Enchondroma

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Abstract

Benign cartilaginous neoplasms are among the most common bone lesions. Enchondromas are the classical presentation of them and are usually found incidentally. Their clinical presentation can range from an asymptomatic lesion in an adult to multiple lesions as part of a syndrome in a younger patient. If the clinical and radiological presentation is characteristic, enchondromas can be treated non-operatively with observation alone. However, in certain circumstances, the differential diagnosis among a benign enchondroma or an atypical cartilaginous neoplasm/low-grade chondrosarcoma can be difficult and might need further investigations and a multidisciplinary approach. In cases of symptomatic lesions, diagnostic uncertainty, or a pathological fracture, curettage and grafting with or without osteosynthesis is usually the treatment of choice.

Keywords

Enchondroma • Benign cartilaginous neoplasm • Chondroma

Definition

Cartilaginous neoplasms are among the most common tumors of the appendicular skeleton and can involve almost any bone. Benign examples of these are enchondroma, osteochondroma, chondroblastoma, and chondromyxoid fibroma.

Enchondromas are the most common benign intraosseous form of cartilaginous neoplasms. They represent approximately 3% of all bone tumors and up to 15% of benign bone tumors. The vast majority are an intramedullary growth of hyaline cartilage, but a peripheral variant also exists around the bone surface (periosteal chondroma) [1, 2].

Syndromes with multiple enchondromas in the skeleton are infrequent, such as Ollier disease and Maffucci syndrome.

Clinical Presentation

Enchondromas are usually solitary tumors that are found incidentally, and therefore, their true incidence is likely to be higher than reported. Most of them are asymptomatic, and are found at any age, but usually from 15–40 years. In cases with multiple tumors and enchondromatosis the diagnosis is earlier in life, usually during the first decade, and they can present themselves with substantial deformity [3].

Small bones of the hands and feet are the most commonly affected bones, and that can occur in more than 50% of the cases, with long bones being next, such as the proximal humerus and distal femur. Axial skeleton involvement is rare in solitary enchondromas. In the hand, enchondromas can be diagnosed as a pathological fracture.

A frequent presentation is a young patient with an enchondroma in a long bone with a benign appearance, and a coexisting pathology in the contiguous joint that is causing symptoms (bursitis of the shoulder, for example). If symptoms and physical exam are also characteristic with this condition, and the cartilagenous lesion has a clear appearance of a benign process , the treatment should be addressed to manage the underlying condition and the cartilaginous tumor observed.

Imaging and Evaluation

Typically, enchondromas appear as central and metaphyseal lesions, with a well-delimitated border and central mineralization. Their appearance depends importantly on the amount of calcification, and they can range in size from

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small punctuate to larger rings. They can also be described as having a popcorn-like appearance (Figs. 7.1 and 7.2). Endosteal scalloping can be observed on plain radiographs as well as in its low-grade malignant or atypical counterpart. In children, mineralization of the lesion might not be completed, and enchondromas can be confused with cystic lesions.

Even when the diagnosis in clearly benign lesions might seem simple, differentiating between an enchondroma and a more aggressive/malignant tumor, especially an atypical cartilaginous neoplasm, remains a diagnostic challenge, even for experienced specialists. A recent study published by our group showed that for 39 cartilaginous lesions, diagnosis and grading had only fair interobserver agreement (kappa = 0.44) between 10 experienced subspecialists, while treatment had only a poor intraobserver agreement (kappa = 0.21) [4]. Similar results have been found for radiologists and pathologists, showing us the complexity of this diagnosis [5, 6].

Various radiographic and clinical features can aid in the differentiation of a benign enchondroma from a chondrosarcoma [7, 8]. Murphey et al. [9] showed that for 187 cartilaginous neoplasms, cortical compromise more than 2/3 of cortical thickness, a neoplasm size >5 cm and the presence or absence of pain were the most prominent symptoms/signs for distinguishing between an enchondroma versus low-grade chondrosarcoma. Conversely, patient age, tumor location, and other variables did not influence the diagnosis. Studies by Ferrer-Santacreu [10, 11] showed that pain on palpation, cortical involvement, and bone scan uptake were essential factors in the diagnosis of low-grade chondrosarcoma as well.

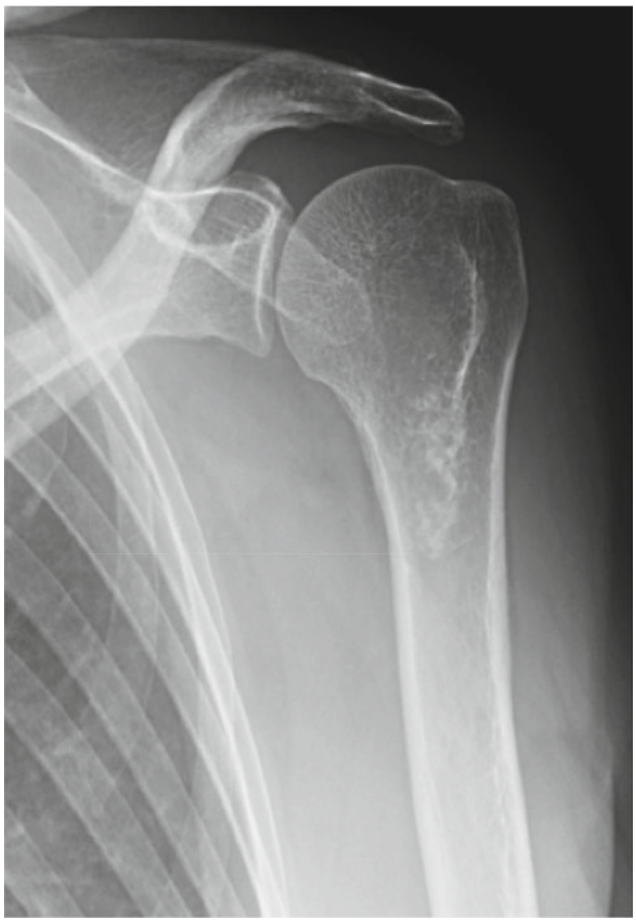

Fig. 7.1 Enchondroma of the left proximal humerus

CT and MRI can both be useful in the evaluation of these lesions. CT scan and axial reconstructions are useful to determine the presence of endosteal scalloping or cortical compromise. MRI can be helpful to evaluate soft tissue masses and edema in cases of impending fracture. Also, it can help demonstrate bone marrow replacement by the tumor and can guide surgical treatment if needed (Fig. 7.3).

18F-fluorodeoxyglucose positron emission tomography (18F FDG PET-CT) has been used to assess metabolic activity and to help differentiate between a benign enchondroma and a chondrosarcoma. A recent metanalysis of eight articles including 166 lesions, showed that maximum standardized uptake value (SUVmax) correlates with the histologic grade in intraosseous chondroid neoplasms, with low SUVmax being supportive of a benign tumor, while elevated SUVmax ≥ 4.4 being 99% specific for chondrosarcoma. A technetium-99 bone scan can also provide useful information. Radionuclide uptake within the lesion can be compared with an internal marker, such as the anterior superior iliac spine. Murphey et al. showed that 82% of chondrosarcomas in their series had lesion uptake higher than that of the anterior iliac crest.

Pathology and Genetics

Distinguishing between an enchondroma and a chondrosarcoma can be difficult even for trained histopathologists, and therefore, the final diagnosis has to be made by a multidisciplinary team in this clinical scenario more than ever. Samples from curettage are often fragmented, and they are composed of hyaline cartilage mixed with bone tissue (Fig. 7.4). Core needle biopsy might be prone to sampling error due to the heterogeneity that these tumors can have, with even high-grade chondrosarcoma having areas of benign hyaline cartilage. For this same reason, needle biopsy to differentiate between an enchondroma and a low-grade chondrosarcoma or an atypical cartilaginous neoplasm is not recommended as a considerable risk of error, and a non-representative sample can be found.

Enchondromas are composed of lobules of hyaline cartilage with low cellularity and atypia. The lobules are usually rimmed by bone, and small nodules of cartilage may be seen

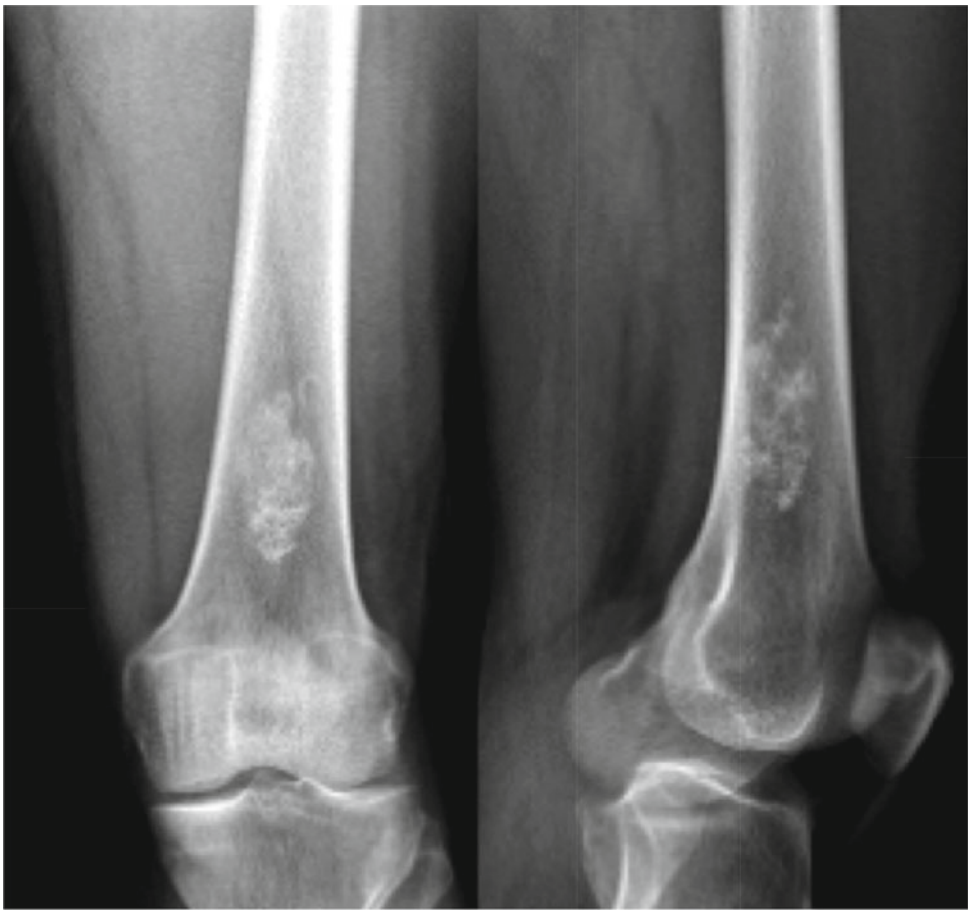

Fig. 7.2 Distal femur AP and lateral X-ray on an 18-year-old male patient without any previous pain who had a knee contusion playing soccer; images show a central lesion with a cartilaginous matrix and calcifications

separated from the mass [2, 12]. As it was previously mentioned, that final histopathological diagnosis depends significantly from the clinical and radiographic appearance. For example, samples from the hand usually present more atypia and cellularity, but with clinical and radiographic manifestations of an enchondroma, they still maintain their benign status, while the same sample from the pelvis might be considered as a malignant variant. In general, binucleation, increased cellularity, atypia, bone permeation, and myxoid changes are indicative of malignancy [13, 14].

A few genetic abnormalities have been found in patients with multiple enchondromatosis with up to 8% of them demonstrating mutations in the gene encoding a Parathyroid hormone-like hormone (PTHLH) receptor (PTHR1) which is involved in enchondral bone formation. However, conflicting evidence exists regarding the real prevalence of these mutations [15, 16]. This being said, the exact cause of enchondromatosis is unknown. Recently, patients with solitary enchondromas as well as Ollier disease and Maffucci syndrome have been found to carry somatic mutations in isocitrate dehydrogenase-1 (IDH1) and 2 (IDH2) genes [17, 18]. This causes malfunction of the tricarboxylic acid cycle resulting in increased levels of the oncometabolite D-2-hydroxyglutarate and a blockade of osteogenic differentiation during the formation of bone and instead cartilaginous tumor formation.

Treatment

As with most benign latent lesions, enchondromas that are asymptomatic can be treated non-operatively with observation alone. Single lesions with a characteristic radiographic appearance do not need to undergo a biopsy since follow up for more than 3–5 years without significant change has been usually considered to be enough for establishing an accurate diagnosis.

Indications for surgical treatment in an enchondroma are continuous symptoms; enlargement or radiographic changes during follow up to rule out a low-grade malignant variant; impending fracture or an actual fracture of the host bone. If surgical treatment is decided, curettage and bone grafting is usually the treatment of choice, with a low rate of recurrence if done adequately.

Several adjuvants for curettage have been described in order to reduce remaining microscopic foci of the tumor.

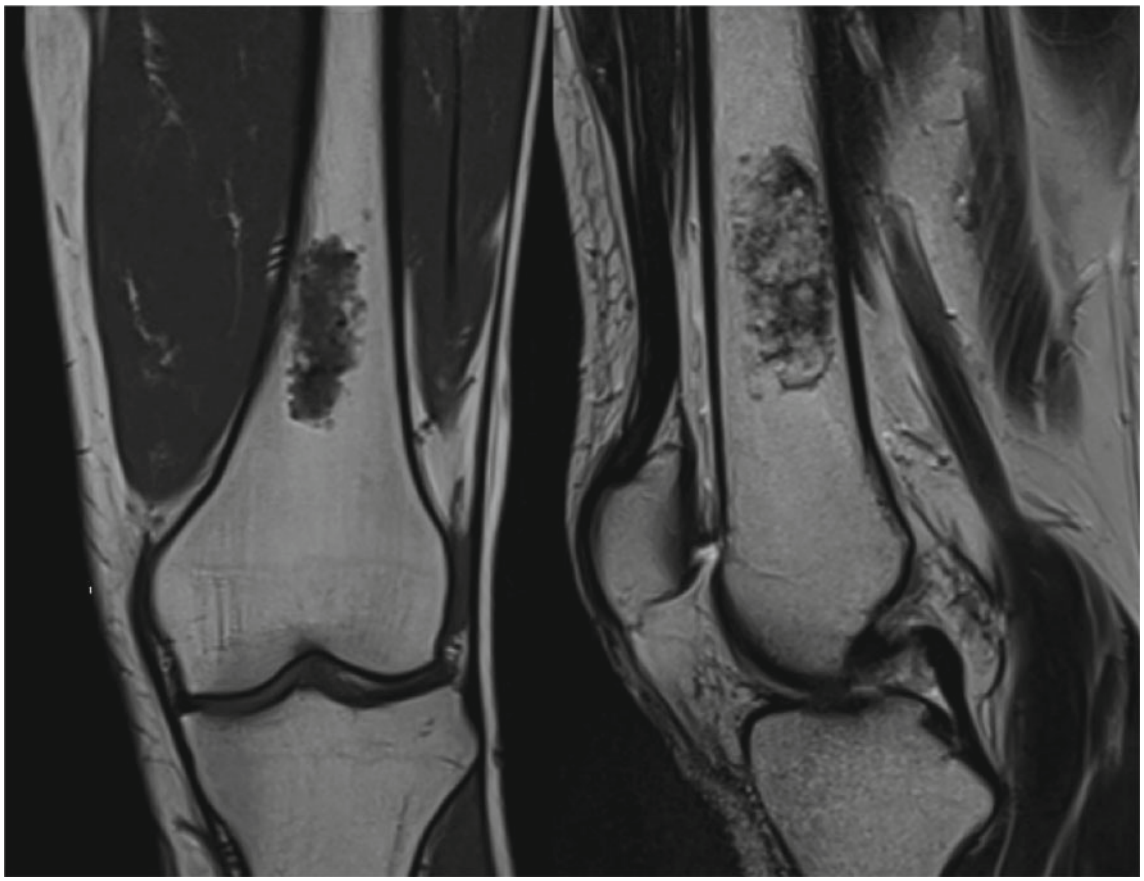

Fig. 7.3 Same case as Fig. 7.2:. coronal and sagittal T1 MRI sequence showing a cartilaginous tumor of 2 x 4 cm without any cortical compromise nor soft tissue mass

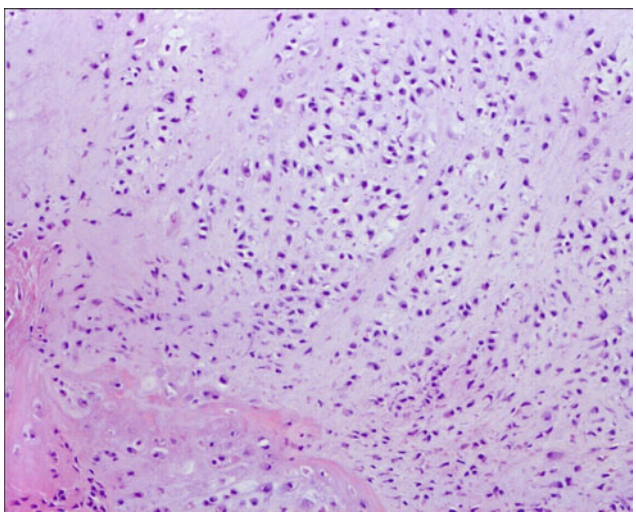

Fig. 7.4 Microscopic histology of enchondroma

Frequently used techniques are the use of thermal ablation with electrocautery and phenol, as well as cryotherapy. Grafting of the tumor can be done with either allo or autograft with excellent results. Other substitutes have been used to fill the cavitary defect after curettage beside bone graft. Filling the defect with methyl methacrylate is another alternative, especially if immediate stability is needed, with other benefits such as the adjuvant properties of thermal ablation and facilitating the postoperative evaluation of recurrence with better visualization of the bone-cement interface. Plate and screw fixation can be used as well if stability is needed on a weakened bone. Modification of activities and weight bear protection is usually recommended to prevent postoperative fractures after curettage, especially in the lower limb.

If a fracture occurs in a lesion suspected to be an enchondroma, treatment depends on the stability of the fracture, the localization of the lesion and the age of the patient. Young patients can usually be treated non-operatively, as fractures tend to heal as long as adequate stability and alignment are maintained. In cases where the lesion is close to the physis, surgical treatment should be delayed to prevent any damage to the growth plate of the bone. If the location of the fracture warrants acute stabilization, special attention should be paid to perform an adequate curettage and not contaminating other compartments. Fixation and osteosynthesis should be

performed after curettage, and adjuvant therapy are performed, filling the defect with bone graft, substitutes, or cement.

Enchondromatosis

Several syndromes have been described in patients with multiple enchondromas, with recent classifications based on spinal involvement and genetic inheritance. The two most frequently described syndromes are Ollier disease and Maffucci syndrome, both non-hereditary and without spinal involvement [19, 20].

Ollier Disease is the most common subtype, with an estimated prevalence of 1/100.000. The lesions usually are distributed unilaterally, but bilateral distribution with lesions in the entire skeleton have been described as well (Fig. 7.4). Malignant transformation is significant, with a rate of 10–40%, being more frequent in long or flat bones, instead of the hands and feet. They also have a higher rate of other non-skeletal malignant tumors, like gliomas, ovarian juvenile granulosa cell tumors, and non-small cell lung cancer.

Maffucci syndrome is characterized by the presence of enchondromatosis with multiple haemangiomas of soft tissue or less commonly lymphangiomas. The disease develops in an important proportion before the first couple of years, and lesions are asymmetrically distributed. Both enchondromas and vascular lesions can transform to malignant tumors, with a higher risk of that happening than with Ollier disease. In the same way, a higher risk of developing intracranial malignancies is seen in these patients.

Similarly, other syndromes without spinal involvement, but with autosomal dominant inheritance have been described, such as Matachondromatosis and Genochondromatosis. Both of them are rare, the first one displaying a combination of multiple enchondromas along with osteochondroma-like lesions and the second one with characteristic chondroma in the clavicle or alteration of the flat bones of the hands or feet.

Syndromes with spinal involvement can be inherited or sporadic as well. Examples of this are Spondyloenchondrodysplasia, an autosomal recessive inherited disease with enchondromas of the appendicular skeleton combined with vertebral dysplasia. Other syndromes like Cheirospondyloenchondromatosis are characterized for marked hand and foot involvement, and Dysspondyloenchondromatosis that combines enchondromatosis with severe irregular vertebral lesions, including segmentation and severe kyphoscoliosis (Fig. 7.5).

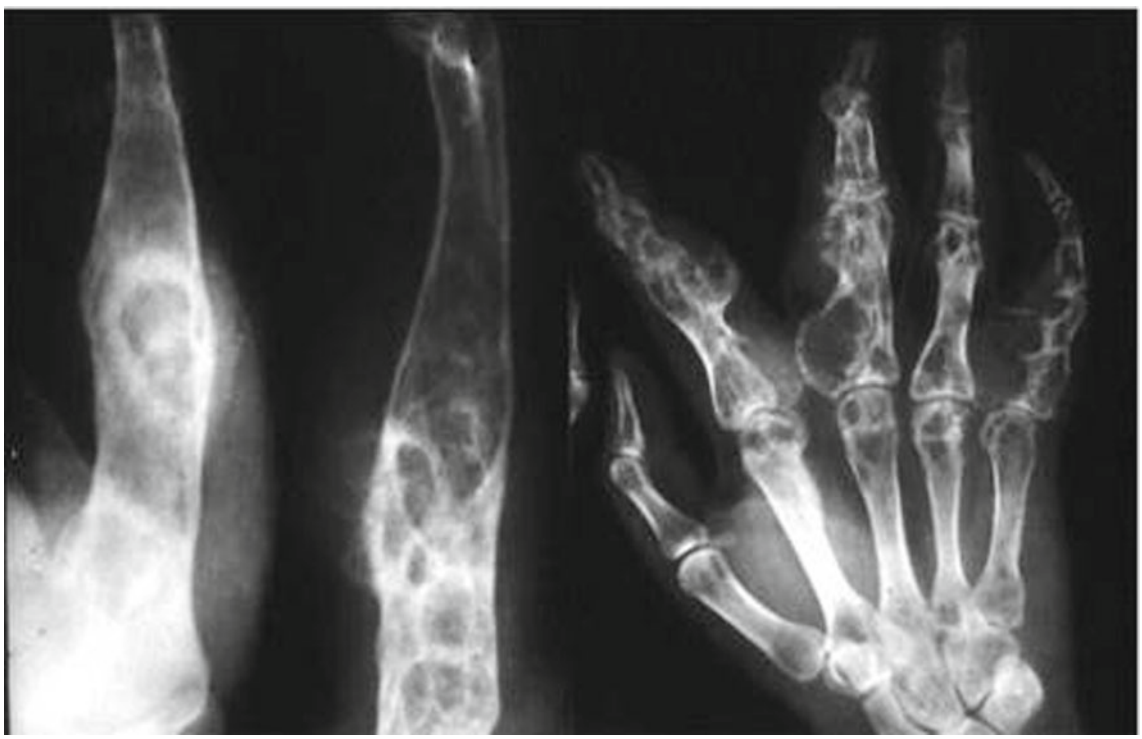

Fig. 7.5 35-year-old patient with enchondromatosis and hand lesions

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