Malignant pigmented villonodular synovitis (PVNS) is a proliferative disorder of synovial tissue in the joint, tendon sheath, and bursa. Although the lesion is benign, it can be locally aggressive and destroy surrounding soft tissue and bone. PVNS belongs to a family of synovial lesions characterized by benign proliferation of synovial-like mononuclear cells, admixed with multinucleated giant cells, lipid- or hemosiderin-laden macrophages, and inflammatory cells. The etiology of PVNS is unclear. Although Jaffe et al. considered the disease to be a reactive inflammatory response, some investigators have regarded it as neoplastic lesion based on its capacity for autonomous growth, monoclonality, metastatic potential, the presence of chromosomal aberrations, and DNA aneuploidy in some cases.

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PVNS has been generally divided into 2 types: diffuse and localized. PVNS, especially the diffuse type, predominantly affects the knee, followed by the hip, ankle, elbow, and shoulder. Although any synovium can be affected, involvement of the temporomandibular joint (TMJ) has rarely been reported. PVNS of the TMJ was first described by Lapayowker et al. in 1973. Since then, approximately 30 cases of PVNS of the TMJ have been reported in the English literature. According to a recent review of the literature, the average age of onset of TMJ lesions was calculated to be 44 years and ranged from 10 to 70 years; approximately 59% of patients were in their thirties and forties. There was no sex predilection. A preauricular swelling was the most common clinical symptom (present in 92% of cases) and the mean duration of symptoms before diagnosis was 11.4 months. All of the cases were unilateral and monoarticular. Seventy percent of cases had localized bony destruction and 22% of cases extended into the middle cranial fossa. The recurrence rate was 7.4%, lower than that of diffuse PVNS of the knee joint, estimated from 8% to 46%.

The diffuse type of PVNS tends to be a more aggressive lesion with multiple recurrences followed by malignant transformation. In some instances of high cellular proliferation with a high mitotic rate, this type of PVNS can be difficult to differentiate from malignant PVNS. Malignancy in PVNS is extremely rare and there has been some confusion regarding its diag-
nosis owing to the rarity of the well-documented cases and the heterogeneous histologic features of this group of tumors. Approximately 30 cases of malignant PVNS (malignant tenosynovial giant cell tumor) have been reported. Only 1 case of malignant PVNS of the TMJ has been reported. Among 30 cases, the development of metastases was observed in 50% of the patients. Interestingly, metastatic lesions have also developed in cases with benign histology. These 3 cases have been considered to represent clinically malignant disease. Here we present an additional case of the clinically malignant PVNS with lung metastasis.

**CASE REPORT**

A 29-year-old man was referred to our hospital complaining of recurrent swelling and pain in the right preauricular area in March 2006. He had a history of benign tumor removal of the TMJ from the outside hospital in 2000. Clinical evaluation revealed a nontender mass in the TMJ area and a limited interincisal opening of 20 mm. He had no other significant medical history, but presented with hearing loss in the right ear secondary to childhood trauma following a fall. A panoramic radiograph demonstrated a previous resection state of the right mandibular condyle, but the recurrent lesion destroying the surrounding structures, such as articular fossa, articular eminence, or zygomatic arch, was detected (Fig. 1, A). An enhanced computed tomography scan demonstrated an expansile soft tissue mass, approximately 7.0 × 7.0 cm, centered in the right TMJ with severe destruction of the temporal bone. It extended superiorly into the middle cranial base infiltrating the dura mater, medially into the sphenoid bone, laterally into the zygomatic arch, and inferiorly, involving the previously operated condylar area (Fig. 1, B). T2-weighted magnetic resonance imaging (MRI) demonstrated a multiple nodular mass with a low signal area, which seemed to represent a ferromagnetic effect of hemosiderin (Fig. 1, C). Although MRI finding strongly favored PVNS, the possibility of malignancy could not be ruled out because of the extensive and irregular bone destruction. A punch biopsy was performed in the preauricular area. Microscopically, there were numerous mononuclear histiocytic cells, interspersed multi-

![Fig. 1. A, Panoramic view showing the destructive lesion around the right mandibular condyle previously operated. B, An enhanced CT demonstrates an expansile soft tissue mass. C, T2-weighted MRI demonstrates a large nodular mass with a low signal intensity that seems to represent ferromagnetic effect of hemosiderin.](image-url)
nucleated giant cells, inflammatory cells, and prominent hemosiderin deposits. These mononuclear cells had an ovoid or polygonal shape with negative reactivity for s 100 and positive reactivity for CD68 immunostaining. Radiographic and microscopic findings yielded a provisional diagnosis of PVNS.

In July 2006, the patient was operated on by a surgical team consisting of both a maxillofacial surgeon and neurosurgeon. Mass resection with partial mandibulectomy and partial craniotomy was performed. A complete removal of the extra- and intracranial mass was attempted, but an infiltrated dural component remained. There was no evidence of involvement of the brain parenchyma. Repair of the dura and reconstruction with a serratus anterior myo-osseous flap were performed.

Grossly, the resected mass was soft, friable, and approximately 8.0 cm in diameter. Its cut surface was dark brown and gray reflecting diffuse bleeding and necrosis. Microscopically, the tumor was infiltrative and grew as diffuse sheets and occasional lobules (Fig. 2, A). The lesions were composed of a variable number of mononuclear histiocytic cells, interspersed multinucleated giant cells, and hemosiderin-laden

Fig. 2. Histopathologic features. (hematoxylin-eosin stain) A, Infiltrative growth of diffuse sheets and lobules of tumor cells, accompanied by numerous hemosiderin deposits (original magnification ×40). B, Ovoid or spindle-shaped, small histiocytic cells (original magnification ×200). C, Larger rounded cells whose cytoplasm often contained a peripheral rim of hemosiderin granules (original magnification ×200). D, Focally dystrophic lacelike calcification in the chondroid areas (original magnification ×200). E, Pseudoalveolar spaces within the tumor nodule and woven bone formation around the periphery of the nodule (original magnification ×100). F, Focal area showing absence of multinucleated giant cells and some atypical cells with bizarre nuclei (original magnification ×200).
The mononuclear cells were composed of 2 types of cells: ovoid or spindle-shaped, small histiocytic cells (Fig. 2, B) and larger rounded cells with cytoplasm often containing a peripheral rim of hemosiderin granules (Fig. 2, C). Other features were focally dystrophic lacelike calcification in the chondroid areas (Fig. 2, D) and woven bone formation around the periphery of tumor nodules (Fig. 2, E). Pseudoalveolar spaces were also detected within the tumor nodule. Although most areas had histologic overlap with usual PVNS, focal area exhibited some atypical cells with bizarre nuclei, and absence of multinucleated giant cells (Fig. 2, F). These features are atypical in conventional PVNS, but in the absence of frank sarcomatous transformation, we could not conclude that these features were indicative of the malignant transformation. Immunohistochemically, the multinucleated giant cells and some mononuclear cells, demonstrated positivity for CD68 (Fig. 3, A), but negativity for S 100 (Fig. 3, B). The Ki-67 labeling index was 6.4%. Considering the imaging, clinical features, and histology, the final diagnosis was PVNS of the TMJ with focal atypical cells.

At 30 months post surgery, there was no sign of recurrence in the TMJ area on MRI scan, but a thoracic CT found a 2.8-cm nodule in the left lower lobe of the lung (Fig. 4, A). Percutaneous transthoracic needle biopsies were performed. Histologic features of the pulmonary lesion were consistent with the primary lesion in the TMJ area and it was diagnosed as metastatic PVNS (Fig. 4, B and C). The patient was referred to the Department of Thoracic Surgery for surgical removal of the metastatic lesion.

**DISCUSSION**

The term “pigmented villonodular synovitis, tenosynovitis, and bursitis” was introduced in 1941 by Jaffe et al. They regarded the synovium of the joint, tendon sheath, and bursa as an anatomic unit that could give rise to a common family of lesions, including the giant cell tumor of tendon sheath (nodular tenosynovitis), localized and diffuse forms of pigmented villonodular synovitis, and rare cases of extra-articular pigmented villonodular synovitis arising from bursae (pigmented villonodular bursitis or diffuse-type giant cell tumor of tendon sheath). Weiss and Goldblum preferred the term “tenosynovial giant cell tumor (TSGCT)” instead of “giant cell tumor of the tendon sheath” and classified it into 2 subtypes. The localized type of TSGCT usually arises in the flexor tendon sheaths of the hand or foot, which is alternatively referred to as “nodular tenosynovitis” or “giant cell tumor of the tendon sheath.” Unlike the localized type, the diffuse type of TSGCT presents as a poorly defined soft tissue mass and is characterized by a locally aggressive growth pattern and a high recurrence rate. It affects relatively younger patients, principally in the third to fifth decades of life and commonly occurs in large joints, such as the knee, where it is often synonymously referred to as “PVNS.” However, some authors have suggested that the term PVNS should be restricted to purely articular lesions and should not be applied to lesions with diffuse extra-articular extension. Therefore, PVNS could be regarded as the intra-articular form of diffuse TSGCT.

Although many cases of PVNS have exhibited diffuse extra-articular extension in the TMJ area, many authors have continued to use the term PVNS instead of diffuse TSGCT. Interestingly, in a review of the literature, we found only 1 relevant case report that used the terminology “diffuse variant TSGCT of the TMJ.” These authors preferred the term diffuse TSGCT for the reasons outlined in the previous paragraph. The distinction of these terms in the description of TMJ lesions according to the growth pattern (intra-articular or extra-articularly extended) may be necessary to predict the clinical behavior and prognosis of these different types, as there are clinical differences between purely articular PVNS and extra-articularly extended PVNS (= diffuse TSGCT) in other joint areas.
Diffuse TSGCT may exhibit atypical histologic features, including a significantly increased mitotic rate, necrosis, monomorphism, spindling of mononuclear cells, the presence of unusually abundant eosinophilic cytoplasm in histiocytelike cells, enlarged nuclei with nucleoli, and stromal myxoid change. These lesions can be difficult to differentiate from malignant TSGCT/PVNS. However, Somerhausen and Fletcher emphasized that none of these features individually, in absence of frank sarcomatous change, seems to be indicative of malignancy and cases with one or more worrisome features should be reported as “atypical” instead of “malignant.” In the current case, the primary lesion demonstrated focal areas exhibiting few multinucleated giant cells and some atypical cells with bizarre nuclei. Except for focal cytologic atypia, there were no features favoring malignant PVNS. However, unfortunately, the current case developed a pulmonary metastasis that also exhibited bland histologic features.

Malignant tenosynovial giant cell tumors are extremely rare. Diagnosis of the disease may be problematic because of the heterogeneous histologic features of malignant TSGCT. Weiss and Goldblum defined malignant TSGCT/PVNS as a lesion in which typical-appearing benign PVNS coexists with frankly sarcomatous areas (synchronous) or when the original lesion is typical of a benign PVNS and a recurrence appears malignant (metachronous). Bertoni et al. expanded these criteria to include synovium-centered primary sarcoma that, although lacking a history of PVNS, had overlap with the histopathologic features of malignant PVNS arising in patients with previous PVNS. The heterogeneous features of the sarcomatous areas have been reported in forms of fibrosarcomatous, myxosarcomatous, malignant fibrous histiocytomalike, or “giant-cell tumorlike” patterns. However, despite the absence of frank sarcomatous change in the histopathology of PVNS, there have been 3 reported cases of metastatic lesions in the lung or lymph nodes. Although this is a very rare event, the current case could be considered an additional case of the clinically malignant form.

In addition to the preference for pulmonary metastasis, chondroblastoma of bone may exhibit histologic...
features similar to the current case. Chondroid metaplasia was detected in both the primary and metastatic lesions of the current case. Rarely, cartilaginous and osseous metaplasia have been reported in PVNS. Two of these cases involved the TMJ and temporal bone. This uncommon event can mimic chondroblastoma of the bone. To make matters more confusing, in the skull, the temporal bone is the most common site of chondroblastoma, whereas PVNS is uncommon in the TMJ area. According to the Armed Forces Institute of Pathology publications, chondroblastomas of the skull have some histologic features similar to PVNS. Chondroblastomas of the temporal bone have mononuclear cells with oval to elongated nuclei with a characteristic longitudinal groove, abundant eosinophilic cytoplasm, a variable number of multinucleated giant cells, and/or brown granular pigment in the cytoplasm, which may also be characteristic features of PVNS. However, it has been reported that differences in immunoreactivity for CD68 and s 100 protein are helpful in distinguishing PVNS from chondroblastomas of the bone. Mononuclear cells in PVNS are positive for CD68 and negative for s 100 protein, whereas those in chondroblastomas have positive reaction for s 100. In the current case, mononuclear and multinuclear giant cells were positive for CD68, but negative for s 100 staining.

Giant-cell tumors (GCT) of bone should be also excluded, especially in cases with pulmonary metastasis, as GCT of the bone can metastasize to the lung. Histologically, GCT differs from the current case by the monomorphism of the mononuclear cells, which exhibit nuclei similar to those of giant cells. In addition, cartilage and calcification formation is uncommon in GCT.

According to recent review of a large series of malignant diffuse-type TSGCT by Li et al., the mean age of the available 28 patients was calculated at 50.3 years. When these investigators compared 24 benign cases and 7 malignant cases in their study, the results demonstrated a significant difference in the mean age of onset for benign and malignant cases, which are 39.5 and 60.9 years, respectively. A slight female predilection has been previously reported, which is similar to the trends observed in the benign counterpart. Lower extremities were the most commonly involved locations, but the miscellaneous involvement of temporomandibular, paravertebral, and sacrococcygeal regions were also detected in 1 case for each region. The only case of malignant PVNS of the TMJ occurred in a 71-year-old female. Her metachronous malignant lesion demonstrated giant-cell tumorlike histologic features as mentioned by Bertoni et al., and she had a local recurrence with a pulmonary metastasis. Recurrence in malignant cases was detected in 71% of reviewed cases by Bertoni et al., which is significantly higher than the rate of diffuse TSGCT, estimated from 8% to 46%. Li et al. found that the development of metastases was seen in 50% of patients with malignant diffuse-type TSGCT, and 66.7% of them died of the disease. Based on this, malignant TSGCT/PVNS seems to be a very aggressive malignancy.

Most common metastatic sites of malignant TSGCT/PVNS were regional lymph nodes, the lung, and the spine. It seems that the histopathologic features of lymph node metastases are not necessarily consistent with those of the primary sarcoma lesion. Although the original lesion showed myxosarcomatous or malignant fibrous histiocytomalike pattern, metastatic tumors to regional lymph nodes displayed giant cell tumorlike sheets with frequent mitoses. In the clinically malignant form, lymph node metastasis also showed usual benign morphology, similar to that of the primary lesion. Unfortunately, there has been no detailed description of the histopathologic features of the pulmonary metastasis from the malignant TSGCT/PVNS.

The diagnosis criteria and treatment modalities for malignant TSGCT/PVNS have not yet been established because of the rarity of this lesion. On the diagnosis of diffuse TSGCT, the risk of clinically malignant PVNS may be considered negligible for treatment decision because this event is extremely rare. The diagnosis of PVNS of the TMJ, as that in other anatomic sites, seems to be confirmed with the more recent cross-sectional imaging techniques, such as MRI, based on the ferromagnetic effect by hemosiderin deposition. Hemosiderin can alter the MRI signal, shortening of both T1 and T2 relaxation times, and then appearing as low signal areas in T1- and T2-weighted images. MRI has superior contrast, suitable for estimating extent of synovial proliferation, joint effusion, bone erosion, and deposition of hemosiderin. Li et al. also demonstrated that some common characteristics of MRI could serve as clues for differential diagnosis of malignant diffuse TSGCTs. These contained dark signal nodules suggestive of hemosiderin, frequent lobulation of varying degrees, and the close topographic association with tenosynovial structures or joint spaces. Although the differential diagnosis contains hematomas, giant-cell tumors, and pseudoaneurysm as the results of hemorrhage, the combination of synovial proliferation, soft tissue mass, deposits of hemosiderin, and bone erosion around the joint is highly diagnostic for PVNS. Although multiple recurrences and regional or distant metastasis have developed following aggressive treatments, such as amputation with radiation therapy, surgical excision with wide surgical margins is the current treatment of choice. Based on a review dem-
onstrating that regional and distant metastases were detected as early as 4 months and as late as 5 years after treatment, long-term follow-up is mandatory to detect late metastasis. As multiple local recurrences and metastatic potential seem to be related to a poor prognosis, strict local control with aggressive surgical treatment and periodic follow-up with imaging for the metastatic lesions may be needed to improve outcomes. Further study of greater numbers of malignant TSGCT/PVNS cases, including the clinically malignant form, is needed to further elucidate this entity and to establish the clinico-pathological criteria for predicting malignant transformation from its benign counterpart.

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Reprint requests:
Seong-Doo Hong, DDS, PhD
Department of Oral Pathology
School of Dentistry
Seoul National University
28-2 Yeongun-dong, Chongro-gu
Seoul 110-749, Korea
hongsd@snu.ac.kr