

Pigmented villonodular synovitis with chondroid metaplasia, resembling chondroblastoma of the bone: a report of three cases

Yoshinao Oda¹, Teiyu Izumi¹, Katsumi Harimaya², Yuichi Segawa¹, Shinichiro Ishihara³, Shizuo Komune⁴, Yukihide Iwamoto² and Masazumi Tsuneyoshi¹

¹Department of Anatomic Pathology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan; ²Department of Orthopaedic Surgery, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan; ³Miyake Neurosurgical Hospital, Iizuka, Japan and ⁴Department of Otolaryngology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

We herein describe three cases of pigmented villonodular synovitis with chondroid metaplasia. Two cases involved the temporomandibular joint, whereas the remaining one case occurred in the hip joint. Histologically, the tumors showed a villous pattern and were mainly composed of histiocyte-like cells and scattered osteoclast-like multinucleated giant cells, accompanied by chondroid areas with occasional lace-like calcification. These features resembled those of chondroblastoma of the bone, with the exception of the villous pattern. The histiocyte-like cells showed positive immunoreactivity for CD68, whereas they were negative for S-100 protein. Some of the previously reported cases of chondroblastoma in the temporal bone may have actually been cases of pigmented villonodular synovitis with chondroid metaplasia. When histologically chondroblastoma-like lesions involve the temporal bone or temporomandibular joint, the possibility of pigmented villonodular synovitis with chondroid metaplasia should also be considered, in addition to chondroblastoma of the bone. The correlation between this lesion and synovial chondromatosis remains uncertain.

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Pigmented villonodular synovitis usually arises from the joint spaces in large joints, such as the knee or hip.¹ Histologically, the lesion is characterized of the presence of a villous pattern, or a pseudoglandular or pseudoalveolar pattern.^{1,2} The tumor is mainly composed of small or large histiocyte-like cells and osteoclast-like multinucleated giant cells. Recently, molecular genetic study demonstrated that only a minority of cells in pigmented villonodular synovitis are actually neoplastic cells and overexpress CFS1, which attract a

secondary non-neoplastic population of histiocytes.³ Cartilaginous and osseous metaplasia is considered to be a rare phenomenon in pigmented villonodular synovitis. Only a single case report has been documented in detail concerning this rare type of tumor.⁴ Here, we report three cases of pigmented villonodular synovitis with extensive cartilaginous metaplasia and focal areas superficially resembling chondroblastoma of the bone. Two out of the three cases involved the temporomandibular joint and temporal bone, which is the most common site of skull chondroblastoma.

Correspondence: Dr Y Oda, MD, Department of Anatomic Pathology, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan.
E-mail: oda@surgpath.med.kyushu-u.ac.jp

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Materials and methods

The surgical specimens of all three cases were fixed in neutral buffered formalin. Hematoxylin and eosin staining and iron staining were performed in six (case 1), two (case 2) and six (case 3) formalin-fixed paraffin-embedded blocks. Immunohistochemical

Table 1 Antibodies used and sources

Antibody	Source	Concentration
CD68	Dako Cytomation, CA, USA	1/300 MW ^a
Factor XIIIa	Behring, Marburg, Germany	1/800 T ^b
S-100 protein	Dako	1/400 T
Desmin	Dako	1/100
Muscle-specific actin	Biomedica, CA, USA	1/200
Vimentin	Dako	1/25
EMA	Dako	1/400
Cytokeratin (AE1/AE3)	NeoMarker, CA, USA	1/400
Ki-67	Dako	1/100 MW

^aMW; pretreated with citrate buffer in a microwave oven for 20 min.

^bT; pretreated with trypsin for 30 min.

staining was performed in sections from a representative paraffin block from each case, using a streptavidin–biotin–peroxidase method (Histofine, Nichirei, Tokyo, Japan). The antibodies employed in this study are listed in Table 1. The Ki-67-labeling index (LI) was estimated by counting the number of positive cells per 1000 tumor cells.

Case Reports

Case 1

A 52-year-old man suffered from a 10-month history of tightness in his right ear. A mass lesion that protruded from the external auditory canal was discerned. CT scan revealed bone destruction of the right mandibular condyle and a soft-tissue mass measuring 2.0×1.8 cm with calcification, which had invaded the temporal bone and temporomandibular joint (Figure 1). After open biopsy, tumor resection was carried out. Follow-up magnetic resonance imaging (MRI) 11 months after surgery revealed no tumor recurrence.

Case 2

A 67-year-old man suffered from a 3-month history of pain in the left ear and swelling of the left cheek. MRI demonstrated a mass lesion, which was destroying the left temporal bone, involving the middle fossa and the temporomandibular joint. Angiography revealed a hypervascular mass. Following open biopsy, tumor resection was performed. Currently, the patient remains free of tumor recurrence 7 years and 3 months after the surgery.

Case 3

A 52-year-old woman complained of a 3-year history of right coxalgia. She had also noticed a mass lesion in her right groin about 6 months earlier. Plain radiography showed bone erosion in the right femoral neck. MRI revealed a tumor measuring

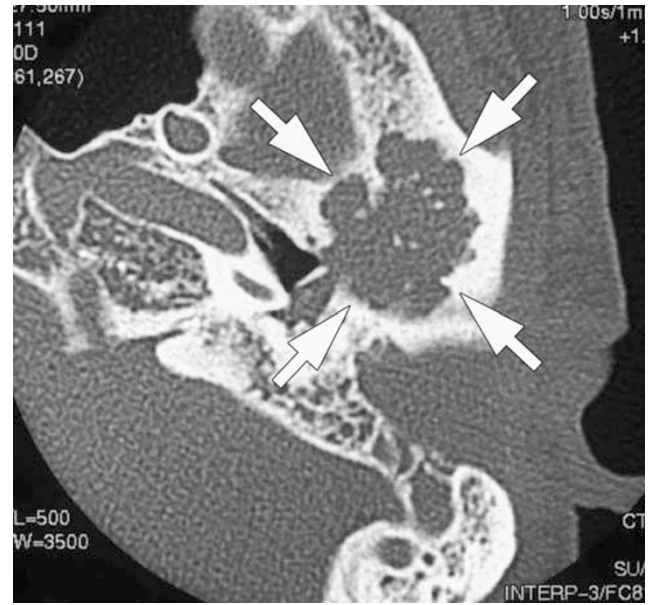


Figure 1 Plain CT scan shows the destruction of the mandibular condyle. Soft-tissue mass in the temporomandibular joint is extending into the temporal bone (arrow), associated with calcification (case 1).

3.0×2.0 cm with fluid beneath the femoral neck, which showed low intensity on T1-weighted images (WI) and low intensity on T2-WI (Figure 2). The preoperative clinical diagnosis was pigmented villonodular synovitis and the patient underwent tumor resection. Postoperative imaging 2 years after the surgery revealed no recurrence.

Results

Macroscopic Findings

The tumors were resected piece by piece in cases 1 and 2. These lesions were described by the operating surgeons as comprising solid brownish or reddish-brown material. The periphery of the lesion was firm, whereas the central areas were friable. In case 3, the joint cavity was filled with bloody joint fluid and a tan to grayish tumor was observed. The cut surface of the resected tumor showed solid and whitish-gray cartilaginous areas with a gritty sensation, accompanied by villous configuration in part (Figure 2b).

Histopathological Findings

All the three cases had similar microscopic features and showed a characteristic villous pattern on low-power view (Figure 3a). In case 1, pseudoalveolar spaces were also encountered within the solid areas (Figure 3b). The tumor was mainly composed of a proliferation of rounded or polygonal mononuclear histiocyte-like cells with pale eosinophilic cyto-

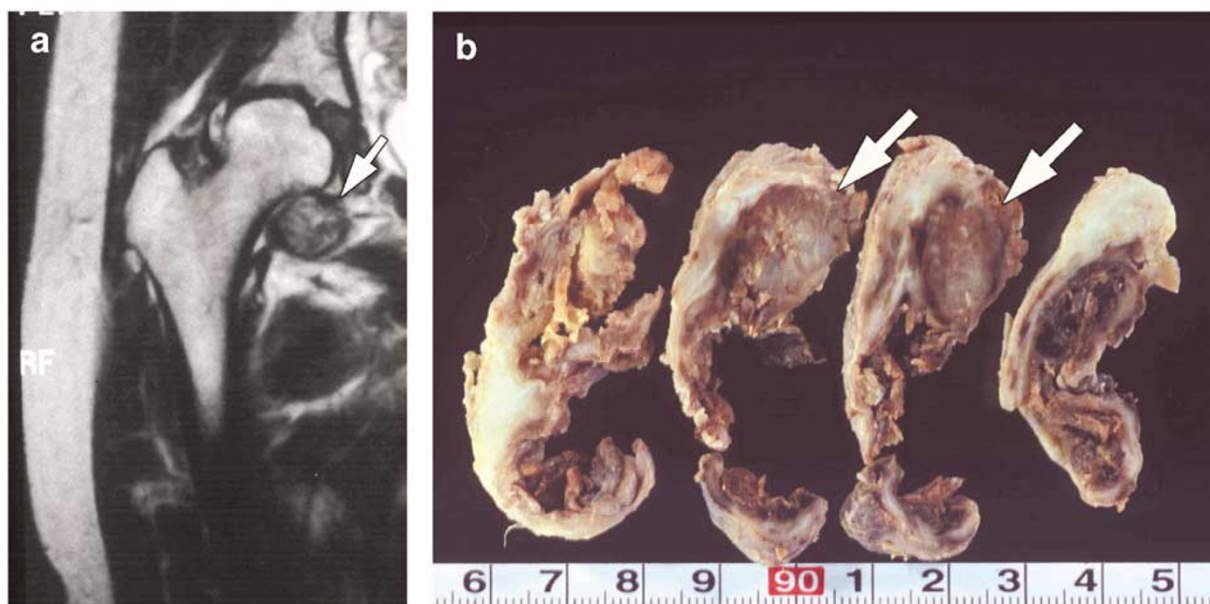


Figure 2 (a) MRI discloses a nodular lesion in the hip joint (arrow), which shows low intensity on T2 WI (case 3). (b) Cut surface of the resected tumor shows whitish-gray cartilaginous tissue (arrow), accompanied by brownish villous configuration in part (case 3).

plasm (Figure 3c). Some mononuclear cells had prominent eosinophilic cytoplasm and grooved nuclei, which mimicked chondroblasts. Mitotic figures were occasionally seen; however, no abnormal forms were detected. Aggregates of osteoclast-like multinucleated giant cells (Figure 3b) and hemosiderin deposits (Figure 3d) were also evident in all the three cases. Iron stain also confirmed the presence of abundant hemosiderin in all cases (Figure 3e). Another characteristic feature was the presence of hyaline chondroid nodules or lobules (Figure 3f and g). The cartilaginous component occupied approximately 20% of whole area in case 1, 30% in case 2 and 30% in case 3, respectively. Moreover, there were focal areas superficially resembling chondroblastoma. Dystrophic lace-like calcification, resembling so-called 'chickenwire calcification' of chondroblastoma, was focally observed in the chondroid areas in all three cases (Figure 3h). Enchondral ossification was also apparent in case 3 (Figure 3i). Secondary changes including reactive bone formation and a florid fibrohistiocytic proliferation were evident in case 1.

Immunohistochemical Findings

The immunohistochemical findings are summarized in Table 2. The histiocyte-like cells were positive for CD68 as well as osteoclast-like multinucleated giant cells in all cases (Figure 4a). The histiocyte-like cells also showed immunoreactivity for Factor XIIIa in cases 1 and 2. The mononuclear cells in the chondroid areas were uniformly positive for S-100 protein (Figure 4b), whereas none of the histiocyte-

like cells showed any positive reaction. A minority of the histiocyte-like cells was positive for desmin in all cases, and positive for muscle-specific actin in cases 1 and 3. The mononuclear cells in both the histiocyte-like and chondroid areas were uniformly positive for vimentin. Concerning the proliferative activities, Ki-67-LIs in the histiocyte-like areas were between 5.7 and 8.7%, whereas those in the chondroid areas were less than 1%.

Discussion

Chondroid metaplasia is a rare phenomenon in tenosynovial giant cell tumors of both localized (giant cell tumor of tendon sheath) and diffused type (pigmented villonodular synovitis). Weiss and Goldblum² stated that cartilaginous and osseous metaplasia is a rare focal finding in giant cell tumor of tendon sheath; however, no such description was observed in pigmented villonodular synovitis. In our three cases, cartilaginous metaplasia was extensively observed, in addition to the typical histological findings of pigmented villonodular synovitis. Until now, only a single such case report has been documented, and that concerned the elbow joint of a 54-year-old man. The tumor was classified as pigmented villonodular synovitis with a cartilaginous component by Pignatti *et al.*⁴

Histopathologically, our cases superficially mimicked chondroblastoma. Two of our three cases involved the temporomandibular joint and the temporal bone. The temporal bone or temporal fossa is one of the most common sites of chondroblastoma,^{5,6} whereas pigmented villonodular synovitis of

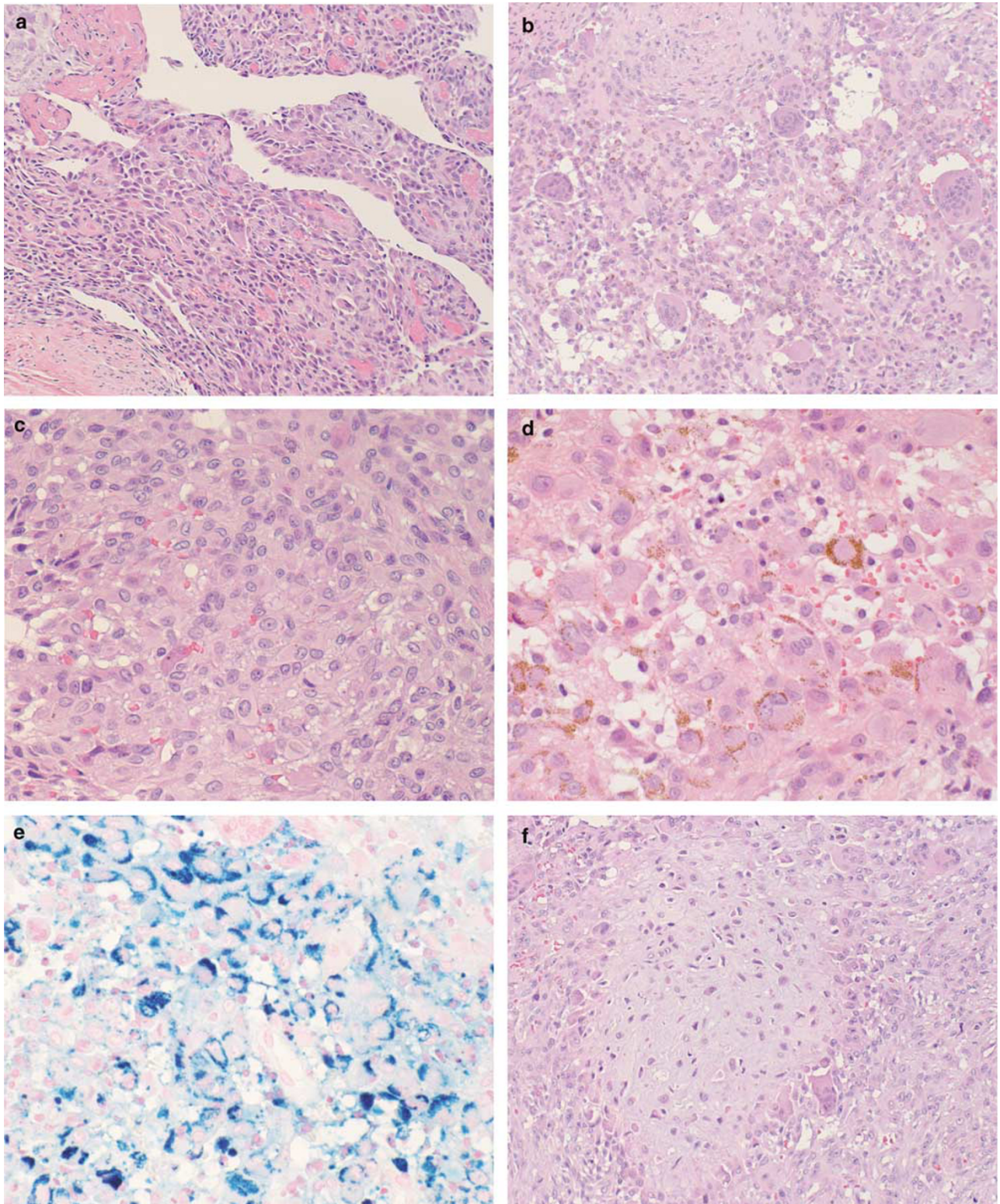


Figure 3 (a) Typical villous pattern (case 3). (b) Pseudoalveolar spaces with scattered osteoclast-like multinucleated giant cells (case 1). (c) Rounded or polygonal histiocyte-like mononuclear cells with eosinophilic cytoplasm (case 1). (d) Large-sized mononuclear histiocyte-like cells contain a peripheral rim of hemosiderin granules (case 2). (e) Iron stain discloses abundant hemosiderin (case 2). (f) Nodules of pink chondroid matrix are present between a proliferation of mononuclear histiocyte-like cells (case 1). (g) Lobular arrangement of hyaline cartilaginous tissue with mildly atypical chondrocytes (case 3). (h) Lace-like calcification between the mononuclear cells in the chondroid area (case 1). (i) Prominent enchondral ossification (case 3).

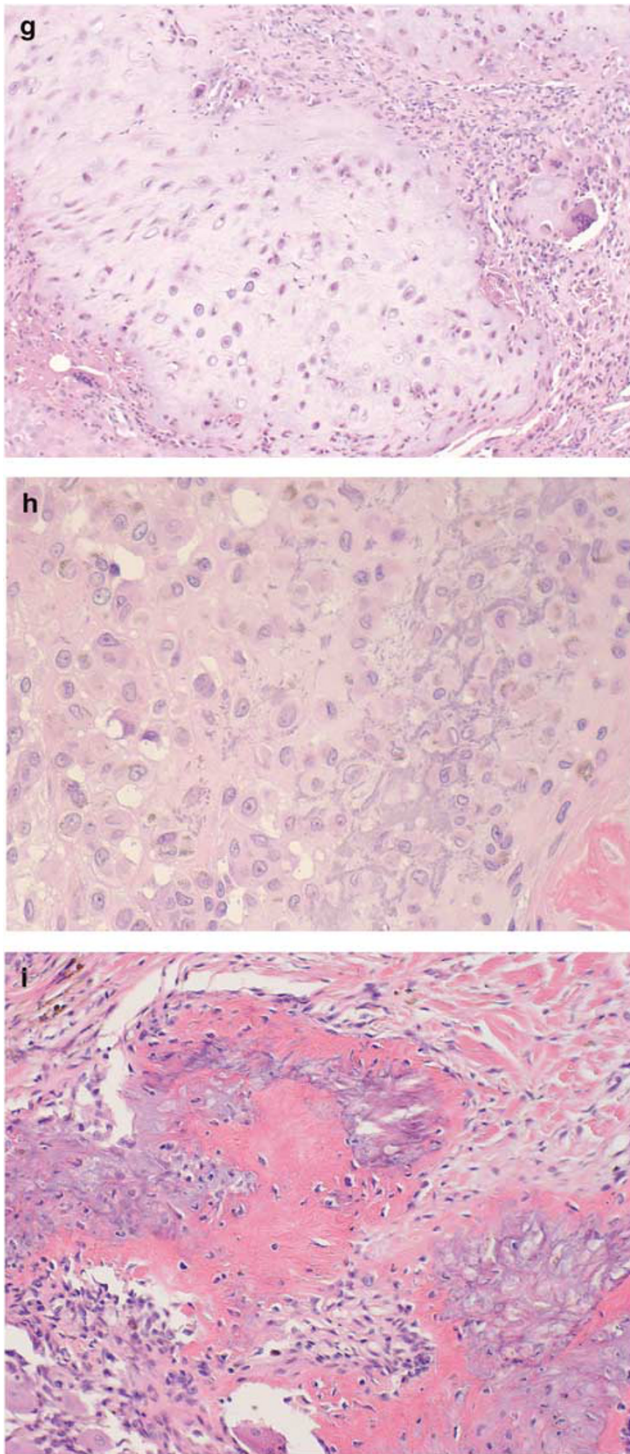


Figure 3 Continued.

temporomandibular joint is not common.⁷ According to the large series of Kurt *et al*,⁵ 23 out of 499 chondroblastomas (4.6%) arose in the temporal bone. Actually, our initial diagnosis of one case (case 1) was chondroblastoma. Brien *et al*⁸ described about their own 15 cases of giant cell tumor of tendon sheath or pigmented villonodular synovitis

with extensive areas of chondroid and/or cartilage differentiation could not be distinguished from chondroblastoma of the bone by histologic or electron microscopic features alone. However, unfortunately they stated these comments in only discussion and their details have not been further documented.⁸ Reviewing the previously reported cases of temporal bone chondroblastoma, large tumors involved the surrounding soft tissue as well as the temporomandibular joint, suggesting pigmented villonodular synovitis by CT scan⁹ or MRI¹⁰ and these tumors histologically were found to contain prominent brown pigments in the mononuclear cells.^{9–11} Interestingly, the AFIP textbook states that some chondroblasts in the skull more commonly contain brown granular pigment in the cytoplasm, compared with other long bone cases.¹² Moreover, histiocyte-like cells in pigmented villonodular synovitis also frequently display eosinophilic cytoplasm and longitudinal nuclear grooves,¹ which are also the characteristic features of chondroblasts.⁶ Considering these reports, there is the possibility that some reported cases of temporal bone chondroblastoma may have actually been cases of pigmented villonodular synovitis with chondroid metaplasia.

Synovial chondromatosis is the other important differential diagnosis of the current cases. One of our cases (case 3) involved the hip joint, wherein synovial chondromatosis often occurs. Janssens *et al*¹³ found three cases of free osteochondroma with well-defined foci of metaplastic cartilage beneath the synovial lining cells, among their own seven cases of pigmented villonodular synovitis in the hip joint. They speculated that pigmented villonodular synovitis and synovial osteochondromatosis may occur simultaneously and may possibly be related entities reacting to a common etiologic factor. Furthermore, Pignatti *et al*⁴ also considered that their case of elbow pigmented villonodular synovitis with chondroid metaplasia had the possibility of being an intermediate form of pigmented villonodular synovitis associated with synovial chondromatosis. In our cases, no free osteochondral or cartilaginous nodules, as seen in typical synovial chondromatosis, were observed in the lesion. Therefore, we considered that the presence of cartilaginous tissue in the current cases was caused by chondroid metaplasia within the pigmented villonodular synovitis. However, the possibility that pigmented villonodular synovitis is actually a reactive synovial lesion to the primary synovial chondromatosis cannot be completely denied (Figure 5).

Tumoral calcium pyrophosphate dihydrate crystal deposition disease (tophaceous pseudogout) is also differential diagnosis of the current cases. It can also affect temporomandibular joint^{14,15} and other atypical location.¹⁴ Tumoral calcium pyrophosphate dihydrate crystal deposition disease may be confused with pigmented villonodular synovitis with

Table 2 Immunohistochemical results

Antibody	Case 1		Case 2		Case 3	
	H	C	H	C	H	C
CD68	+ patchy	—	+	—	+	+ patchy
Factor XIIIa	+	—	+	—	—	—
S-100 protein	—	+	—	+	—	+
Desmin	+ focal, weak	—	+ focal	—	+ focal, weak	—
Muscle-specific actin	+ focal	—	—	—	+ focal	—
Vimentin	+	+	+	+	+	+
EMA	—	—	—	—	—	—
Cytokeratin (AE1/AE3)	—	—	—	—	—	—
Ki-67 labeling index (%)	8.2	<1	5.7	<1	6.4	<1

C, chondroid area; H, histiocyte-like area.

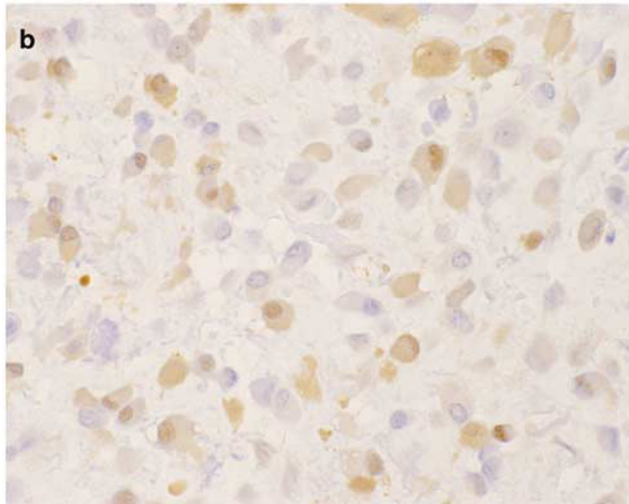
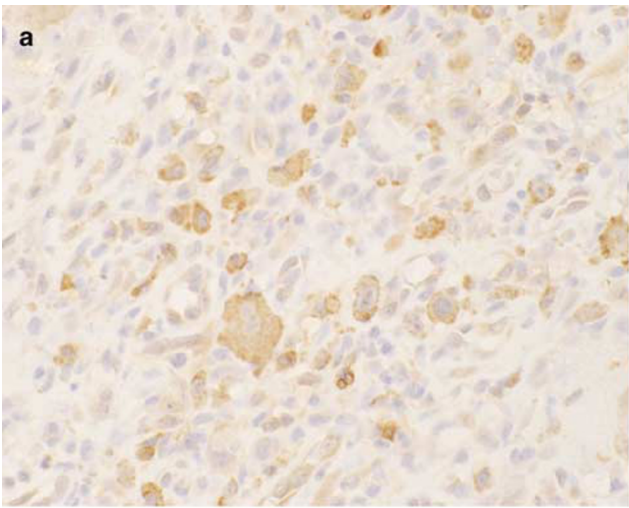


Figure 4 (a) Polygonal mononuclear histiocyte-like cells and osteoclast-like multinucleated giant cells are positive for CD68 (case 3). (b) Mononuclear cells with eosinophilic cytoplasm in the chondroid areas show immunoreactivity for S-100 protein (case 3).

chondroid metaplasia, because it commonly shows foreign body granuloma reaction and metaplastic chondroid tissue.¹⁴ Tumoral calcium pyrophosphate

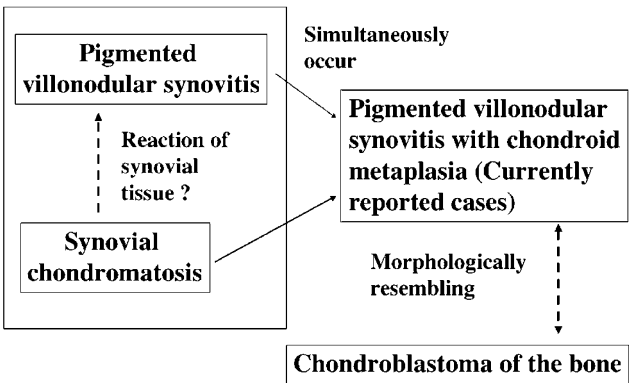


Figure 5 Possible correlations between pigmented villonodular synovitis, synovial chondromatosis, and the currently reported cases of pigmented villonodular synovitis with chondroid metaplasia.

dihydrate crystal deposition disease is characterized by the presence of small to large islands of intensely basophilic calcified crystalline material, which exhibit positive birefringence. In our cases, no such crystalloid material could be detected throughout the lesions.

Immunohistochemical studies were helpful to distinguish pigmented villonodular synovitis from chondroblastoma. Mononuclear histiocyte-like cells in all three cases showed immunoreactivity for CD68 and were negative for S-100 protein. In contrast, mononuclear cells in chondroblastoma are positive for S-100 protein,^{6,12} whereas they are negative for CD68. In the current cases, mononuclear cells in morphologically distinct chondroid nodules were positive for S-100 protein.

In summary, we have described three cases of pigmented villonodular synovitis with chondroid metaplasia. Histologically, these lesions mimicked chondroblastoma. When similar lesions involve the temporal bone or temporomandibular joint, the possibility of pigmented villonodular synovitis with chondroid metaplasia, as well as chondroblastoma, should also be considered. As regards their relation-

ship with synovial chondromatosis, further studies enabling the analysis of more cases are needed.

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Conflict of interest

There are no conflicts of interest to disclose by any of the authors.

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