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Maffucci's syndrome combined with dedifferentiated chondrosarcoma

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Summary. We report a rare case of Maffucci's syndrome combined with dedifferentiated chondrosarcoma in the right shoulder girdle developing from pre-existing enchondroma. In this case, magnetic resonance imaging was useful in diagnosing dedifferentiated chondrosarcoma before surgery. T2-weighted imaging was used to distinguish between the cartilaginous component and the dedifferentiated one. Histologically, there was enchondroma in the humerus and grade 2 chondrosarcoma in the scapula. Further, the dedifferentiated tumor had three mesenchymal elements: osteosarcoma, malignant fibrous histiocytoma, and fibrosarcoma. This histological heterogenicity may be due to mesodermal dysplasia of Maffucci's syndrome.

Maffucci's syndrome, a rare, congenital, nonhereditary mesodermal dysplasia, is characterized by multiple enchondromas and soft tissue hemangiomas. The incidence of malignant tumors associated with the disease is high, with more than 50% of these being malignant transformations of enchondromas to chondrosarcomas [11]. This report details the case of a 72-year-old woman diagnosed as having Maffucci's syndrome combined with dedifferentiated chondrosarcoma in the right shoulder girdle developing from pre-existing enchondroma.

Dedifferentiated chondrosarcoma was first fully described in 1971 by Dahlin and Beabout [5]; however, dedifferentiated chondrosarcoma associated with multiple enchondromas is rare. Three dedifferentiated chondrosarcomas occurring in patients with multiple enchondromas (Ollier's disease) were described by Dahlin and Unni [6]. To our knowledge, dedifferentiated chondrosarcoma arising in an enchondroma in Maffucci's syndrome has not previously been reported.

In this case, magnetic resonance imaging (MRI) was used to distinguish between the cartilagenous component and the dedifferentiated one. Histologically, the dedifferentiated lesion had three elements; osteosarcoma, malignant fibrous histiocytoma, and fibrosarcoma.

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Case report

A 72-year-old woman presented with a 6-month history of right shoulder pain. During the first 4 months, she was treated conservatively at Shinminato City Hospital for periarthritis of right shoulder joint. At that time, radiographs showed no evidence of any malignant change in a pre-existing enchondroma (Fig. 1a). Thirty years previously her right small finger had been amputated because of recurrent enchondroma.

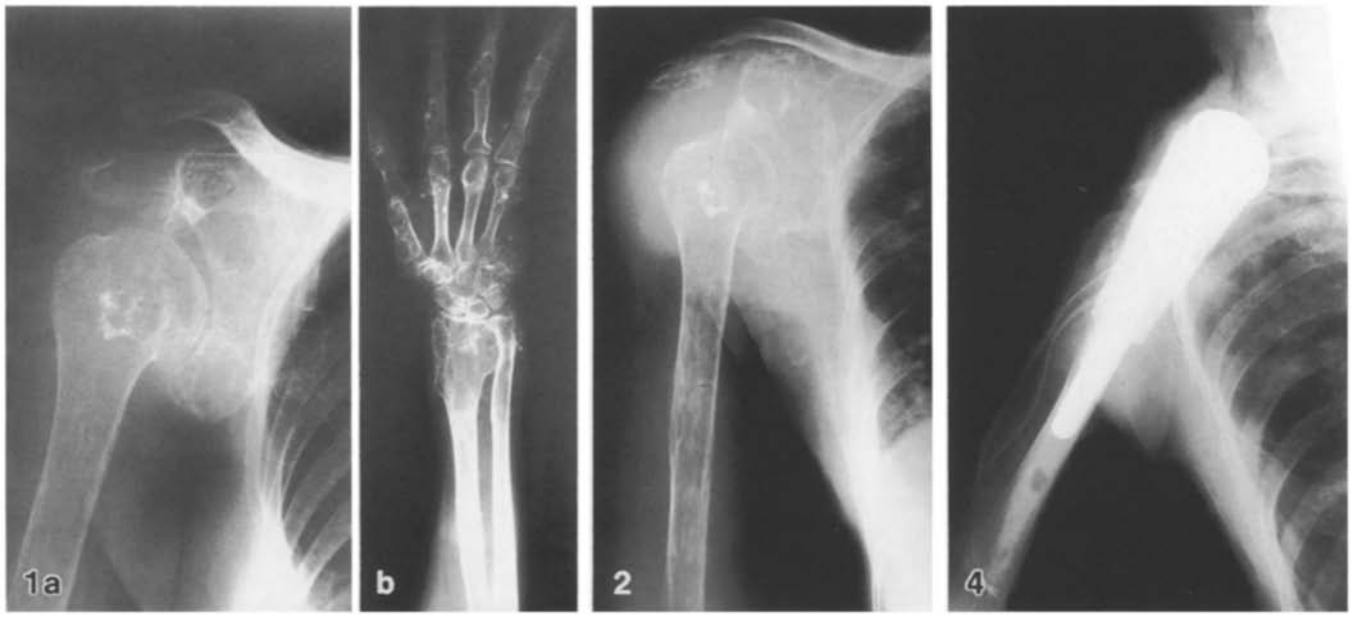
A diagnosis of Maffucci's syndrome was made based on the presence of multiple enchondromas in the phalanges, metacarpals, radius, ulna, humerus, and scapula of the right upper extremity and multiple subcutaneous hemangiomas in the right hand and elbow (Fig. 1b). The woman had had no history of malignancy prior to this time.

A physical examination showed remarkable swelling of the right shoulder and severe limitation of the range of motion of the shoulder joint. The skin had a slightly erythematous change, and the mass, located in the posterior lateral aspect of the shoulder, was firm, immobile, and tender to palpation.

Radiographs of the right shoulder demonstrated an expansile, destructive lesion involving the humerus and scapula (Fig. 2). A pulmonary metastasis was observed in the radiograph of the chest. A radionuclide bone scan showed markedly increased uptake in the scapula, humerus, and soft tissue component of the shoulder girdle tumor; however, the bone scintigram did not permit specific location of the uptake. No other sites demonstrated abnormal uptake. Computed axial tomography (CAT) showed a low density area and spotty calcification in the scapula and humerus, but did not allow distinction between extraosseous extension of the lesion and normal muscle.

Magnetic resonance imaging (MRI) demonstrated the existence of two components in the tumor. The tests were performed with a 1.5-tesla system (Signa; General Electric Medical Systems) with the right upper extremity placed in a surface coil. On the T1-weighted images [repetition time (TR) = 500 ms; echo time (TE) = 20 ms] by the spin echo method, both the intraosseous lesions in the humerus and scapula and the extraosseous lesion posterior to the shoulder girdle showed low signal intensity similar to normal muscles. However, the T2-weighted image (TR = 2500 ms; TE = 80 ms) demonstrated increased signal intensity in the lesion of the humerus and scapula compared to normal fatty marrow. The intraosseous tumor was arranged in a lobular pattern. Further, the signal intensity of the scapular lesion was higher than that of the humeral lesion. The extraosseous lesion showed even and low signal intensity relative to the intraosseous lesion in the T2-weighted image. Partial discontinuity of the cortex of the humerus and scapula was also observed (Fig. 3).

After complete clinical evaluation, the patient's condition was diagnosed as malignant transformation of enchondroma to chondrosarcoma with dedifferentiated components. Wide excision was performed according to the Tikhoff-Linberg procedure [12] to relieve the severe pain. Reconstruction was achieved using a cement-



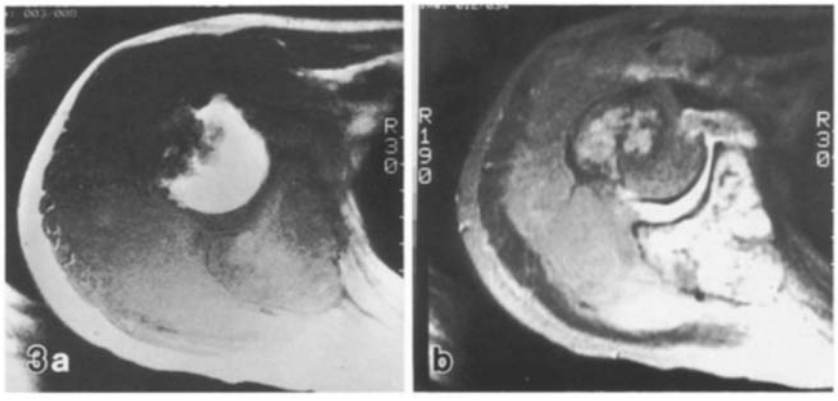


Fig. 1. a Plain radiograph taken at Shinminato City Hospital showed spotty calcification in the humerus and scapula. Expansion of the scapula was observed; however, destructive change was not seen at this time. **b** Plain radiograph showed multiple enchondromatoses and calcification in subcutaneous hemangiomas. The small finger had been amputated 30 years previously

Fig. 2. Plain radiograph 6 months after onset of symptoms showed an expansile and destructive lesion involving the humerus and scapula. A huge soft tissue mass was also seen

Fig. 3. a On T1-weighted imaging (TR = 500 ms; TE = 20 ms), the intraosseous lesions in the humerus and scapula as well as the extraosseous dedifferentiated portion showed low signal intensity, similar to normal muscle, when compared with normal fatty marrow. **b** On T2-weighted imaging (TR = 2500 ms; TE = 80 ms), increased signal intensity compared with normal marrow was seen in the lesion of the humerus and scapula. The intensity of the scapular lesion was higher than that of the humeral lesion. The dedifferentiated portion was visible as low signal intensity similar to normal fatty marrow. The intraosseous lesion grew in a lobular pattern

Fig. 4. After wide excision using the Tikhoff-Linberg procedure, the shoulder was replaced by a cemented Neer prosthesis

ed Neer prosthesis (Fig. 4). Four weeks after surgery, the patient died of respiratory failure due to multiple pulmonary metastases. Pain relief as a result of surgery was satisfactory.

Pathological findings

The intraosseous lesion was a semitranslucent, partially calcified and lobulated, cartilaginous tumor. A small area of cortical destruction was seen at the dorsal aspect of the humerus and scapula. A gray, fleshy, anaplastic tumor abutted the cartilagenous component. Enchondromas were present in the humerus, high grade chondrosarcoma in the scapula, and a highly malignant spindle cell sarcoma in the extraosseous lesion (Fig. 5). Using the classification system described by Evans et al. [8], the condrosarcoma in the scapula was grade 3 as more than two mitoses were observed in each high power field. There was also a small of enchondroma in the lower focus edge of the lesion in the scapula.

Closer examination revealed that the dedifferentiated lesion had three mesenchymal elements, consisting of osteosarcoma, fibrosarcoma, and malignant fibrous histiocytoma (Fig. 6). Small foci of malignant osteoid formation seen were near the edge of enchondroma in the humerus. Most of the fibrogenic area showed a "storiform" or "herring-bone" pattern. There were histiocytic cells which showed grooving or indentation of nuclei in a small area of this fibrogenic tumor. The dedifferentiated tumor was classified as a fibroblastic osteosarcoma according to the definition by Dahlin and Unni [6].

The pulmonary metastatic lesions were found to be malignant spindle cell sarcoma. There was no evidence of osteoid production by the spindle cells.

Discussion

The syndrome of enchondromatosis with hemangiomatosis was first described by Maffucci in 1881 [13]. In 1942, Carleton et al. [4] reviewed 20 cases of this syndrome and named it Maffucci's syndrome. Lewis and

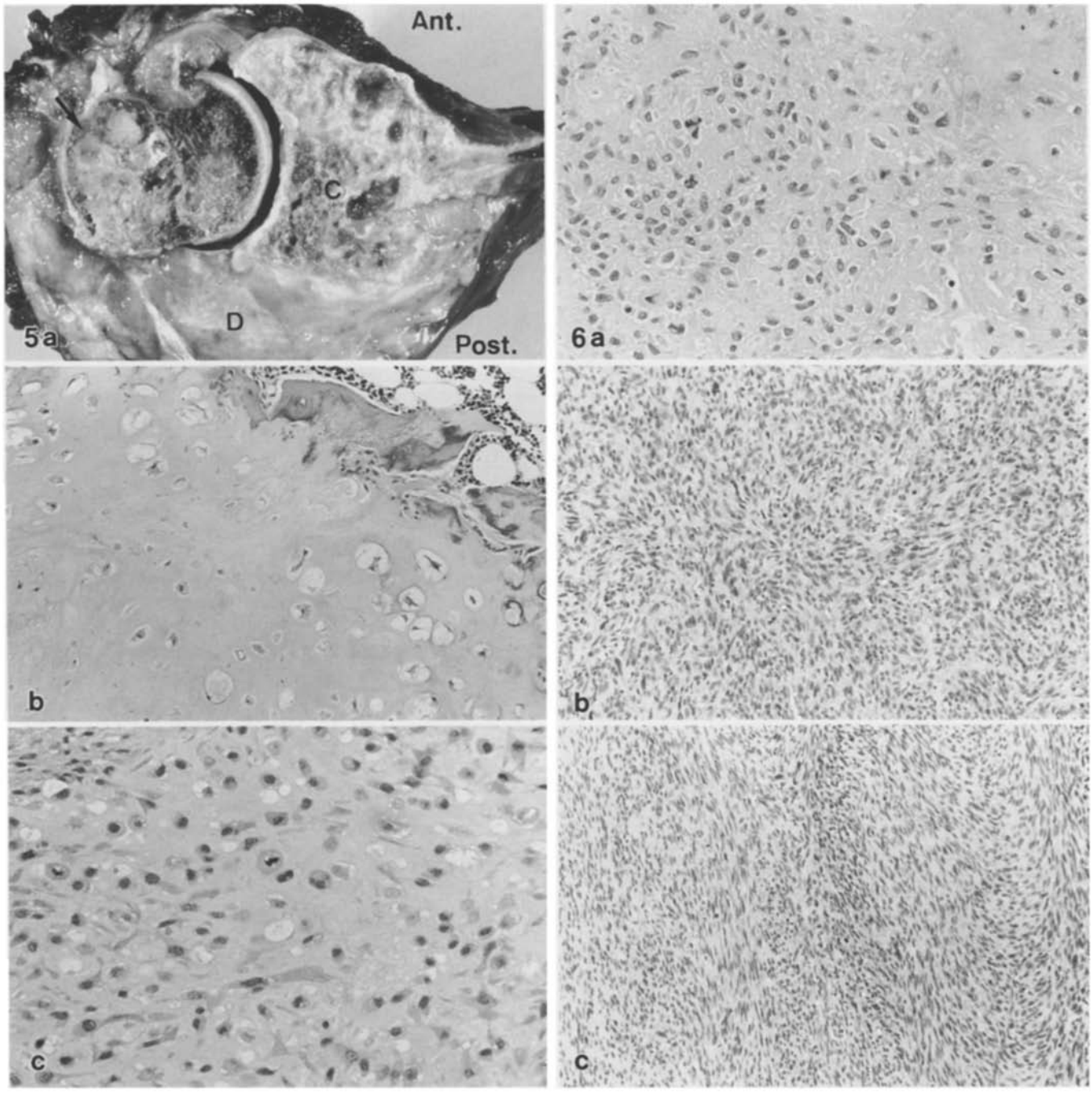


Fig. 5. a Dedifferentiated fibrous tumor *(D)* situated posteriorly in the shoulder girdle. A semitranslucent cartilaginous lesion was seen in the humerus (*black arrow*, enchondroma) and scapula (*C*, chondrosarcoma). The posterior cortex of the scapula was thinned and partially ill defined. **b** Histologically, the lesion in the humerus was a benign enchondroma (hematoxylin – eosin, × 300). **c** The lesion in the scapula was a grade 3 chondrosarcoma in Evans' classification; more than two mitoses were observed in each high power field (hematoxylin – eosin, × 300)

Fig. 6. a There were small foci of neoplastic osteoid production by spindle cells near the edge of the humeral enchondroma (hematoxylin – eosin, × 150). **b** The fibrogenic area showed "storiform" pattern, which is commonly seen in malignant fibrous histiocytoma (hematoxylin – eosin, × 75). **c** A "herringbone" pattern was also observed in a dedifferentiated area (hematoxylin – eosin, × 75)

Ketcham [11] recorded sarcomatous transformation in 16 of 105 cases with Maffucci's syndrome, with an overall malignancy rate of 23%. The incidence of chondrosarcoma in enchondromatosis including Maffucci's syndrome and Ollier's disease was between 15.2% and 23% [11, 17, 18]; most of these chondrosarcomas were low grade. Dahlin and Unni [6] described three cases of dedifferentiated chondrosarcoma in Ollier's disease. However, this report is the first documentation of the occurrence of dedifferentiated chondrosarcoma developing in a patient with Maffucci's syndrome.

In this case, T2-weighted images showed different intensities within the cartilaginous lesion; the dedifferentiated area was, therefore, anticipated. It has been re-

ported that chondrosarcoma in patients with Maffucci's syndrome has a higher signal intensity that the enchondroma in a T2-weighted image [19]. While distinguishing between chondrosarcoma and benign enchondroma may be difficult radiographically and histologically [15], T2-weighted imaging may differentiate between chondrosarcoma and benign enchondroma. In this patient, the signal intensity of the chondromatous lesion in the scapula was clearly higher than in the humerus. Thus, examination by MRI should be performed for tissue characterization as well as for finding out the tumor extension and for anatomical information. T2-weighted images can also be used to plan treatment for patients with enchondromatosis if T2-values can distinguish between chondrosarcoma and chondroma or between dedifferentiated chondrosarcoma and low grade chondrosarcoma.

Histologically, tumor cells may have the potential to dedifferentiate in various directions. In a study of 79 dedifferentiated tumors, Dahlin and Unni reported that 43 cases showed osteoid production and were judged to be osteosarcoma, while 33 were judged to be fibrosarcoma [6]. However, three additional studies found that malignant fibrous histiocytoma was the most frequent outcome of dedifferentiation [3, 10, 14]. Cases of rhabdomyosarcomatous and cytokeratinous differentiation were reported as well [7, 16]. In the case reported here, the dedifferentiated tumor had three mesenchymal elements: osteosarcoma, fibrosarcoma, and malignant fibrous histiocytoma. This histological heterogenicity may be due to mesodermal dysplasia of Maffucci's syndrome. One portion was judged to be osteosarcoma because there were small foci of osteoid production by the spindle cells. It may be unnecessary to characterize the dedifferentiated portion, especially in cases which have various mesenchymal elements.

Although most dedifferentiated chondrosarcomas feature a well-differentiated chondrosarcomatous component, Campanacci et al. [2] reported 7 of 25 chondromatous lesions to be grade 2 chondrosarcoma according to Broders' classification [1]. Dahlin and Unni reported that the cartilaginous component was considered more active and the lesion was grade 2 in 19 of the 79 cases they examined [6]. In this case, the cartilaginous lesion in the humerus was definitely enchondroma, while that in the scapula was a grade 3 chondrosarcoma according to Evans' classification or a grade 2–3 chondrosarcoma by Broders' system. The origin of the dedifferentiated portion was not evident: the dedifferentiated chondrosarcoma in the humerus may have been complicated by the secondary chondrosarcoma arising from the enchondroma in the scapula or the dedifferentiated chondrosarcoma arising from the scapula may have been complicated by the enchondroma in the humerus.

The prognosis for dedifferentiated chondrosarcoma is commonly poor [3, 6, 9]. Highly anaplastic cells frequently metastasize to distant organs. In this case, histological examination revealed that the pulmonary metastatic lesions consisted of highly anaplastic spindle cells which had no characteristic features. Although chemotherapy is needed to obtain good results, the patient's general condition did not allow the intensive chemotherapy which would have been necessary to prolong her survival.

In this case of Maffucci's syndrome combined with dedifferentiated chondrosarcoma, T2-weighted MRI was useful to distinguish between the dedifferentiated component and the cartilaginous one. In addition, the dedifferentiated tumor was discovered to have three mesenchymal elements: osteosarcoma, fibrosarcoma, and malignant fibrous histicytoma.

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