intracranial	No*	NED (52)
11	M	34	3.3	No	No	Yes	Yes	Yes	120	Condyle and tomporal bone resorption	Yes	NED (47)
12	F	57	3.6	No	No	Yes	Yes	No	48	Tomporal bone resorption and around the mandibular ramus	No*	NED (47)
13	F	23	4.1	No	Yes	No	Yes	Yes	12	Tomporal bone resorption	Partly	NED (39)
14	M	34	2.4	No	No	No	Yes	No	12	Tomporal bone resorption, invasion of skull base	No	NED (42)
15	F	39	3.1	Yes	Yes	Yes	Yes	No	12	Tomporal and sphenoid bone resorption	No	NED (41)
16	F	40	2	No	No	Yes	Yes	Yes	48	Condyle resorption	No	No data
17	M	32	6.4	No	No	No	Yes	Yes	12	Condyle and tomporal bone resorption, around the condyle	Yes	NED (24)
18	F	50	3.7	Yes	No	Yes	Yes	No	12	Condyle resorption, around the condyle, cystic	Yes	NED (3)
19	M	49	5.5	No	No	Yes	Yes	Yes	12	Tomporal bone resorption, around the condyle, calcification	Yes	NED (24)
20	F	44	3.4	No	Yes	Yes	Yes	No	12	Around the condyle	No	NED (14)
21	M	52	2.2	Yes	No	Yes	Yes	Yes	6	Tomporal bone resorption	No	NED (6)
22	F	37	5.7	Yes	No	No	No	Yes	18	Condyle and mandibular ramus resorpation, invasion of intracranial	Yes	NED (12)
23	M	47	3.4	No	Yes	No	Yes	No	36	Tomporal bone resorption	Yes	NED (101)
24	F	35	3.9	No	No	Yes	Yes	Yes	36	Tomporal bone resorption and around the condyle	No	NED (7)
25	F	39	3.5	No	No	No	No	Yes	24	Around the condyle	Partly	NED (97)
26	F	46	3.9	Yes	Yes	No	Yes	Yes	180	Condyle and tomporal bone resorption, around the condyle	Partly	No data
27	M	40	4	No	No	No	Yes	Yes	12	Condyle and tomporal bone resorption, around the condyle	Yes	NED (173)
28	F	43	2.5	No	No	No	Yes	Yes	24	Tomporal bone resorption	No※	NED (170)
29	F	48	2.5	No	Yes	Yes	Yes	Yes	12	Condyle resorption	Yes	NED (163)
30	M	38	4.5	Yes	No	Yes	Yes	Yes	24	Condyle resorption	Yes	No data
31	F	16	2	Yes	No	No	No	No	12	Condyle and tomporal bone resorption	Yes	LR (74) AWD (157)
32	M	42	3.5	Yes	No	Yes	Yes	No	7	Tomporal bone resorption	No*	NED (151)

Abbreviations: M, male; F, female; MD, Maximum diameter; CM, Chondroid metaplasia: FM, Foamy Macrophages; IS: Involvement of synovium; JS: Joint syndroms; PD, Preoperative duration; NED: no evidence of disease; AWD: alive with disease; DOOD: died of other disease. *These patients had articular disc ressection. ※These patients had radiotherapy after surgery.

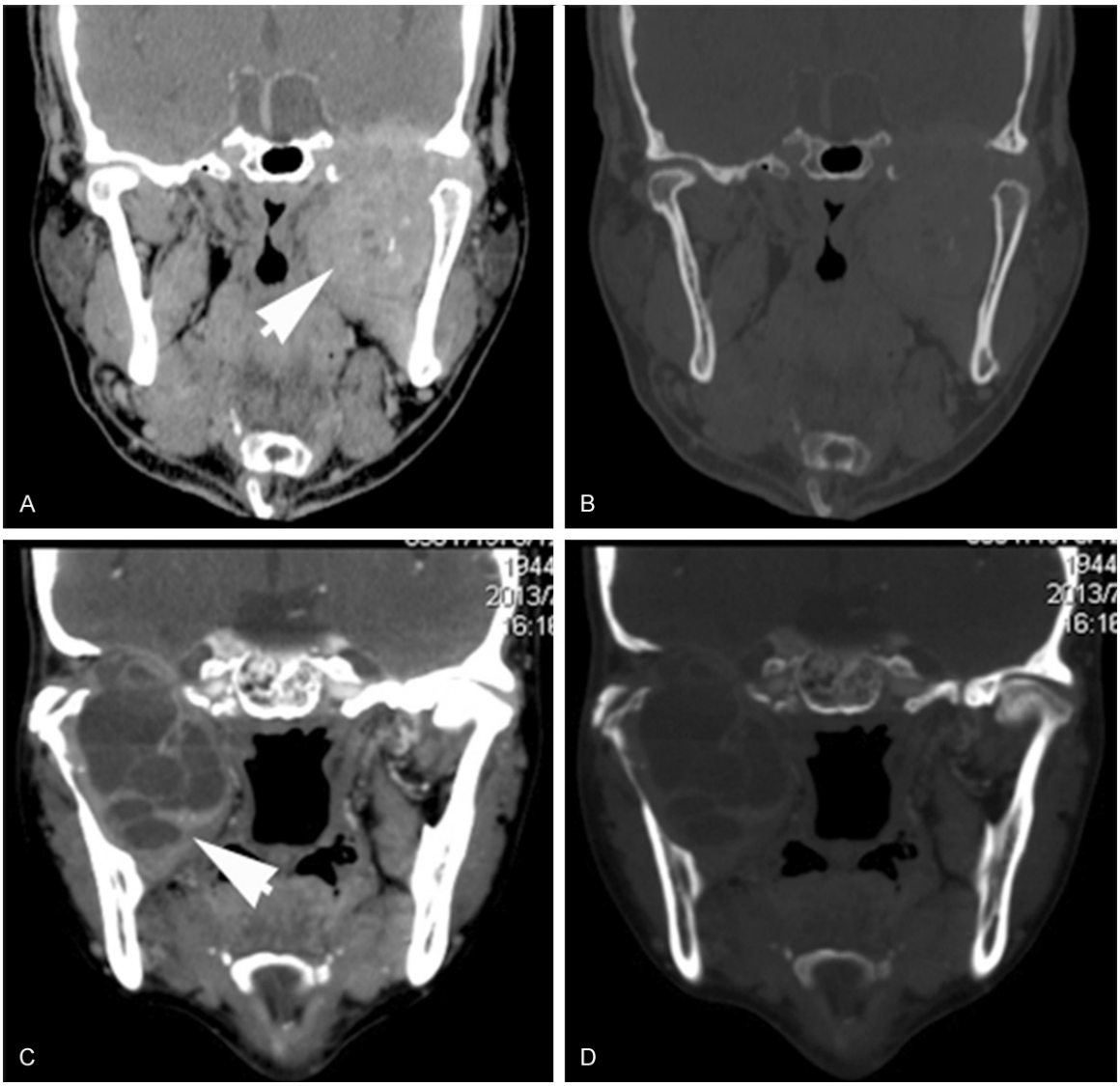

Figure 1. Imaging of D-TGCT. A, B: The tumor can be observed in the soft tissue surrounding the condyle, with widening joint space and involvement of the intracalvarium (Case 8); C, D: The tumor destroyed the mandibular ramus and condyle, which is multicystic (Case 22).

nests, adenoids or crack-like arrangements, with a large cell volume, abundant cytoplasm, eosinophils, and round, oval or kidney-shaped nuclei. They could be vesicular and deviated, and prominent nucleoli could sometimes be observed. Pigmentation in half-rings could be found in the cytoplasm of some cases (**Figure 3**). Synovium-like monocytes might be actively growing. In 34.3% (11/32) of cases, 1-3 mitotic Figures/10 HPF were shown. Small histiocytoid cells were small, round, oval or short spindle-shaped, with little cytoplasm and light staining. Multinucleated giant cells were of different sizes and had uneven distributions, and the number of nuclei ranged from several to dozens. Foamy macrophages were found in 28% (9/32) of cases, though they were mostly focal and located at the tumor margin. Only one case (Case 20) showed many foamy macrophages. The appearance of foamy macrophages was often associated with the infiltration of many small focal lymphocytes.

In 53% (17/32) of cases, the tumor tissue was found to be migrating with the synovium tissue or joint disc (**Figure 3**, **Table 2**). Obvious soft tissue or bone tissue invasion was found in 75% (24/32) of cases; 44% (14/32) of cases showed

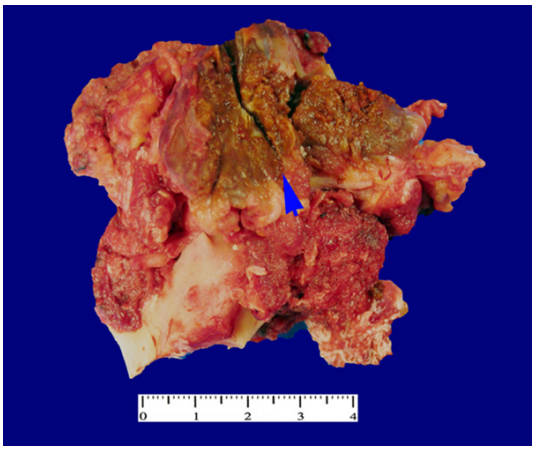

Figure 2. General appearance of D-TGCT. The tumor is in the temporomandibular joint area, with the section surface in dark red, showing no obvious capsule (Case 1).

varying levels of cartilaginous metaplasia, and the cartilage components took varying forms from myxoid matrix to maturely differentiated hyaline cartilage. Some cases even showed a "chicken wire" calcification similar to chondroblastoma and cartilaginous bone on the basis of cartilaginous metaplasia (**Figure 3**). A large area of obstructive necrosis was found in one case, while another case was associated with synovium chondromatosis.

Immunohistochemistry

Clusterin was expressed in the synovium-like monocytes of all patients, with positive staining in the cytoplasm. Clusterin expression was also found in the area of cartilaginous metaplasia. Desmin was expressed in small amounts in the synovium-like monocytes in 34% (11/32) of cases, with dendrites being seen in the cytoplasm. CD163 was expressed in all small histiocytoid cells, and CD68 was expressed in some, with positive staining in the cytoplasm. CD68 was expressed in multinucleated giant cells. S-100-positive nuclei were found in the metaplastic chondrocytes in cartilaginous metaplasia, while the surrounding synovium-like monocytes, small histiocytoid cells and multinucleated giant cells were S-100 negative (**Figure 4**).

Treatment and follow-up

All patients underwent surgery as the primary treatment. Complete or partial condylar resection was performed in 18/32 patients, the articular disc was resected with condyle preservation in 4/32 patients, and extended tumor resection was performed in the remaining 10 patients. Two patients underwent postoperative radiotherapy, and the remaining patients did not undergo other treatment. All patients were followed up routinely.

Follow-up information from 29 (91%) patients was collected (including 26 primary cases and 3 cases of recurrence). The follow-up time was 3-173 months, with a mean of 67 months. Except for one patient who died from another cause, all patients achieved disease-free survival. Among the 26 primary cases, 3 patients (11%) developed postoperative recurrence in 7-19 months, with an average of 13 months. Among the 3 cases of recurrence, the condyle was preserved during the first surgery, and no postoperative radiotherapy was performed; two cases showed no recurrence in postoperative follow-up after the secondary surgery, and the remaining case relapsed after 74 months. No metastasis occurred in any patients (**Table 2**).

Discussion

D-TGCT has been called extra-articular PVNS. However, it is often accompanied by intra-articular lesions, which mostly occur in large joints such as the knee, hip and shoulder, with few cases of TGCT occurring in the temporomandibular joint. The available literature consists mainly of individual case reports of D-TGCT (diffuse PVNS). The study with the most cases is that of Le et al. published in 2013, and this study mainly described the imaging characteristics of 8 cases of D-TGCT in the temporomandibular joint area [7]. To date, no study with a large sample size has reported the histopathologic characteristics of D-TGCT in the temporomandibular joint area. The present study summarized 32 cases of D-TGCT in the temporomandibular joint area treated in our hospital from 2000 to 2013. We had slightly more female patients than male patients (M:F = 1:1.13), and the dominance in female patients is also observed for TGCT of the hand (M:F = 1:1.46) [8] and D-TGCT of other large joints (M:F = 1:1.27) [9]. D-TGCT of other large joints can occur at any age, but it mainly occurs around 30-40 years and often shows clinical symptoms of joint pain and movement disorders. Due to the low incidence of D-TGCT in the temporomandibular joint area with non-specific

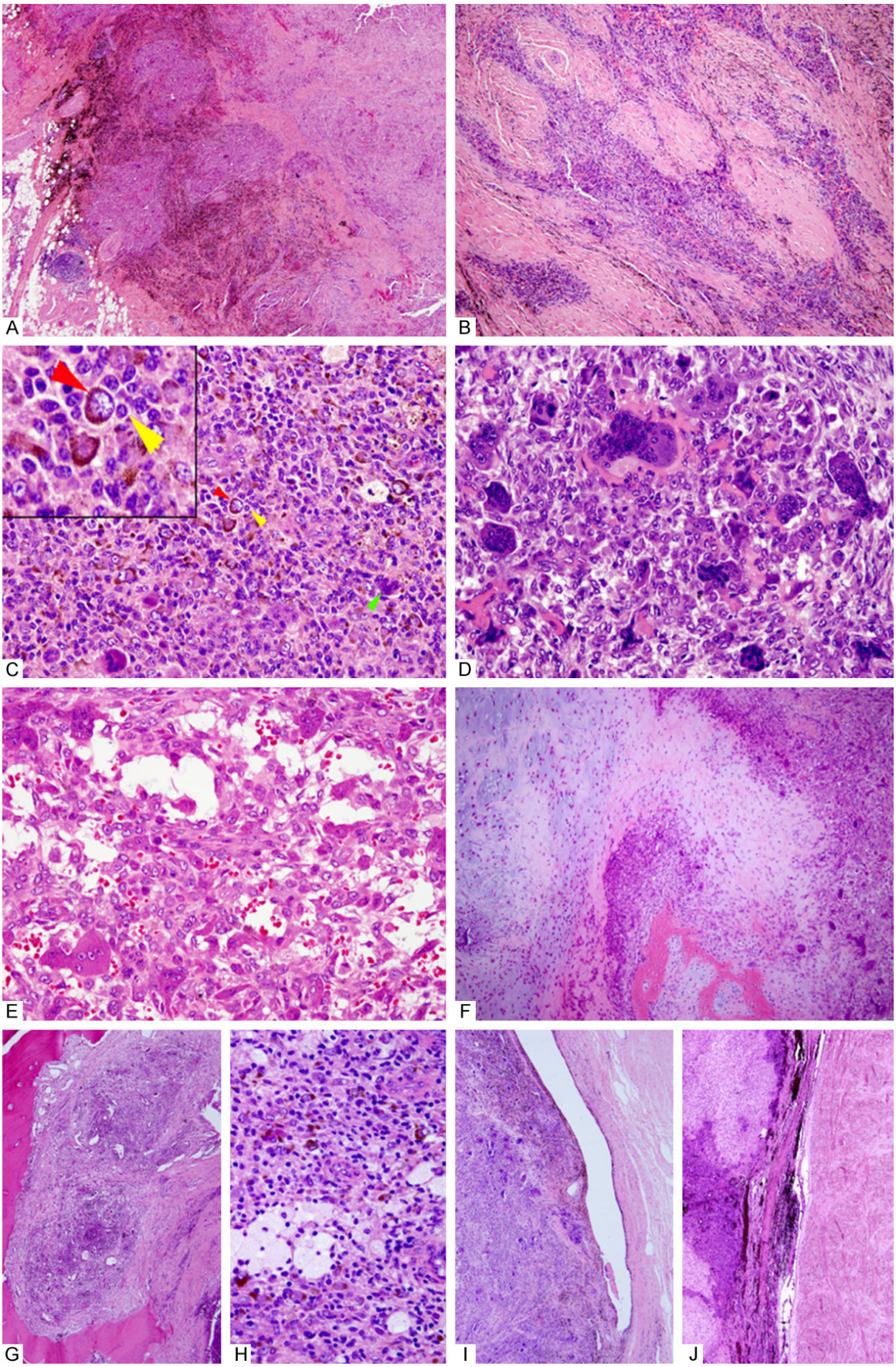
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Figure 3. Histological characteristics and H&E staining of D-TGCT. A: The lesions show no obvious boundaries, and involve the surrounding soft tissue (Case 30), ×40; B: The tumor cells are arranged in the form of pellets and are spotty, with fibrous tissue in the interval (Case 3), ×100; C: The lesion is composed of synovium-like monocytes (red arrow), small histiocytoid cells (yellow arrow), and multinucleated giant cells (green arrow), with some synovium-like monocytes containing semi-circular pigment (Case 10), ×400; D: The multinucleated giant cells are of different sizes and have uneven distributions, and the number of nuclei range from several to dozens (Case 16), ×400; E: The synovium-like monocytes are in adenoid or crack-like arrangements (Case 5), ×400; F: Cartilage and bone metaplasia was found in some patients (Case 5), ×100; G: The tumor invaded the bone tissue (case 18), ×40; H: Foamy histiocytes were observed in some patients (Case 20), ×400; I: The extension of the lesion and synovial tissue were observed in some patients (Case 19), ×40; J: The relation of the joint disc and the lesion is shown (Case 3), ×40.

clinical symptoms, patients often receive a clinical diagnosis of parotid mass or temporomandibular joint disorder [10-13]. Our youngest patient was 16 years old, and our oldest was 65 years old; their mean age of 42 years is similar to the age of onset of D-TGCT at other sites. Because the temporomandibular joint area is close to the skull base and the external auditory canal, the patients in this study showed not only restriction in the ability to open the mouth and occlusal discomfort due to limited joint mobility but also symptoms of pus in the ear, hearing loss, and headaches, which may be due to invasive growth of the tumor into the temporal bone, thereby involving the external auditory canal.

D-TGCT originates in the cells covering the surface of the synovium and primarily consists of three cell types, including synovium-like monocytes, small histiocytoid cells and multinucleated giant cells, though foamy tissue cells are found in some cases. Synovium-like monocytes are the true tumor cells, and their immune phenotype is the same as that of the normal synovium cells [14]. These cells are large in volume and 1.5-5 times the size of small histiocytoid cells [9]. Semi-circular pigment can be found in the cytoplasm with varying amounts of mitosis, though the level of mitosis shows no clear relationship with the biological behavior of the tumor such as recurrence or malignant transformation. Among the patients in this study, 1-3 mitosis figures/10HFP were observed in 34.3% of the cases, with no obvious correlation to tumor recurrence. In the literature, the number of mitosis figures in some cases may reach ≥10/10HPF [9, 15]. In 2009, Jennifer et al. found that clusterin is positively expressed in normal synovial tissue, as well as in the synovium-like monocytes of L-TGCT and D-TGCT [14]. Clusterin is a chaperone glycoprotein associated with follicular dendritic cells involved in lipid recycling and apoptosis [16], suggesting that synovium-like monocytes have the features of follicular dendritic cells. The immunophenotypes of the tumor tissue of patients in this study are similar to those reported in the literature. In all cases, clusterin was expressed in the synovium-like monocytes to varying degrees. Des was expressed in the synovium-like monocytes in 34% of cases, which is close to the 43-45% reported in the literature [9, 17]. Additionally, dendrites were observed in cells with positive Des staining. Although positive expression of clusterin in synovium-like monocytes can be an indicator for the differential diagnosis of other giant cell-containing lesions, it is not a specific marker for TGCT [16], and attention should be paid when using this marker clinically. Although foamy macrophages were common in the individual case reports (56%), they were found in only 24% of cases from the large study previously reported [9], which is similar to the 28% found among patients in this study.

For cases of TGCT that are not in the temporomandibular joint area, cartilaginous metaplasia is uncommon. Among the 9 cases of TGCT with cartilaginous metaplasia reported in the literature, 8 cases occurred in the temporomandibular joint area [18-20], suggesting that cartilaginous metaplasia is common in cases of TGCT in the temporomandibular joint. In this study, cartilaginous metaplasia was seen in varying amounts and at different stages of differentiation in 44% (14/32) of cases. Additionally, ossification and calcification on the basis of the cartilaginous metaplasia could be observed. Benjamin et al. believed that foamy macrophages could not be found in cases of TGCT associated with cartilaginous metaplasia [20]. However, in this study, foamy macrophages were found in 2/14 of the cases with cartilaginous metaplasia.

The microscopic migration of the tumor tissue against the synovium or joint disc tissue is strong evidence of the diagnosis of D-TGCT.

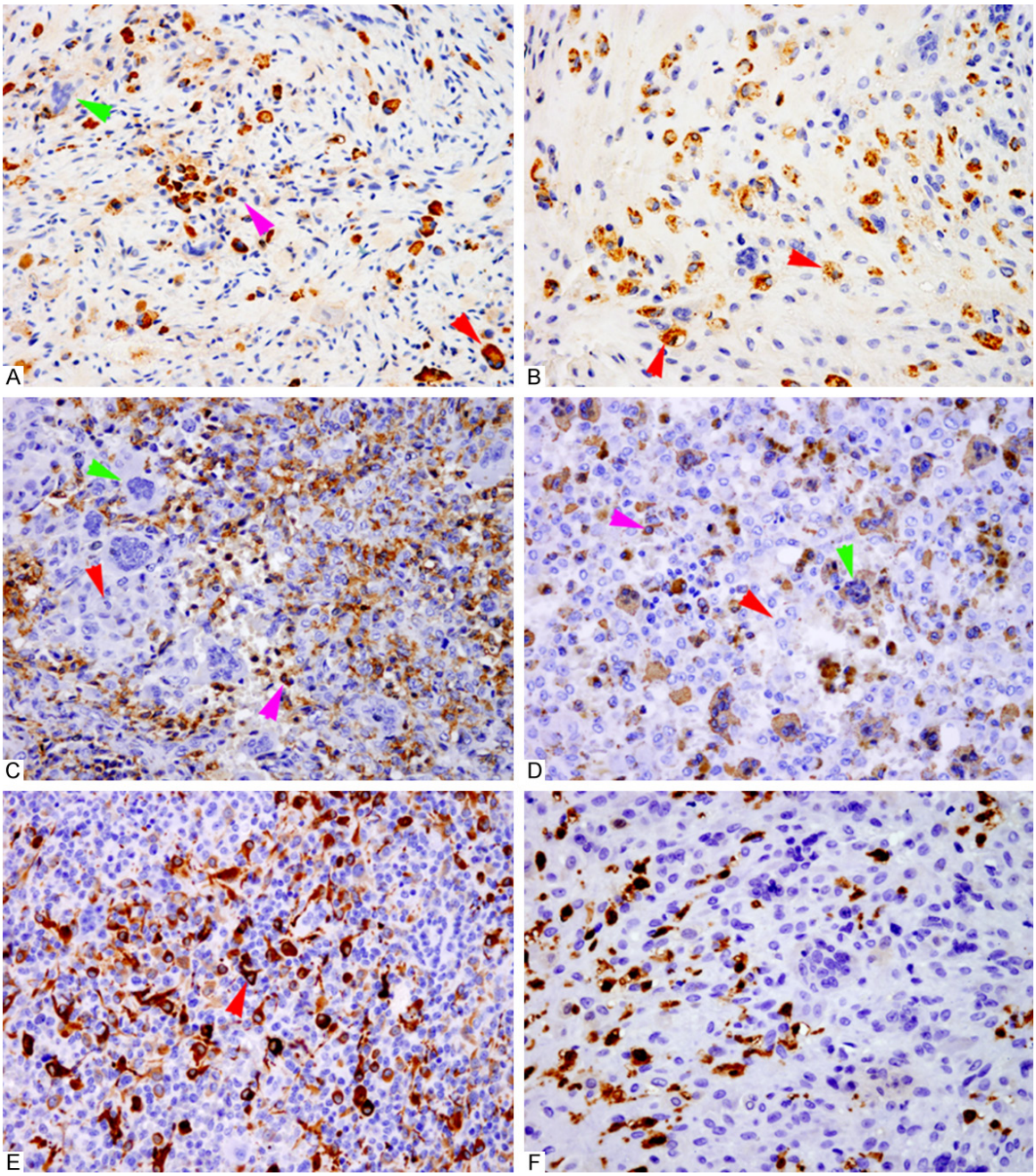

Figure 4. Immunohistochemical staining for D-TGCT, IHC, ×400, EnVision TM. A: Clusterin was expressed in the synovium-like monocytes (red arrow) but not in the small histiocytoid cells (purple arrow) or multinucleated giant cells (green arrow) (Case 16); B: Clusterin was expressed in the cells associated with differentiated chondrocytes of the cartilaginous metaplasia region (Case 16); C: CD163 was expressed in the small histiocytoid cells (purple arrow) but not in the synovium-like monocytes (red arrow) or multinucleated giant cells (green arrow) (Case 22); D: CD68 was expressed in the multinucleated giant cells (green arrow) and some small histiocytoid cells (purple arrow) but not in synovium-like monocytes (red arrow) (Case 25); E: Des was expressed in some synovium-like monocytes, and dendrites are shown in the cytoplasm of the synovium-like monocytes (red arrow) (Case 20); F: S-100 staining was positive in the chondrocytes of the cartilaginous metaplasia region and negative in the surrounding cells (Case 5).

Therefore, the sampling coverage should be as wide as possible. Imaging findings are also very conducive to making the diagnosis. Joint space widening was present in 75% of patients with D-TGCT in the temporomandibular joint area, and the tumor was closely related to the con-

dyle [7], which was surrounding the joint area or centered on the joint area. In practice, the diagnosis also needs to differentiate between the lesions showing overlapping histological figures. For cases of D-TGCT occurring in the temporomandibular joint area, the differential diagnosis often needs to consider giant cell granuloma of the mandible and the temporal bone, chondroblastoma, synovial chondromatosis, and giant cell tumor. The diagnosis should be based on the integration of clinical data, imaging findings, and morphological data. Giant cell granuloma often occurs in maxillofacial and small bones, and the patient may have a history of trauma or infection. Lesions occurring in the mandible are usually in the front of the mandible. For the few cases that occurred in the temporomandibular joint area, the lesion was centered on the condyle or medial temporal bone rather than on the joint cavity. Giant cell granulomas contain abundant spindle fibroblasts, have an inflammatory background full of various inflammatory cells, and lack the false adenoid structure and synovium-like monocytes with hemosiderin phagocytosis. Multinucleated giant cells often locate at the perihematom or in clusters, have small volume and few nuclei, and show the formation of reactive new bone. Chondroblastoma often occurs in adolescents, usually among males, and the lesions are generally located in the epiphysis of the long bones; they rarely involve the articular cartilage or synovium. Chondroblastoma rarely occurs in the temporomandibular joint area, and cases tend to center on the condyle and present as condyle enlargement [21, 22]. Chondromatosis of the synovium often occurs in middle-aged individuals, and the lesions are radiographically confined to the joint; it is common to see the cartilaginous nodule separate from the joint cavity or be reattached on the articular surface. Chondromatosis of the synovium may be associated with calcification and ossification. Intraosseous islands and multinucleated giant cells are common, often with synovial cells covering the nodular surface, but there is no flaky hyperplasia of synovium-like monocytes. Giant cell tumors rarely occur in craniofacial bones; those that occasionally occur in the temporal bone are often centered on the temporal bone, and typical lesions show infiltration in a large number of osteoclast-like multinucleated giant cells with large volumes and many nuclei. These cells do not cluster, and the background is made of neoplastic interstitial monocytes and macrophage precursor monocytes, in which the interstitial monocytes are the true tumor cells. No migration between synovial tissue and lesions was found, and cartilage metaplasia was rare. The centers of osteosarcoma and chondrosarcoma lesions that contain cartilage-like matrix are located in the bone, and the tumor cells generally have obvious heteromorphisms showing invasive growth in, but not limited to, the bone.

Compared to L-TGCT and PVNS, D-TGCT is mainly characterized by its invasive growth. In the 2013 WHO classification, although TGCT is classified as benign, the ICD-O of D-TGCT was coded as "1" [4], suggesting that TGCT may have some characteristics of intermediate tumors. In this study, 75% of patients had tumor invasion of the bone tissue or surrounding soft tissue on microscope examination, and the invasion was obvious. The recurrence rate among patients with D-TGCT in the non-temporomandibular joint area is 33-50% [4], but the reported recurrence rate of D-TGCT in the temporomandibular joint is 9-11% [23, 24]. In a recent report, Joshi K et al. reviewed PVNS cases (including localized PVNS and diffuse PVNS) in the temporomandibular joint area and found that the recurrence rate among 66 cases of diffuse PVNS with complete clinical data was 7.6% (5/66) [6]. In the present study, the recurrence rate among the 29 primary cases was 11% (3/26) (follow-up information of 3 patients was not collected), and the 3 patients with recurrence had undergone resection with maintenance of the condyle. A study on D-TGCT in the non-temporomandibular joint area reported a recurrence rate of 33%, and only 2/50 (4%) patients underwent amputation due to invasion of the surrounding tissue [9]. In the present study, 18/32 (56%) patients underwent condylar tissue resection, suggesting that the surgical procedure may be a factor in the different recurrence rates among patients with D-TGCT at different sites.

The efficacy of postoperative radiotherapy remains inconclusive [24]. However, a recent review reported that postoperative radiotherapy can control invasive growth and limit recurrence in cases with positive resection margin [6]. For cases of D-TGCT that are not in the temporomandibular joint area, some scholars believe that low-dose radiation therapy may be

considered to reduce the recurrence rate among recurrent cases and those with invasive growth [25]. Among patients in the present study, 2 underwent radiotherapy. These patients were followed for 48 months and 170 months and showed no sign of recurrence, but whether this is related to radiotherapy requires further investigation with a large sample size.

Conclusion

In summary, D-TGCT of the temporomandibular joint is a rare tumor. Among patients in the present study, the average age was 42, and there were slightly more females than males. Imaging studies showed that the lesions centered on the temporomandibular joint area, and the tumors originated in the cells covering the surface of the synovium. The lesions mainly consisted of synovium-like monocytes, small histiocytoid cells and multinucleated giant cells. Synovium-like monocytes are the true tumor cells and are commonly characterized by semi-circular pigment in the cytoplasm, positive staining for clusterin, migration of the lesions against the synovium and articular disc, and the presence of cartilaginous metaplasia. In the pathological diagnosis, the clinical characteristics, imaging findings, endoscopic findings, and immunohistochemical phenotype should be comprehensively considered to differentiate from cases of giant cell granuloma, chondroblastoma, and synovial chondromatosis. D-TGCT in the temporomandibular joint area is invasive, and complete resection of the tumor should be the goal of treatment.

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Disclosure of conflict of interest

None.

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References

[1] Jaffe HL, Lichtenstein L, Sutro CJ. Pigmented villonodular synovitis, buritis and tenosynovitis. Arch Path Lab Med 1941; 31: 731-765.

[2] O'Connell JX. Pathology of the synovium. Am J Clin Pathol 2000; 114: 773-784.

[3] Martin RC 2nd, Osborne DL, Edwards MJ, Wrightson W, McMasters KM. Giant cell tumor of tendon sheath, tenosynovial giant cell tumor, and pigmented villonodular synovitis: defining the presentation, surgical therapy and recurrence. Oncol Rep 2000; 7: 413-419.

[4] Fletcher CD, Bridge JA, Hogendoorn PC, Mertens F. So-called fibrohistiocytic tumours. WHO Classification of Tumors of Soft Tissue and Bone. In: Fletcher CD, Bridge JA, Hogendoorn PC, Mertens F, editors. Lyon, France: IARC; 2013.

[5] Lapayowker MS, Miller WT, Levy WM, Harwick RD. Pigmented villonodular synovitis of the temperomandibular joint. Radiology 1973; 108: 313-316.

[6] 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.

[7] Le WJ, Li MH, Yu Q, Shi HM. Pigmented villonodular synovitis of the temporomandibular joint: CT imaging findings. Clin Imaging 2014; 38: 6-10.

[8] Lancigu R, Rabarin F, Jeudy J, Saint Cast Y, Cesari B, Fouque PA, Raimbeau G. Giant cell tumors of the tendon sheaths in the hand: review of 96 patients with an average follow-up of 12 years. Orthop Traumatol Surg Res 2013; 99 Suppl 4: S251-254.

[9] Somerhausen NS, Fletcher CD. Diffuse-type giant cell tumor: clinicopathologic and immunohistochemical analysis of 50 cases with extraarticular disease. Am J Surg Pathol 2000; 24: 479-492.

[10] Aoyama S, Iwaki H, Amagasa T, Kino K, Okada N, Kishimoto S. Pigmented villonodular synovitis of the temporomandibular joint: differential diagnosis and case report. Br J Oral Maxillofac Surg 2004; 42: 51-54.

[11] Cascone P, Filiaci F, Paparo F, Mustazza MC. Pigmented villonodular synovitis of the temporomandibular joint. J Orofac Pain 2008; 22: 252-255.

[12] Stryjakowska KK, Martel M, Sasaki CT. Pigmented villonodular synovitis of the temporomandibular joint: differential diagnosis of the parotid mass. Auris Nasus Larynx 2005; 32: 309-314.

[13] Yu GH, Staerkel GA, Kershisnik MM, Varma DG. Fine-needle aspiration of pigmented villonodu-

lar synovitis of the temporomandibular joint masquerading as a primary parotid gland lesion. Diagn Cytopathol 1997; 16: 47-50.
[14] 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.
[15] Ushijima M, Hashimoto H, Tsuneyoshi M, Enjoji M. Giant cell tumor of the tendon sheath (nodular tenosynovitis). A study of 207 cases to compare the large joint group with the common digit group. Cancer 1986; 57: 875-884.
[16] Grogg KL, Macon WR, Kurtin PJ, Nascimento AG. A survey of clusterin and fascin expression in sarcomas and spindle cell neoplasms: strong clusterin immunostaining is highly specific for follicular dendritic cell tumor. Mod Pathol 2005; 18: 260-266.
[17] Folpe AL, Weiss SW, Fletcher CD, Gown AM. Tenosynovial giant cell tumors: evidence for a desmin-positive dendritic cell subpopulation. Mod Pathol 1998; 11: 939-944.
[18] 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.
[19] Oda Y, Izumi T, Harimaya K, Segawa Y, Ishihara S, Komune S, Iwamoto Y, Tsuneyoshi M. Pigmented villonodular synovitis with chondroid metaplasia, resembling chondroblastoma of the bone: a report of three cases. Mod Pathol 2007; 20: 545-551.
[20] 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.
[21] Kim SM, Hong SW, Ryu DJ, Huh JK. Chondroblastoma of the temporomandibular joint lateral capsule: a case report. Cranio 2015: 33: 306-11.
[22] Bui P, Ivan D, Oliver D, Busaidy KF, Wilson J. Chondroblastoma of the temporomandibular joint: report of a case and literature review. J Oral Maxillofac Surg 2009; 67: 405-409.
[23] De Benedittis M, Turco M, Petruzzi M, Cortelazzi R. Extra-articular diffuse-type giant cell tumour of the temporomandibular joint. Int J Oral Maxillofac Surg 2013; 42: 380-385.
[24] Lee JH, Kim YY, Seo BM, Baek SH, Choi JY, Choung PH, Kim MJ. Extra-articular pigmented villonodular synovitis of the temporomandibular joint: case report and review of the literature. Int J Oral Maxillofac Surg 2000; 29: 408-415.
[25] van der Heijden L, Gibbons CL, Dijkstra PD, Kroep JR, van Rijswijk CS, Nout RA, Bradley KM, Athanasou NA, Hogendoorn PC, van de Sande MA. The management of diffuse-type giant cell tumour (pigmented villonodular synovitis) and giant cell tumour of tendon sheath (nodular tenosynovitis). J Bone Joint Surg Br 2012; 94: 882-888.