Best Cases from the AFIP

Maffucci Syndrome: Radiologic and Pathologic Findings[1]

Editor's Note.—Everyone who has taken the course in radiologic pathology at the Armed Forces Institute of Pathology (AFIP) remembers bringing two beautifully illustrated cases for accession to the Institute. In recent years, the staff of the Department of Radiologic Pathology has judged the "best cases" by organ system, and recognition is given to the winners on the last day of the class. Beginning with the July 2001 issue of *RadioGraphics*, one of these cases is published with each issue of the Journal, written by the winning resident. Radiologic-pathologic correlation is emphasized, and the causes of the imaging signs of various diseases are illustrated.

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History

An 18-year-old man visited the Department of Plastic Surgery at our hospital complaining of functional and aesthetic problems with his hands caused by soft-tissue swelling. He particularly had problems using his left hand when working on the computer. He had developed multiple palpable nodular masses on both hands since the age of 2 years. The skin of his right hand showed areas of bluish discoloration consistent with hemangiomas, which had been present since childhood. At initial assessment at the age of 11 years, the diagnosis of Ollier disease had been made. In the following years, more hemangiomas developed and the osseous protuberances on both hands grew larger. At the age of 18 years, radiographs of the hands also showed multiple phleboliths, typical of cavernous hemangiomas, and the diagnosis was changed to Maffucci syndrome.

Imaging Findings

Radiographs of the hands at the age of 11 years showed multiple well-defined, irregularly expanded, radiolucent lesions in the digits of both hands. A small calcification was apparent adjacent to the right ulnar styloid (Fig 1). Radiographs of the hands at the age of 18 years also revealed multiple lytic lesions distributed centrally and eccentrically in the phalanges and metacarpals of both hands. The sharp delineation between the eccentric lesions and medullary bone was suggestive for an intracortical location of these lesions. The typical ring-and-arc appearance with stippled calcifications in the matrix was seen in both kinds of lesions. Multiple small round calcifications in the surrounding soft tissues, suggestive of phleboliths, were also present at this time (Fig 2). Cortical thinning was seen in almost all lesions, with areas of complete absence of the cortex.

Index terms: Enchondroma, 43.1543 • Extremities, neoplasms, 43.1543 • Fingers and toes, neoplasms, 43.1543 • Hand, abnormalities, 43.1543 Maffucci syndrome, 43.1543

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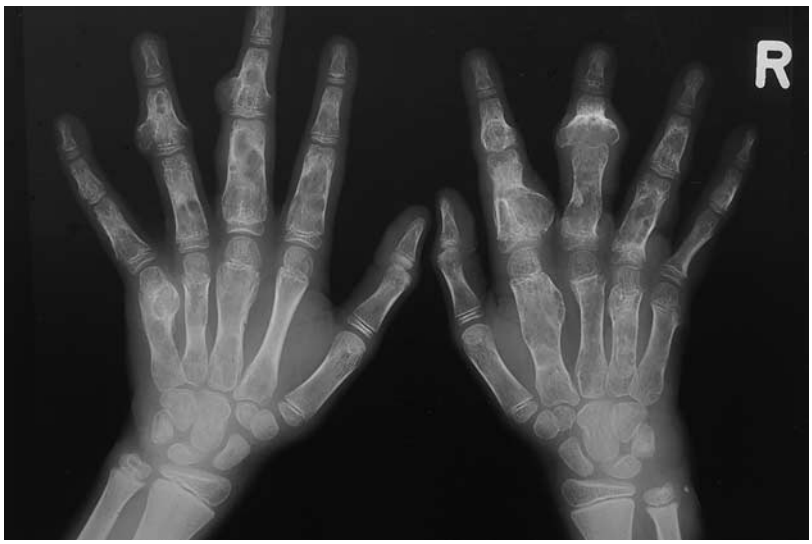
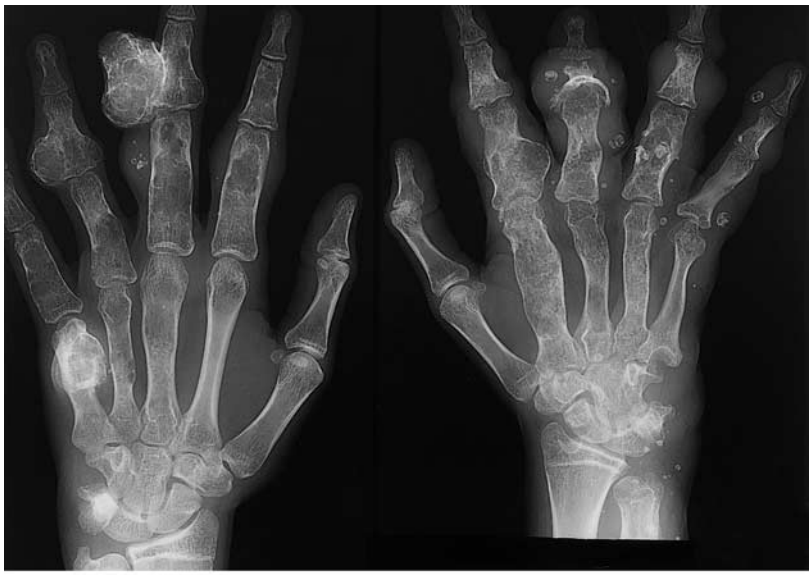
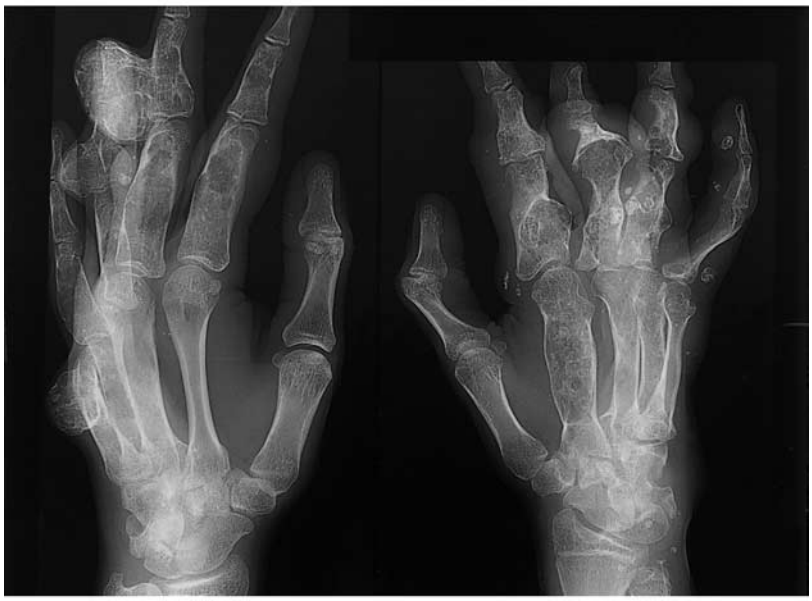


Figure 1. Radiograph of the hands obtained at the age of 11 years shows multiple radiolucent lesions with osseous expansile remodeling. The calcified matrix is not easily appreciated on this image. There is a small calcification adjacent to the right ulnar styloid.

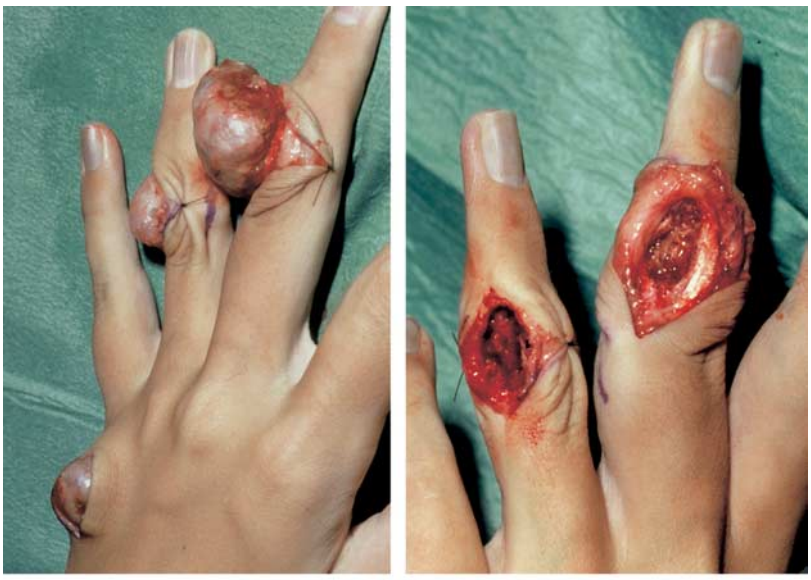


a.



b.

Figure 2. Frontal **(a)** and oblique **(b)** radiographs of the hands obtained at the age of 18 years show the typical ring-and-arc appearance of chondroid lesions in the matrix of the osseous lesions. The well-defined round calcifications in the soft-tissue masses are typical of phleboliths.



a. b.

Figure 3. **(a)** Photograph of the left hand obtained during surgery shows the grayish enchondromas, clearly visible after incisions were made and the skin was moved aside. **(b)** Photograph of the left hand obtained during surgery shows the appearance after removal of the enchondromas.

Pathologic Evaluation

Gross pathologic evaluation showed lobular fragments of grayish tissue (Fig 3a). All pieces were firm with an osseous rim on the outside and more elastic or myxoid, gritty tissue centrally. The gritty material represented mineralized matrix. At microscopic analysis, there was preexistent cortical and cancellous bone in the peripheral parts of the tissue fragments. The more central parts consisted of tissue composed of lobules of hyaline and myxoid chondroid matrix with paucicellular and more cellular areas (Fig 4a). Enchondral ossification of the matrix (Fig 4b) and few double nuclei were seen (Fig 4c). There were no signs of cytonuclear atypia and no mitotic figures. One fragment showed an enchondroma bordering on the endosteal surface with local extension into the medulla, an appearance suggestive for an intracortical origin of this lesion (Fig 4d). The histomorphologic appearance confirmed the diagnosis of multiple enchondromas.

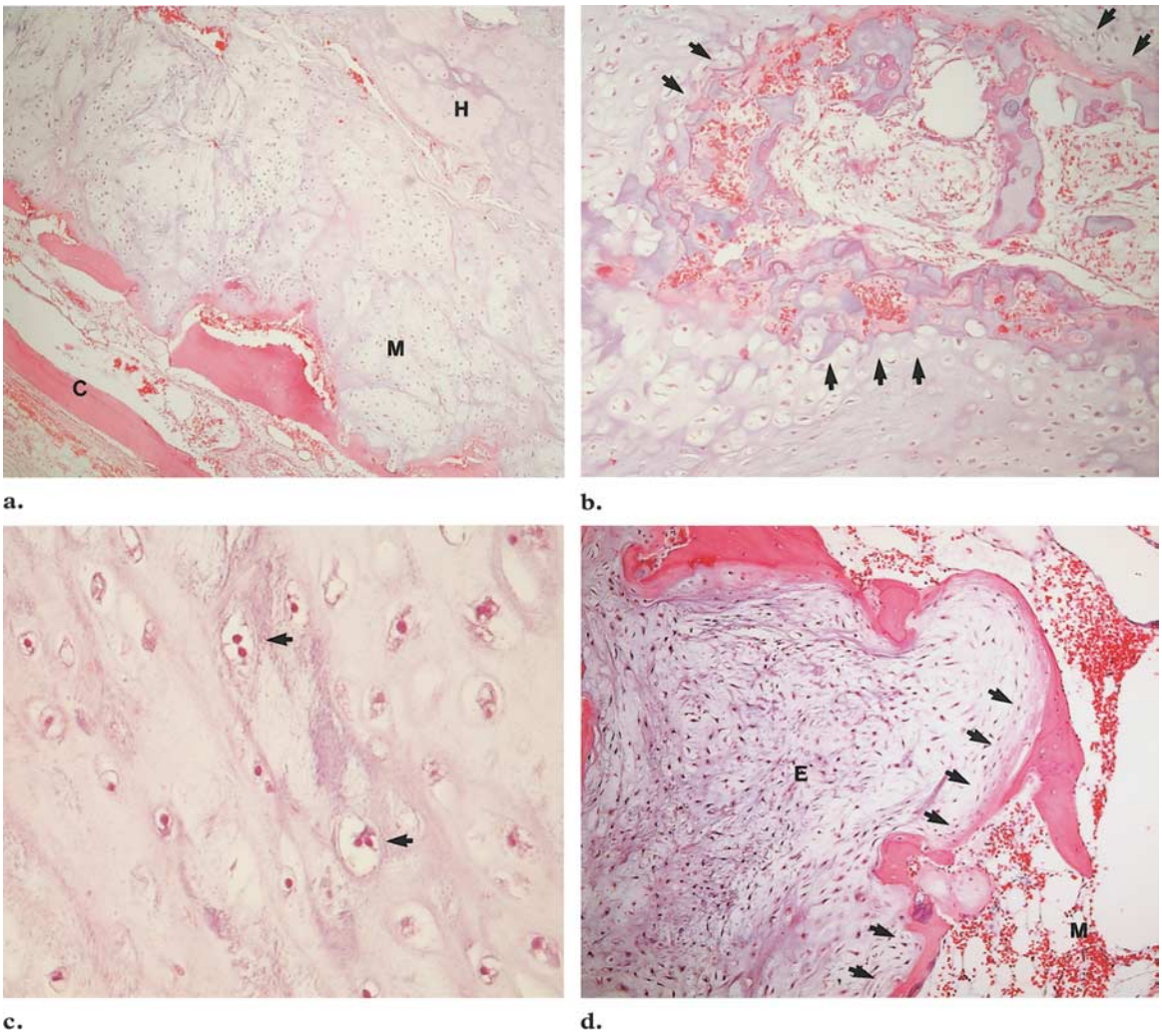


Figure 4. **(a)** Photomicrograph (original magnification, ×50; hematoxylin-eosin stain) shows a moderately cellular cartilaginous tumor with a partly hyaline (*H*), partly myxoid (*M*) matrix bordering on preexisting cortical bone (*C*). **(b)** Photomicrograph (original magnification, ×100; hematoxylin-eosin stain) of the same tumor shows an area with enchondral ossification (arrows). **(c)** High-power photomicrograph (original magnification, ×400; hematoxylin-eosin stain) of the same tumor shows occasional double nuclei (arrows) but no cytonuclear atypia. **(d)** Photomicrograph (original magnification, ×100; hematoxylin-eosin stain) shows an enchondroma (*E*) bordering on the endosteal surface (arrows) and locally extending into the medulla (*M*), an appearance suggestive of an intracortical location of the lesion.

Discussion

Maffucci syndrome was first described in 1881. This rare, nonhereditary syndrome is characterized by multiple enchondromas combined with hemangiomas and less commonly lymphangiomas (1). Maffucci syndrome is sometimes confused with Ollier disease, which was described 19 years later and consists of multiple enchondromas without hemangiomas. Since then, other manifestations of enchondromatosis have been described, with more regionally confined types of disease and more generalized dysplasia (2–4).

The dyschondroplasia in Maffucci syndrome is of unknown origin. There is a derangement of cartilaginous growth, which results in migration of cartilaginous rests from the epiphyseal plate into the metaphyseal regions. Proliferation of these bits of cartilaginous tissue leads to development of intraosseous chondromas, which are usually located within the metaphysis (5,6). Intracortical enchondromas have been described by some authors (7).

In 25% of cases, the clinical symptoms of Maffucci syndrome are present at birth or manifest in the 1st year of life; in 45% the onset of symptoms is before the age of 6 years, and in 78% the symptoms start before puberty (1). The skeletal and vascular lesions in the extremities are usually asymmetrically distributed, with unilateral

changes seen in about 50% of patients (1,8). The hemangiomas in Maffucci syndrome are mostly located in the subcutaneous soft tissues and appear as blue subcutaneous nodules, which can be emptied by means of manual compression. Involvement of the viscera and mucous membranes by hemangiomas has also been reported (1,9). In three cases described by Nakamura et al (10), the first abnormality noted was diffuse swelling of the dorsum of the hand or foot, compatible with adipose tissue with lymphangiectasia. The skeletal lesions show a predilection for involvement of the tubular bones. The most frequent sites of enchondromas are the metacarpals and the phalanges of the hands and less commonly the feet (1). The skeletal lesions can manifest as painless swelling of a digit or as a pathologic fracture.

A review of the literature shows a discrepancy in the rate of malignant transformation of the skeletal lesions in Maffucci syndrome. In 1973, Lewis and Ketcham (1) reported sarcomatous transformation of an enchondroma in 15.2% of 105 cases. Sun et al (11) reported a prevalence of 56% in nine patients, and Kaplan et al (9) reported a 30% prevalence of chondrosarcoma in 65 reported cases. In Ollier disease, the prevalence of malignant transformation of the skeletal lesions is 25%–30% (8,12). The number of involved bones appears to have no relationship with the risk of development of a skeletal malignancy in Maffucci syndrome (8). Chondrosarcoma is the most frequent musculoskeletal malignancy encountered, although malignant transformation of the skeletal lesions to fibrosarcoma and of the vascular lesions to hemangiosarcoma, hemangioendothelioma, or lymphangiosarcoma has been reported as well (1,5,8,9,11,13). Malignancies other than musculoskeletal have also been reported in Maffucci syndrome and include glioma, gastrointestinal adenocarcinoma, pancreatic carcinoma, and ovarian tumor. The overall prevalence of malignancies associated with Maffucci syndrome is 23%–100% in different studies (1,8,9).

In our patient, only the upper limbs were affected. The left hand showed osseous expansile remodeling with soft-tissue swelling and venous malformations. The proximal phalanx of the second digit, the proximal and middle phalanges of the third and fourth digits, and the fifth metacarpal were affected. There was limitation of flexion of the second to fifth digits. On the right side, there was a soft-tissue swelling of the forearm with a vague blue coloration suggestive of a venous malformation at palpation. There were also multiple areas with a vague blue coloration on the dorsum of the hand. The proximal phalanx of the second digit, the whole of the third digit, and the terminal phalanges of the fourth and fifth digits showed deformities and osseous protuberances. The third digit was also shortened. Movement of the elbow, wrist, and hand on the right side was restricted by osseous expansile remodeling at these locations, and flexion in some digits was particularly affected.

Radiographs, particularly of the hands and feet, are often pathognomonic in Maffucci syndrome. The radiolucent skeletal lesions are well demarcated and show expansile remodeling of the affected bone with predominant thinning of the cortex and endosteal scalloping. Matrix mineralization in the osseous lesions is frequent and shows the typical arc-and-ring appearance of chondroid lesions (6). Deformities of the extremities may be caused by interrupted skeletal growth during development (1). In the soft tissues, phleboliths—which are typical of cavernous hemangiomas—and soft-tissue calcifications may be seen (5).

Management of Maffucci syndrome aims at relief of symptoms and early detection of malignancies (8,14). Although the prevalence of malignant change in skeletal lesions in Maffucci syndrome and Ollier disease is quite similar, it is important to differentiate between these two conditions because of the greater risk of developing nonmusculoskeletal malignancies in the former (9,12). Operative procedures for the skeletal lesions, such as corrective osteotomy and lengthening of an arm or leg, have been reported. Curettage and packing with bone graft material is another surgical method (6). Sclerotherapy, irradiation, and surgery for the vascular lesions have been described (14). Skeletal or soft-tissue lesions that enlarge or become painful without antecedent trauma should raise the suspicion of malignancy and need to undergo biopsy (1).

Because of the functional impairment of the left hand in our patient, surgery was performed on three of the protruding osseous lesions of the third, fourth, and fifth digits of the left hand. The mass caused by marked osseous expansion from the enchondroma on the dorsoulnar side of the middle phalanx of the third digit was easily peeled out of the soft tissues up to its origin on the middle phalanx (Fig 3a). The extensor tendons and the ulnar collateral ligaments of the proximal interphalangeal joint were exposed, and the mass was removed with an osteotome without problems. The same procedure was applied to the bony protuberance on the dorsoulnar side of the middle phalanx of the fourth digit. The defect created in this phalanx was large and had to be

filled with a cancellous bone graft taken from the left iliac crest (Fig 3b). The lesion on the dorsum of the fifth metacarpal was removed, and the defect was also filled with a cancellous bone graft. The postoperative recovery was without problems, and the patient underwent hand exercises under the guidance of a specialized physiotherapist. At follow-up 3 months later, the patient was satisfied with the functional and cosmetic results.

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