Multiple Enchondromatosis (Ollier's Disease)

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Abstract

Multiple enchondromatosis (Ollier's disease) is a rare, nonhereditary developmental abnormality involving defective endochondral ossification. It is characterized by multiple intraosseous and subperiosteal cartilaginous tumors, ranging in size from microscopic foci to bulky masses. The skeleton is most frequently affected unilaterally, but bilateral involvement is also observed. The association of enchondromatosis with multiple hemangiomas of soft tissue was reported in 1881 by Maffucci (18 years before Ollier), and this clinical presentation is generally referred to as "Maffucci's syndrome."

Definition

- A rare, nonhereditary developmental abnormality involving defective endochondral ossification. It is characterized by multiple intraosseous and subperiosteal cartilaginous tumors, ranging in size from microscopic foci to bulky masses.
- The skeleton is most frequently affected unilaterally, but bilateral involvement is also observed.
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Synonyms

- Chondrodysplasia
- Skeletal enchondromatosis

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Etiology

- It represents an anomaly of skeletal development, without hereditary or familial influence, and is apparently related to heterotopic proliferation of epiphyseal chondroblasts with consecutive failure of endochondral ossification and shortening of the involved long bones.

Epidemiology

Age

- The disease is diagnosed in childhood, most of the times.

Sex

- There is no sex difference.

Sites of Involvement

- The hands and feet are the most common sites of involvement, followed by the femur, humerus, and forearm.
- Flat bones can be involved in severe cases.

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- In most cases, it occurs in a single extremity or one side of the body. In bilateral involvement, one side of the body is more severely affected than the other.
- The ribs and scapula are rarely involved.

Clinical Symptoms and Signs

- Most of the patients show symptoms within several years after birth. They display skeletal deformities such as short stature or localized swelling.
- Occasionally, pathologic fracture can be a presenting symptom.
- Involved bones and extent of skeletal involvement vary from patient to patient. It can present as multifocal in one or two bones or, in severe cases, can be present as generalized skeletal involvement.

Image Diagnosis

- Enchondromatosis has characteristic radiographic findings, making it possible to diagnose by plain radiography.
- The lesions involve the metaphysis and diaphysis and appear as linear or pillar-shaped radiolucent lesions that are oriented obliquely to the long axis of the bone. Calcification is also a feature (Figs. 17.1).
- "Popcorn"-like cartilaginous-type calcification is typically present.
- In some cases, bone erosion and hypertrophy of the cortical surface can be observed.
- A portion of the lesion can regress while the bone is growing, and after normal growth has stopped, there is usually no increase in size.
- However, if there is a change in size after normal growth has stopped, malignant transformation should be considered.
- In Maffucci's syndrome, the cartilaginous lesions are associated with benign soft tissue hemangiomas which, characteristically, show small rounded calcified images, corresponding to phleboliths.

Image Differential Diagnosis

Secondary Low-Grade Chondrosarcoma

- Clinically in the patients with multiple enchondromas, if the new lesion occurs or the pain is aggravated, we have to consider the possibility of chondrosarcoma.
- Bone permeation and a change in the calcification pattern of any previously known lesion must be suspected of malignant transformation.

Pathology

Gross Features

- The affected bones are often expanded and somewhat shortened due to the presence of bluish masses or islands of cartilage that are arranged as multiple nodules, measuring from one to several centimeters, surrounded by normal bone marrow.
- The lesion may extent through the cortical bone to involve the periosteum or the surrounding soft tissue.

Histological Features

- Histologically, the microscopic appearance of enchondromatosis in both Ollier's disease and Maffucci's syndrome is quite similar to that seen in enchondroma (Fig. 17.3).
- However, increased cellularity is a common feature of the lesions of enchondromatosis, regardless of the site involved, with enlarged nuclei and double-nucleated cells (Fig. 17.4). These histological characteristics can lead to a misdiagnosis of chondrosarcoma.

Pathologic Differential Diagnosis

Low-Grade Chondrosarcoma

- Especially in the metaphysis of the long bone in middle-aged to elderly patients.
- Grossly, mucoid or myxoid changes are frequently observed in chondrosarcoma and only rarely in chondromatosis.
- Enchondromatosis lesions do not show cortical erosion. Also, histologically, marked myxoid change of the stroma and cytologic features of malignancy are observed in chondrosarcoma.
- Separation of cartilage lobules by fibrous bands is seen in low-grade chondrosarcoma.
- In addition, the most important differential diagnostic feature is intramedullary invasion. In chondrosarcoma, the trabeculae of preexisting bone are embedded in the tumor tissue – entrapment of native trabeculae.
- Radiographically, enchondromas of the small bones of the hands and feet show cortical thinning; however, microscopic permeation into the cortical tissue is not observed.

Ancillary Techniques

Genetics

- IDH1 and IDH2 mutations were found in majority of the Ollier's disease and Maffucci's syndrome patients.
- In the patients with Ollier's disease, heterozygous mutation in the PTH receptor gene, *PTHR1*, was reported.
- Also in cases from the nonrecurrent enchondromatosis, specific copy number alterations were found at *FAM86D*, *PRKG1*, and *ANKS1B*, and loss of heterozygosity with copy number loss of chromosome 6 was also found in two cases of enchondromatosis.
- In several different groups of enchondromatosis, patients expressed loss of function mutations in the *PTPN11* gene, recessive mutations of ACP5, and heterozygous missense mutations in COL2A1.

Prognosis

- The prognosis is dependent on the lesion extent and disease severity.
- In Ollier's disease, the incidence of malignant transformation is 25 %, and it is considered to be higher in Maffucci's syndrome. The majority of these cases are low-grade chondrosarcoma.
- Chondrosarcoma develops by age 40 in approximately 25 % of patients with Ollier's disease.
- High-grade osteosarcoma and dedifferentiated chondrosarcoma have been described in Ollier's.

Treatment

- There is no specific ways to treat Ollier's disease or Maffucci's syndrome; however, treatment should primarily focus on alleviating symptoms due to skeletal deformities.
- Skeletal deformity can be surgically corrected or, in severe swelling or deformity cases, amputation can be done.

Images

See Figs. 17.1, 17.2, 17.3, 17.4, 17.5, 17.6, 17.7, and 17.8 for illustrations of Ollier's disease.

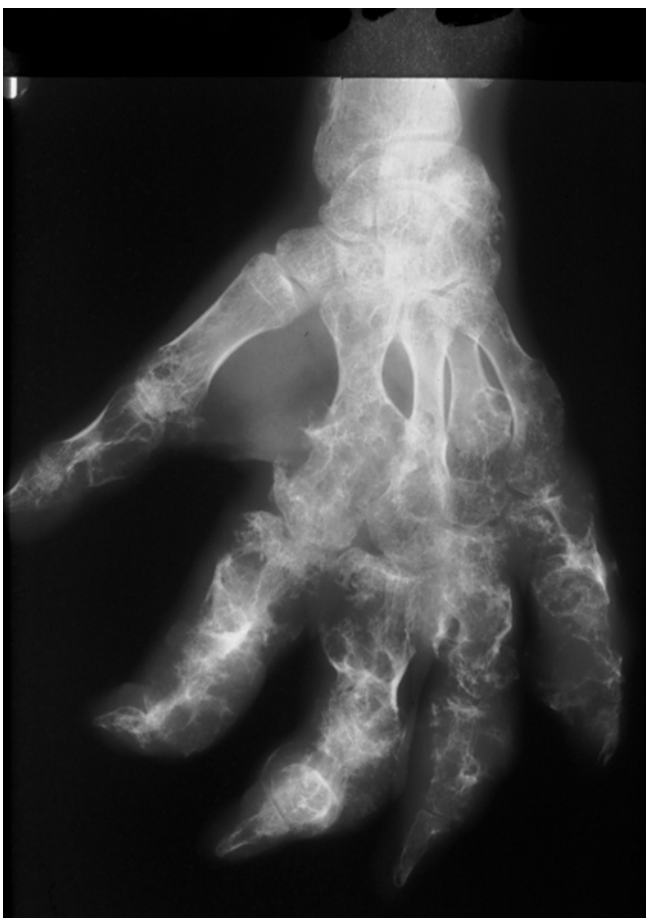

Fig. 17.1 Radiograph shows multiple enchondromas involving whole digits and metacarpal bones leading to extreme deformity

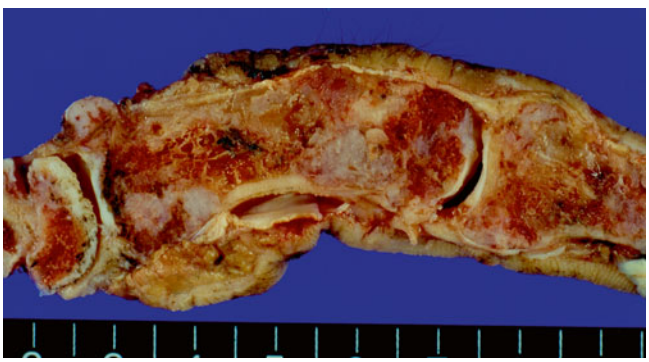

Fig. 17.2 Gross specimen, as illustrated in Fig. 17.1, shows numerous *grayish-blue* cartilage masses within the marrow cavity of the phalangeal bones

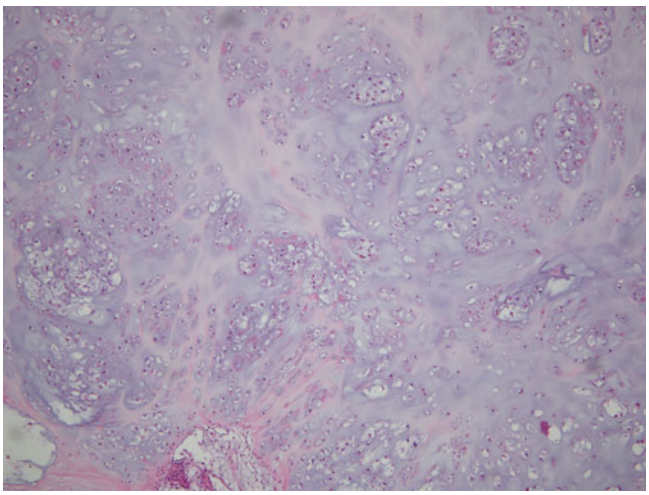

Fig. 17.3 Low-power microscopic view shows lobulated cartilage masses and rich cellularity

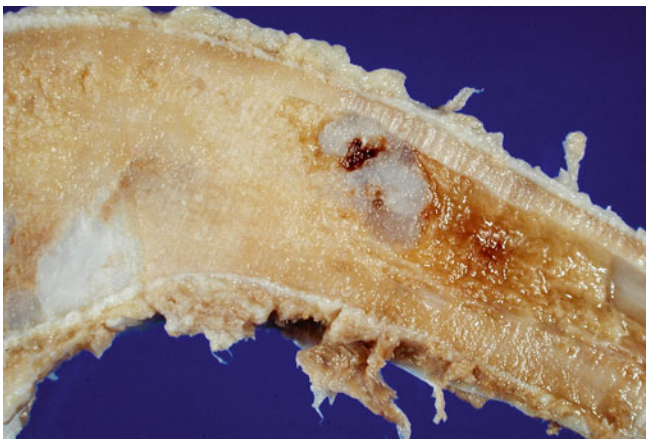

Fig. 17.5 Specimen photography showing several medullar enchondromas in a same bone

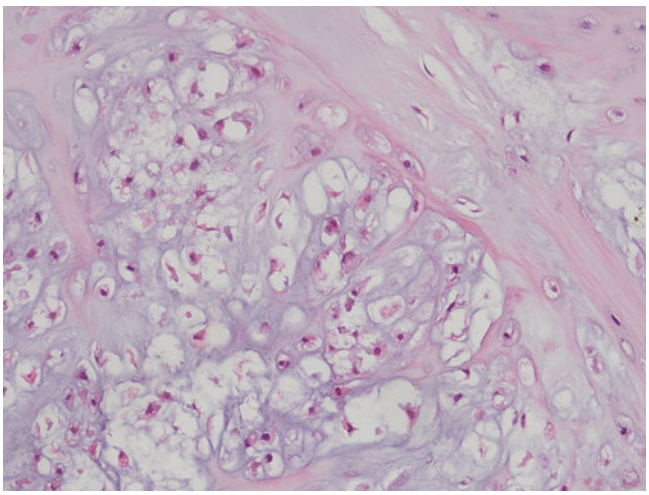

Fig. 17.4 At the periphery of the cartilage lobule, there are enlarged nuclei and binucleation of the chondrocytes, associated with myxoid matrix degeneration

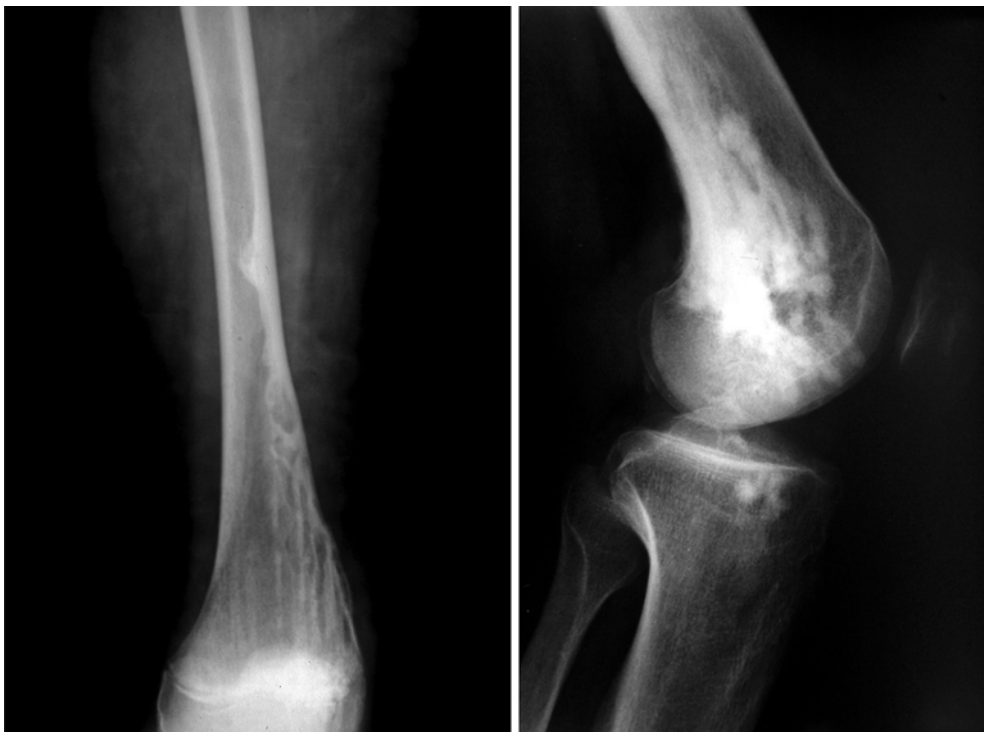

Fig. 17.6 AP and lateral radiographs of a case of Ollier's disease showing characteristic finger-like longitudinal chondromatous proliferations

Fig. 17.7 Macroscopic demonstration of fingerlike chondromatous proliferations in Ollier's disease

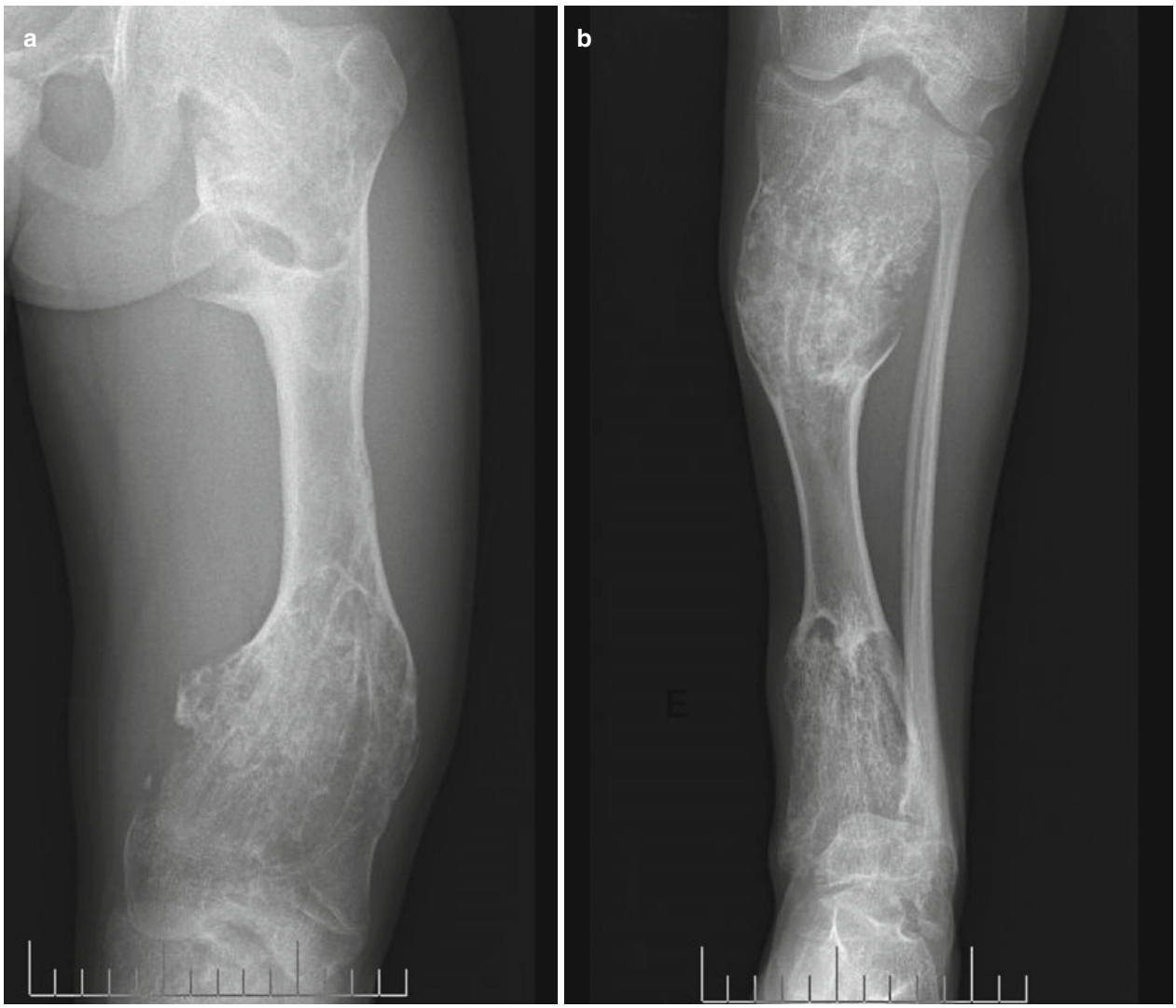

Fig. 17.8 Enchondromatosis (Ollier's disease). Radiographs of femur (**a**) and tibia (**b**) showing multiple deformities caused by large enchondroma lesions in metaphyseal location. Lesions present characteristic elongated ridges and disseminated calcified spots

Recommended Reading

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