Abstract. – OBJECTIVE: This study investigated radiographic images and the differential diagnosis of intracranial diffuse tenosynovial giant cell tumor (D-TGCT) in order to better understand the disease and improve the rate of preoperative diagnosis.

PATIENTS AND METHODS: Images and clinical data of patients with D-TGCT were retrospectively analyzed. Routine Computer Tomography (CT), routine Magnetic Resonance Imaging (MRI), and contrast-enhanced MRI were performed for nine cases. Susceptibility-weighted imaging (SWI) was also performed for one case.

RESULTS: We reviewed nine patients (6 males and 3 females) aged between 24 and 64 years, with a mean age of 47.33 ± 14.92 years. The most frequent complaints were hearing loss (5/9, 55.6%), pain (4/9, 44%), masticatory symptoms (2/9, 22.2%), and mass (4/9, 44.4%), with a mean duration of 22 ± 21.43 months. All cases were centered on the base of the skull, and showed hyper-density soft-tissue mass with osteolytic bone destruction on CT. The tumor signal mainly showed iso-intensity or hypo-intensity on T1WI compared with that in the brain parenchyma in all patients. On T2WI, nine lesions mainly showed hypo-intensity. Among these nine lesions, three displayed cystic region showing hyper-intensity on T1WI compared with that in the brain parenchyma in all patients. On T2WI, nine lesions mainly showed hypo-intensity. Among these nine lesions, three displayed cystic region showing hyper-intensity on T2WI and hypo-intensity on T1WI (Figure 2A, 2B) in the lesion. Nine lesions showed hypo-intensity on DWI sequences. SWI images presented low signal in two cases, showing the "flowering effect". Nine patients showed heterogeneous enhancement, and two patients had meningeal thickening.

CONCLUSIONS: Intracranial D-TGCT is extremely rare, but must be differentiated from other tumors. Osteolytic bone destruction in the area of the skull base with hyper-density soft-tissue mass and hypo-intensity on T2WI images are indicative of D-TGCT.

Key Words: Tenosynovial giant-cell tumor, Intracranial, Tomography, X-ray computed, Magnetic resonance imaging.

Introduction

Diffuse tenosynovial giant-cell tumor (D-TGCT), also called Pigmented villonodular synovitis, is a benign proliferative disease of the synovium that usually involves joints and tendon sheaths. D-TGCT occurs in large joints of the extremities, of which a single joint is most involved. The tumor can be destructive. D-TGCT was initially reported to be an inflammatory disease related to chromosomal translocations detected by cytogenetics. Research also suggests that chronic inflammation may cause the disease, and that repeated trauma and hemarthrosis are possible risk factors.

The current best treatment option is surgical resection. The cell biology of D-TGCTs indicates that they have a malignant tendency, and they are prone to malignant transformation after multiple recurrences. The lesions can grow longitudinally around the tendon to form tiny satellite lesions. If the clinician does not have a comprehensive understanding of the tumor and the surgical resection fails to consider this feature, the small satellite lesions around the tumor may not be removed and can lead to tumor recurrence. Thus, preoperative MRI diagnosis and differential diagnosis are particularly important. If the imaging diagnosis is D-TGCT, attention should be paid to surrounding satellite lesions and the resection extended to minimize the chance of tumor recurrence as much as possible to prevent lesions from becoming malignant.

D-TGCT rarely occurs in the temporomandibular joint (TMJ); most case reports in literature describe disease of the skull base. In our study, several cases were collected and reviewed in our hospital. Here we describe their radiologic imaging, clinical appearance, and treatment in order to raise awareness of the disease.
Patients and Methods

Subjects
We selected nine patients whose D-TGCT diagnoses were confirmed by surgery and pathology in our hospital from July 2015 to December 2021. Clinical features including age, sex, symptoms, radiological imaging, and pathological findings were recorded (Table I).

Imaging Examination Methods
Routine CT, conventional, and contrast enhancement MRI were performed in nine cases, and the case 2 was examined with SWI. CT scans were performed using GE Discovery 64-slice spiral CT machine with a slice gap of 5 mm and a slice thickness of 5 mm. MR images of patients, scanned on 3.0-T MRI scanners (Magnetom Trio TIM/Prisma, Siemens Healthcare, Germany), were retrieved from the Picture Archive and Communication System at the hospital. The sequence acquisition parameters were as follows:
- 2D sequence T1-weighted [repetition time (TR): 250 ms; echo time (TE): 2.5 ms] in the sagittal plane and cross-sectional scanning;
- the turbo spin echo (SE) sequence T2-weighted imaging (TR 4500 ms, TE 100 ms) in the cross-sectional plane, a layer thickness 5 mm, no spacing interval, and two excitation imaging.

On axial diffusion-weighted imaging (DWI), a SE echo planar imaging sequence was used with TR 3,700 ms and TE 102 ms, b-values of 0 and 1,000, a layer thickness of 5 mm, and a layer spacing of 1.8 mm. During enhanced scanning, patients were injected with contrast agent [gadopentetate dimeglumine (Beijing Beilu Pharmaceutical Co., China)] at a dose of 0.2 ml/kg.

Image Analysis
All images were jointly read by two senior diagnostic radiologists who observed the lesion location, size, shape, adjacent bone changes, signal characteristics, and reinforcement mode of TGCT, recorded the results separately, discussed and compared them, and then reached a consensus.

Surgery and Pathological Examination
Seven patients underwent surgical total resection. Two patients underwent CT-guided biopsy at first go to hospital and chose surgical total resection when the size of tumor changed. All lesions underwent routine paraffin-embedded sectioning and HE staining.

Statistical Analysis
SPSS 22.0 statistical analysis software (IBM Corp., Armonk, NY, USA) was used for data processing. Statistical results were expressed as mean ± standard deviation. The incidence of hearing loss and the differences in CT and intraoperative performance between the two groups were compared using Chi-squared test. A value of p<0.05 was the criterion for statistical significance.

Results

Patient Characteristics
Patient clinical information is presented in Table I. We reviewed nine patients (six males and three females) between 24 and 64 years old, of mean age 47.33 ± 14.92 years. Five cases occurred on the right side and four cases occurred on the left. The most frequent complaints were hearing loss (5/9, 55.6%), pain (4/9, 44%), masticatory symptoms (2/9, 22.2%), and a mass (4/9, 44.4%), with a mean symptom duration of 22 ± 21.43 months.

Radiological Characteristics

The shape, size, and maximum diameter plane of the enhanced tumor on MRI imaging
The tumor manifested as irregular shape masses, grew diffusely, and infiltrated the surrounding tissues. The size of the tumor was 32-60 mm, and the maximum diameter was the upper-to-lower diameter, which was significantly larger than the transverse diameter and anterior-to-posterior diameter (Table II).

Density of computed tomography
All cases present soft tissue masses of mixed density with higher density area and osteolytic bone destruction expansion into the skull base bone (Figure 1G, 1H) and unclear boundary. The CT findings are summarized in Table II.

Signal of magnetic resonance imaging
The tumor presented mainly iso-intensity or hypo-intensity on T1WI compared with the signal of the brain parenchyma in all patients (Figure 1A, 2B). On T2WI, nine lesions mainly showed
Image findings of tendon sheaths affected by diffuse tenosynovial giant cell tumors of the skull base

hypo-intensity (Figure 1B). Among these nine lesions, three displayed cystic regions showing hyper-intensity on T2WI and hypo-intensity on T1WI (Figure 2A, 2B) in the lesion. Nine lesions showed hypo-intensity on DWI sequences (Figures 1C, 2D). SWI images presented low signal in case 2, showing the “flowering effect” (Figure 1F). Nine patients showed heterogeneous enhancement (Figure 1D). The MRI findings are summarized in Table II.

### Surrounding invasion of tumors

Temporal meningeal enhancement around the tumor was observed in two patients (Figure 1E). In four patients, the lesions grew into the external auditory meatus after destroying the anterior wall (Table II). In one case, the tumor involved the facial nerve root with enhancement, forming soft tissue masses in the cerebellar-pontine region (case 1). The tumor invaded the bone of the mastoid region in two cases (Table II). Compression of the Eustachian tube was observed in nine patients with mastoiditis. According to the extent of bone destruction on CT images, the patients were divided into Group A (involving external auditory meatus, mastoid process, and tympanum) and Group B (not involving external auditory meatus, mastoid process, and tympanum). The incidence of hearing loss in Group A (5/6) was higher than that in Group B (0/3; \( p < 0.05, \chi^2=5.625 \)). There was no significant difference between group A (5/1) and Group B (3/3; \( p > 0.05, \chi^2=0.563 \)) between CT images and intraoperative diagnosis of bone destruction.

### Tumor Recurrence and Follow-Up

The tumor had no recurrence at three years after the operation in three cases. Three patients had no recurrence two years after the operation. In one case, the tumor had no recurrence one year after the operation. The remaining two patients were lost to follow-up after the operation (Table I).

### Pathological Radiological Manifestations

Postoperative pathological examination revealed foam cells, multinucleated giant cells, and hemosiderin-laden macrophages. The pathological diagnosis was a diffuse giant cell tumor of the tendon sheath (Figure 1I).

### Table I. General information of nine cases of D-TGCT at the base of the skull.

<table>
<thead>
<tr>
<th>No.</th>
<th>Age</th>
<th>Sex</th>
<th>Nationality</th>
<th>Side</th>
<th>Chief complaint</th>
<th>Duration of symptom month</th>
<th>Operation resection</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>56</td>
<td>M</td>
<td>Han</td>
<td>right</td>
<td>Hearing loss, pre-auricular mass</td>
<td>8</td>
<td>Total resection</td>
<td>Loss to follow-up</td>
</tr>
<tr>
<td>2</td>
<td>60</td>
<td>M</td>
<td>Han</td>
<td>left</td>
<td>Facial nerve paralysis, Hearing loss, Pre-auricular mass</td>
<td>48</td>
<td>Total resection</td>
<td>Recurrence-free survival (1 year)</td>
</tr>
<tr>
<td>3</td>
<td>64</td>
<td>F</td>
<td>Han</td>
<td>right</td>
<td>Confused when chewing</td>
<td>1</td>
<td>Total resection</td>
<td>Recurrence-free survival (1 year)</td>
</tr>
<tr>
<td>4</td>
<td>59</td>
<td>M</td>
<td>Han</td>
<td>left</td>
<td>Temporal mass</td>
<td>60</td>
<td>Total resection</td>
<td>Recurrence-free survival (1 year)</td>
</tr>
<tr>
<td>5</td>
<td>24</td>
<td>M</td>
<td>Han</td>
<td>right</td>
<td>Earache, Hearing loss</td>
<td>3</td>
<td>Biopsy, Total resection</td>
<td>Recurrence-free survival (2 year)</td>
</tr>
<tr>
<td>6</td>
<td>46</td>
<td>F</td>
<td>Han</td>
<td>left</td>
<td>Earache, Hearing loss</td>
<td>36</td>
<td>Total resection</td>
<td>Recurrence-free survival (3 year)</td>
</tr>
<tr>
<td>7</td>
<td>36</td>
<td>F</td>
<td>Han</td>
<td>left</td>
<td>Temporal mass</td>
<td>12</td>
<td>Total resection</td>
<td>Recurrence-free survival (3 year)</td>
</tr>
<tr>
<td>8</td>
<td>54</td>
<td>M</td>
<td>Han</td>
<td>right</td>
<td>Mastoid process pain when chewing</td>
<td>24</td>
<td>Biopsy, Total resection</td>
<td>Recurrence-free survival (3 year)</td>
</tr>
<tr>
<td>9</td>
<td>27</td>
<td>M</td>
<td>Han</td>
<td>left</td>
<td>Earache, Hearing loss</td>
<td>6</td>
<td>Total resection</td>
<td>Loss to follow-up</td>
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</table>
The 2013 WHO classification of D-TGCT soft-tissue tumors includes the following groups: segmental (single nodule), diffuse (multiple nodules), and malignant, among which the segmental type is the most common. D-TGCT can occur at any age but is more common in adults aged 30-50 years; one patient in our case series was diagnosed to have it at the age of 24, consistent with a previous study. D-TGCT often involves the fingers and knee joints, followed by the ankles, hips, elbows, shoulder joints, and spine. D-TGCT of the TMJ is very rare, and involvement of the skull base is even rarer. In this study, in all nine cases, the tumor occurred in the temporal skull base and was diffuse.

Symptoms in patients with this disorder are nonspecific and include a painful or painless pre-auricular mass, TMJ symptoms, and hearing impairment. Local numbness may occur in some cases, due to compression of the trigeminal nu-
nucleus and facial nerve. Age of onset, progressive hearing impairment, and TMJ symptoms were specific in this case.

Pathologically, most D-TGCT were rich in monocytes, foam cells, multinucleated giant cell, and hemosiderin-laden tissue macrophages, consistent with the results of this study. In addition, other studies have shown that there is a 1p13 chromosomal translocation in most D-TGCT cases, with overexpression of the colony-stimulating factor 1 (CSF1) gene. Colony-stimulating factor receptor 1 (CSF1R) is a protein located on the cell surface that controls the generation and differentiation of macrophages. Overexpression of CSF1, a ligand for CSF1R, can form a CSF1 gradient that recruits CSF1R-expressing cells (such as macrophages) involved in tumor formation, thereby promoting tumor growth through a “paracrine landscape” effect in D-TGCT. This mechanism provides a potential site for targeted drug action by CSF inhibitors to treat D-TGCT.

Accurate preoperative diagnostic imaging can facilitate more precise treatment plan formulation and prognostic evaluation. D-TGCT usually showed an irregular mass with unclear boundaries, which was related to its aggressive biological behavior. MRI images showed diverse appearances as a result of different proportions of hemosiderin, fibers, lipids, stroma, and cellular components. MRI provides better characterization and

<table>
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<tr>
<th>Case</th>
<th>Size (mm)</th>
<th>Shape</th>
<th>Osteolytic bone destruction</th>
<th>Hyper-density soft tissue</th>
<th>Density</th>
<th>T1</th>
<th>T2</th>
<th>DWI</th>
<th>Enhancement</th>
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<tbody>
<tr>
<td>1</td>
<td>37<em>50</em>32</td>
<td>Mass</td>
<td>TB, MT</td>
<td>(+)</td>
<td>Heterogeneous</td>
<td>Iso-intensity, Hypo-intensity</td>
<td>Hypo-intensity (main)</td>
<td>Hypo-intensity</td>
<td>Moderately heterogeneous</td>
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<tr>
<td>2</td>
<td>58<em>45</em>36</td>
<td>Mass</td>
<td>TB, MD, EAC</td>
<td>(+)</td>
<td>Heterogeneous</td>
<td>Iso-intensity, Hypo-intensity</td>
<td>Hypo-intensity (main)</td>
<td>Hypo-intensity</td>
<td>Moderately heterogeneous</td>
</tr>
<tr>
<td>3</td>
<td>33<em>35</em>27</td>
<td>Mass</td>
<td>TB</td>
<td>(+)</td>
<td>Heterogeneous</td>
<td>Iso-intensity, Hypo-intensity</td>
<td>Hypo-intensity (main)</td>
<td>Hypo-intensity</td>
<td>Moderately heterogeneous</td>
</tr>
<tr>
<td>4</td>
<td>61<em>54</em>47</td>
<td>Mass</td>
<td>TB, ZB</td>
<td>(+)</td>
<td>Heterogeneous</td>
<td>Iso-intensity, Hypo-intensity</td>
<td>Hypo-intensity (main)</td>
<td>Hypo-intensity</td>
<td>Moderately heterogeneous</td>
</tr>
<tr>
<td>5</td>
<td>46<em>47</em>39</td>
<td>Mass</td>
<td>TB, EAC</td>
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<td>Heterogeneous</td>
<td>Iso-intensity, Hypo-intensity</td>
<td>Hypo-intensity (main)</td>
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<td>6</td>
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<td>Mass</td>
<td>TB, SB, EAC</td>
<td>(+)</td>
<td>Heterogeneous</td>
<td>Iso-intensity, Hypo-intensity</td>
<td>Hypo-intensity (with cystic signal)</td>
<td>Hypo-intensity</td>
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</tr>
<tr>
<td>7</td>
<td>57<em>60</em>49</td>
<td>Mass</td>
<td>TB, ZB</td>
<td>(+)</td>
<td>Heterogeneous</td>
<td>Iso-intensity, hypo-intensity</td>
<td>Hypo-intensity (main)</td>
<td>Hypo-intensity</td>
<td>Moderately heterogeneous</td>
</tr>
<tr>
<td>8</td>
<td>42<em>39</em>52</td>
<td>Mass</td>
<td>TB, SB, MD, TP</td>
<td>(+)</td>
<td>Heterogeneous</td>
<td>Iso-intensity, Hypo-intensity</td>
<td>Hypo-intensity (with cystic signal)</td>
<td>Hypo-intensity</td>
<td>Moderately heterogeneous</td>
</tr>
<tr>
<td>9</td>
<td>42<em>39</em>59</td>
<td>Mass</td>
<td>TB, EAC, MT</td>
<td>(+)</td>
<td>Heterogeneous</td>
<td>Iso-intensity, Hypo-intense</td>
<td>Hypo-intensity (with cystic signal)</td>
<td>Hypo-intensity</td>
<td>Moderately heterogeneous</td>
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</tbody>
</table>

*TB temporal bone, SB sphenoid bone, ZB zygomatic bone, EAC external auditory canal, MT mastoid, MD mandible, TP tympanum. (+) hyper-density soft-tissue mass. The size of the lesion was measured on enhanced MRI examination.
delineation of the tumor, showing intermediate and hypo-intensity signal intensity on T1-weighted imaging, and multiple intensity (hypo-intensity, hyper-intensity, iso-intensity) on T2-weighted sequencing. The low signal area on T2WI represents hemosiderin with paramagnetic effect, which can shorten T2 relaxation time. Iso-intensity and hyper-intense areas represent tumor tissue and cystic lesion on T2WI, respectively. In this study, nine patients have been found to have the hypo-intensity area, two patients the cystic hyper-intensity area and seven patients the iso-intensity area on T2WI. Extended hypo-intensity (the “flowering effect”) on DWI or SWI sequences were caused by the presence of hemosiderin with paramagnetic effect. On CT imaging, classic features of D-TGCT usually presented as soft tissue masses of mixed density with higher density area as a result of hemosiderosis and destructive expansion into the skull base bone, consistent with the imaging results in our study. Neale et al. suggested that the destruction of bone in D-TGCT lesions was mainly associated with the activation of osteoclast differentiation by monocyte and multinucleated giant cell-expressed antigenic phenotypes, similar to those of osteoclasts. All cases showed bone destruction of the skull base, two of which invaded the skull base through the destruction area of the tumor in this study. The extent of lesions and bone destruction can be observed on CT examinations. In this study, there was no significant difference between CT images and intraoperative diagnosis of bone destruction. The incidence of hearing loss in patients with in-

Figure 2. Magnetic resonance imaging (MRI) of a 46-year-old man with diffuse tenosynovial giant cell tumor (D-TS-GCT) in left TMJ. A, T2; (B), T1; (C), Gd-DTPA; (D), DWI (b=100).
Intracranial D-TGCT is extremely rare but must be differentiated from other tumors. Osteolytic bone destruction in the area of the skull base with hyper-density soft-tissue mass and hypo-intensity on T2WI images are indicative of D-TGCT.

**Conclusions**

Intracranial D-TGCT is extremely rare but must be differentiated from other tumors. Osteolytic bone destruction in the area of the skull base with hyper-density soft-tissue mass and hypo-intensity on T2WI images are indicative of D-TGCT.

**Conflict of Interest**

The Authors declare that they have no conflict of interests.

**Authors’ Contributions**

Shanshan Zhao drafted the manuscript. Shanshan Zhao, Jie Bai, and Yong Zhang analyzed and interpreted data. Shanshan Zhao and Eryuan Gao acquired the data. Shanshan Zhao and Jie Bai conceived and designed the study. All authors read and approved the final version of the manuscript.
Ethics Approval
The study was approved by the Ethics Committee of the First Affiliated Hospital of the Zhengzhou University of China. The privacy and safety of subjects were adequately protected in accordance with clinical study guidelines (Protocol code: 2019-KY-231).

Informed Consent
Informed consent was obtained from all individual participants in the study.

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References
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