Osteochondroma and Hereditary Multiple Osteochondromas

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Franklin H. Sim

Abstract

Osteochondroma is the most common bone tumor, mainly affecting patients under 20 years of age. It presents in 90% of the cases as a solitary lesion. The remaining cases are part of the multiple hereditary osteochondromas syndrome. The pathogenesis is not entirely clear. Osteochondromas usually develop at the metaphysis of long bones. Malignant transformation is rare in solitary lesions, but more common in hereditary syndromes. Solitary osteochondromas are asymptomatic and may be diagnosed incidentally through X-rays. Differential diagnosis includes benign and malignant lesions.

Keywords

Osteochondroma • Cartilage • Exostoses • Bone tumor • Benign bone lesion

Definition

The World Health Organization defines osteochondroma as "a cartilage capped bony projection arising on the external surface of bone containing a marrow cavity that is continuous with that of the underlying bone." The generic term exostosis indicates any outgrowth of bone and should not be mistakenly used as a synonym of osteochondroma. Solitary osteochondroma occur as non-familial, sporadic lesions. The terms hereditary multiple osteochondromas (HMO), hereditary multiple exostosis (HME), diaphyseal aclasis, multiple cartilaginous exostosis and hereditary multiple exostosis have all been used to characterize growth of multiple osteochondromas.

F. H. Sim (✉)
Mayo Clinic, Rochester, MN 55905, USA
e-mail: sim.franklin@mayo.edu

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Epidemiology

Osteochondroma is the most common neoplasm affecting bone, however its true prevalence is difficult to define as many patients are asymptomatic and the tumor is never identified. Nevertheless it is estimated that osteochondromas comprise around 35% of all primary benign bone tumors and 10% of all tumors. In the pediatric population the occurrence of 35.2 per million inhabitants per year has been reported.

Approximately 90% of all osteochondromas present as solitary lesions. The remaining cases are part of the multiple hereditary osteochondromas syndrome.

The majority of osteochondromas affect children and adolescents, with approximately 80% of lesions occurring in the first two decades of life. Around 60% of the patients are male.

Locations

Osteochondromas usually develop in bones that are formed through the process of enchondral ossification. Most often the metaphysis of a long tubular bone is affected, rarely the diaphysis. The most commonly involved sites, in descending order, are the distal femur, proximal humerus, and proximal tibia (Fig. 6.1).

The pelvis is involved in approximately 5% of cases [1] while the involvement of the spine is around 3% [2]. The posterior elements of the lumbar and cervical spine are most often affected. Involvement of the spine has been reported to be associated with development of spinal cord compression and subsequent neurologic deficit [3–8]. The small bones of the hand and feet may be involved in the context of multiple osteochondromas [9–12]. Osteochondroma may involve the scapula in up to 5% cases and it can lead to snapping syndrome and pseudowinging of the scapula [13,14]. Rarely a lesion may involve the ribs or the sternum (Figs. 6.2 and 6.3) [15]

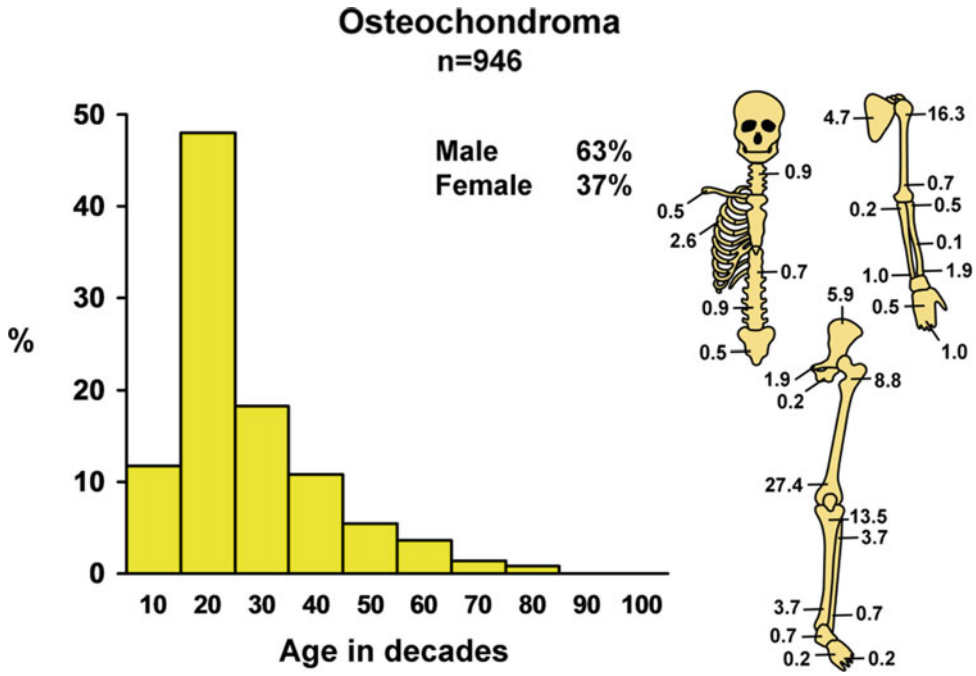

Fig. 6.1 Epimediology and location on skeleton osteochondroma

Etiology and Pathogenesis

There has been an increasing debate about the true nature of osteochondromas. Some authors consider osteochondromas a growth disturbance) [16] (developmental aberration hypothesis) while others defend it is a true benign neoplasm. In the past, the typical justaphyseal location has led to the hypothesis that osteochondromas arises from a portion of the physeal cartilage and its growth [17]. Cartilage metaplasia, defective bone remodeling [18], dysfunction of the periosteum [19] have all been suggested to play a role in the pathogenesis of osteochondromas. The alteration in the direction of normal bone growth resulting from aberrant epiphyseal development has been suggested as the main cause of osteochondromas [16, 20]. Secondary osteochondromas have been reported after radiation therapy [21, 22] and after fractures involving the growth plate [23]. However, cytogenetic studies have identified two loci and subsequent mutation in genes suggested that loss or mutation of EXT1 and EXT2 genes are important in the pathogenesis of both solitary and multiple osteochondromas, therefore compelling evidence of the neoplastic origin of these lesions [24–26].

Hereditary multiple osteochondromas is the most common genetic skeletal dysplasia, with an estimated prevalence of 1/50 000 and is inherited as an autosomal dominant disorder with full penetrance [27] (Fig. 6.4).

HMO has been associated with mutations in the EXT1 gene on chromosome 8q24.11–q24.13) and in the EXT2 gene on chromosome 11p12-p11. To date, there have been

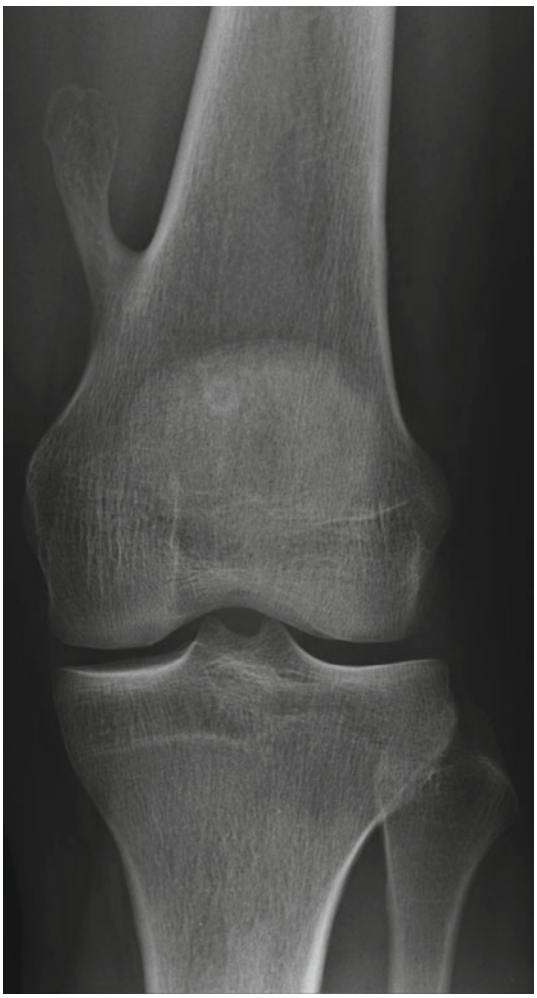

Fig. 6.2 Pediculated osteochondroma: typical aspect on X-ray

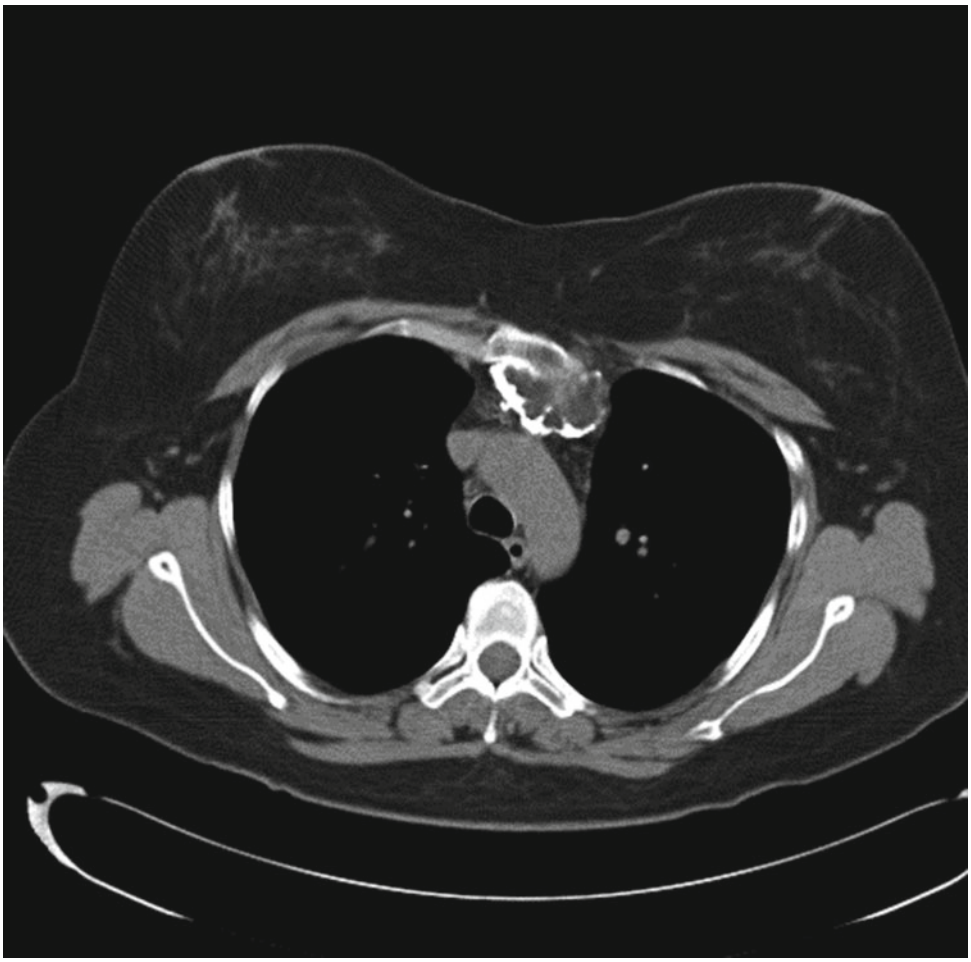

Fig. 6.3 CT showing osteochondroma of the sternum

close to one hundred different EXT1 and fifty different EXT2 mutations reported [26, 28, 29]. Inactivating mutations (frame shift, nonsense and splice-site) represent approximately 80% of the causing mutations of HMO [26]. Missense mutations are less common [30]. In solitary osteochondromas mutation on these genes are reported mainly in the cells from the lesion itself [31].

Pathology

The macroscopic features of an osteochondroma depend whether the lesion is pedunculated or sessile (Fig. 6.5). Sessile osteochondromas are usually round with a thin cartilage cap while pedunculated lesions resemble a mushroom with a bony stalk and a cartilage cap. The cap has a smooth surface and usually ossifies in the skeletal maturity when it should measure no more than a few millimeters. Overlying the cap often a bursa is found.

Microscopically a thin periosteal layer covers the cartilaginous cap. The thin cartilaginous cap is composed of chondrocytes in lacunae arranged in clusters with abundant chondroid matrix. The base of the cartilaginous cap resembles the appearance of the physeal growth plate with maturation via endochondral ossification to regular bone trabeculae. The intertrabecular space is usually filled with fatty or hematopoietic marrow.

Natural History

Osteochondroma usually grow and ossify during skeletal development (Fig. 6.6). Although rare, spontaneous regression of a solitary osteochondroma has been reported.

The lesions should stop growing with skeletal maturity. Lesions that continue to grow after skeletal maturity must be carefully evaluated for the possibility of malignant transformation. Malignant transformation is extremely rare in solitary osteochondromas (less than 1%).

In hereditary multiple osteochondromas malignant transformation is more frequent. Clinically based studies report rates ranging from 0 to 5%.

The most common tumor associated with osteochondromas and HMO is peripheral chondrosarcomas, however

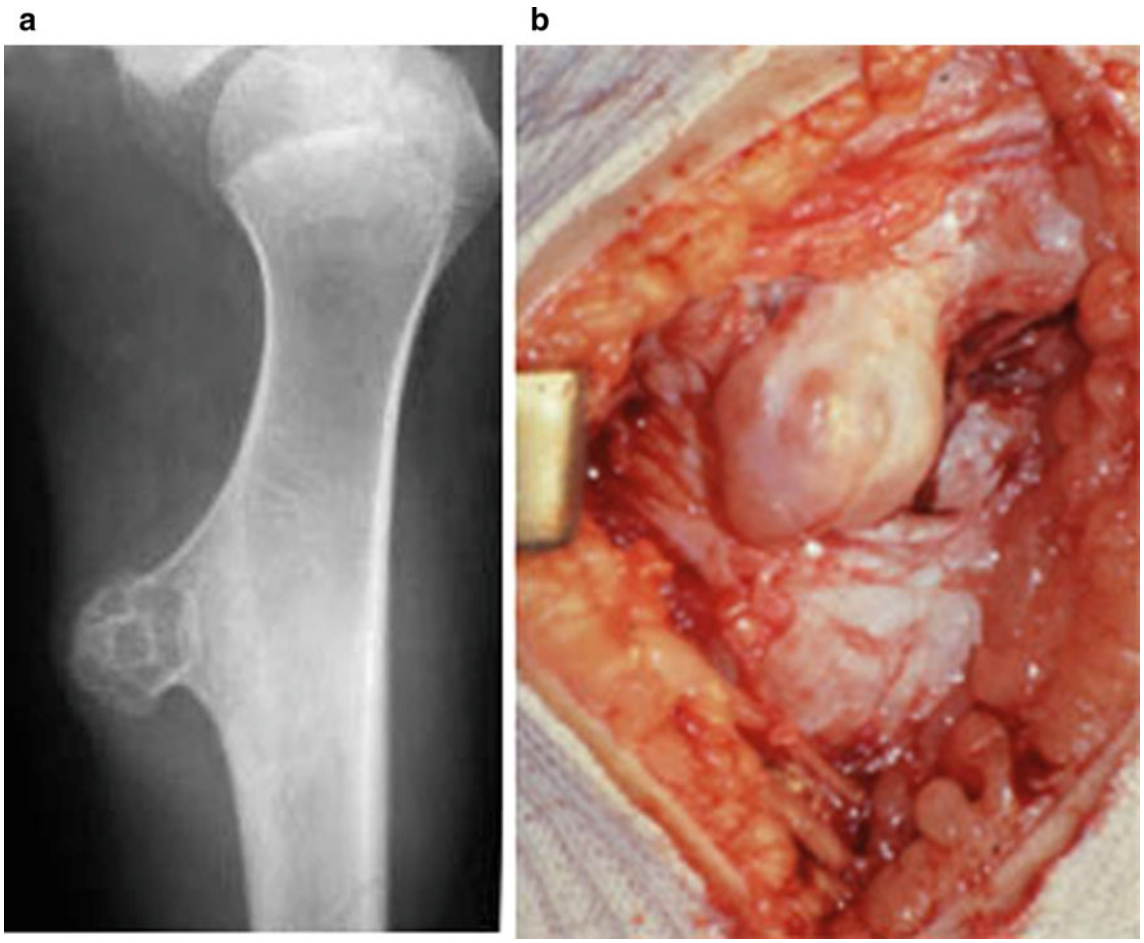

Fig. 6.4 Femur osteochondroma: **a** radiological aspect **b** intraoperative aspect

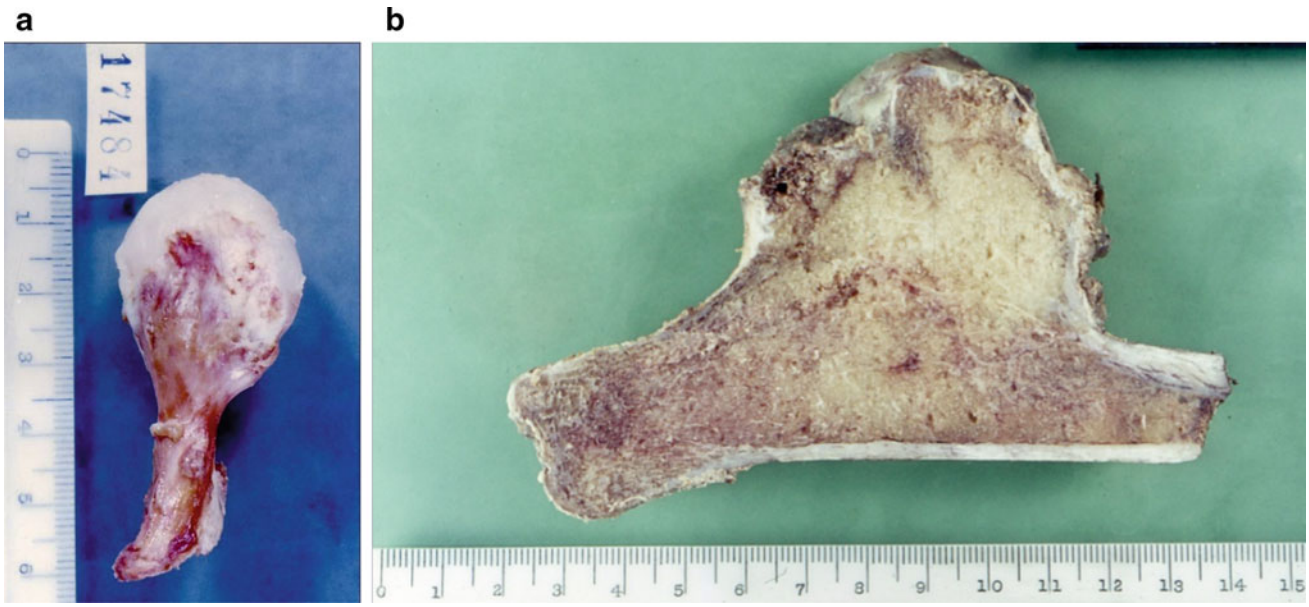

Fig. 6.5 Macroscopic aspect of osteochondroma **a** pediculated osteochondroma **b** sesile osteochondroma

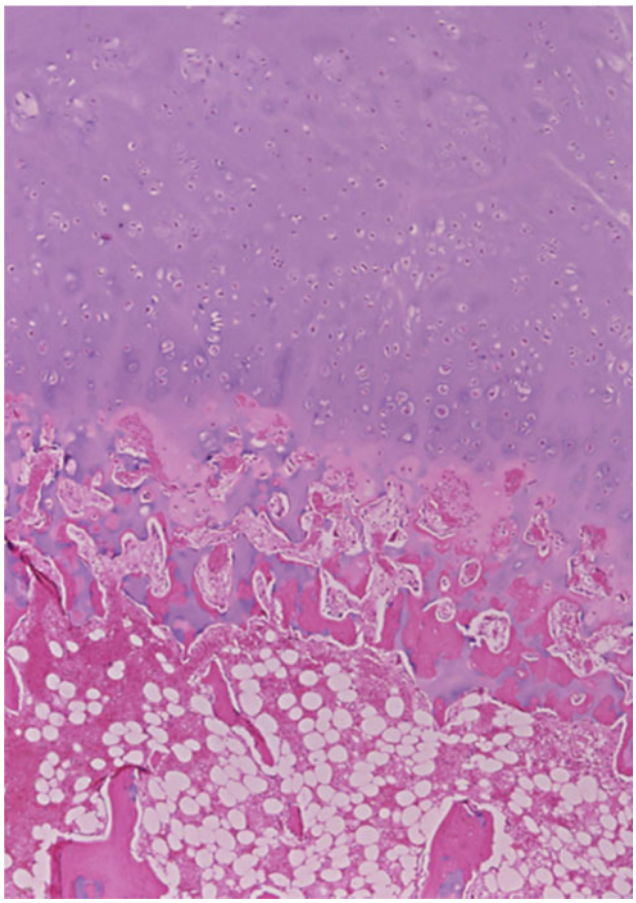

Fig. 6.6 Histology of an osteochondroma

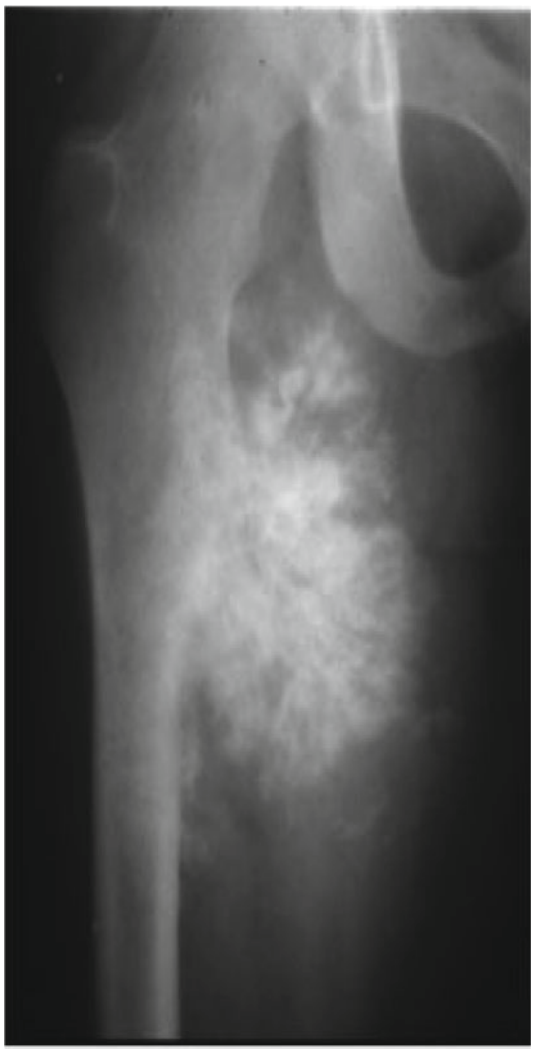

Fig. 6.7 Chondrosarcoma arising in an osteochondroma

osteosarcoma has also been reported. Chondrosarcoma arising in an osteochondroma is typically a low-grade neoplasm (Fig. 6.7).

The diagnosis of malignant transformation is challenging and requires clinical, imaging and histologic information. Growth beyond skeletal maturity and radiographic and advanced imaging evidence of an enlarged cartilaginous cap (greater than 2 cm) are features associated with malignant transformation. Histologically the columnar pattern of the chondrocytes is lost. There is permeation of the bone and nodules of cartilage extending into soft tissues with mitotic activity, atypia and necrosis.

Clinical Manifestation

A large number of solitary osteochondromas are asymptomatic and may be diagnosed incidentally. Initial presentation may be related to a painless palpable mass. Mechanical irritation of the surrounding tissues may result in the development of a bursa around the cartilaginous cap. Overlying tendons and muscles can also be irritated, resulting in pain and reduced range of motion. Occasionally an osteochondroma can produce symptoms due to pressure on nearby nerves. This is specially true for osteochondromas arising in the proximal fibula. Rarely venous thrombosis and pseudoaneurysms of arteries may result from direct pressure from a osteochondroma.

A fracture of the osteochondroma stalk may produce acute pain. Osteochondroma of the spine may cause spinal cord or nerve root compression and patients may present with neurologic defict.

In hereditary multiple osteochondromas there is a wide clinical variation on the number of lesions. Multiple deformities of both upper and lower extremities have been reported in association with HMO. These include ankle valgum, genu valgum and ulnar deviation of the wrist with relative shortening of the ulna. Most often there is bilateral symmetric involvement of the extremities. Unusual sites for solitary osteochondromas (Fig. 6.8), such the pelvis are more commonly affected in HMO.

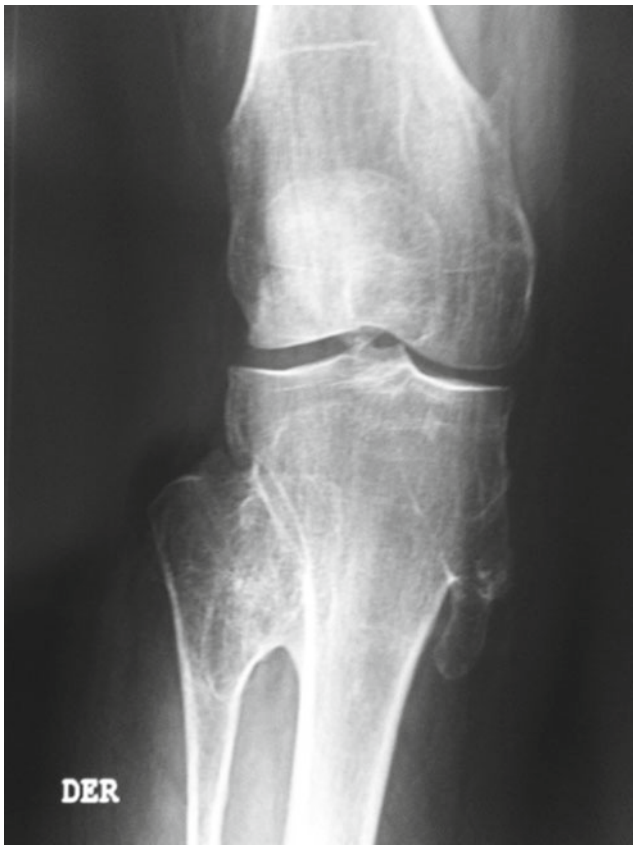

Fig. 6.8 Osteochodromatosis

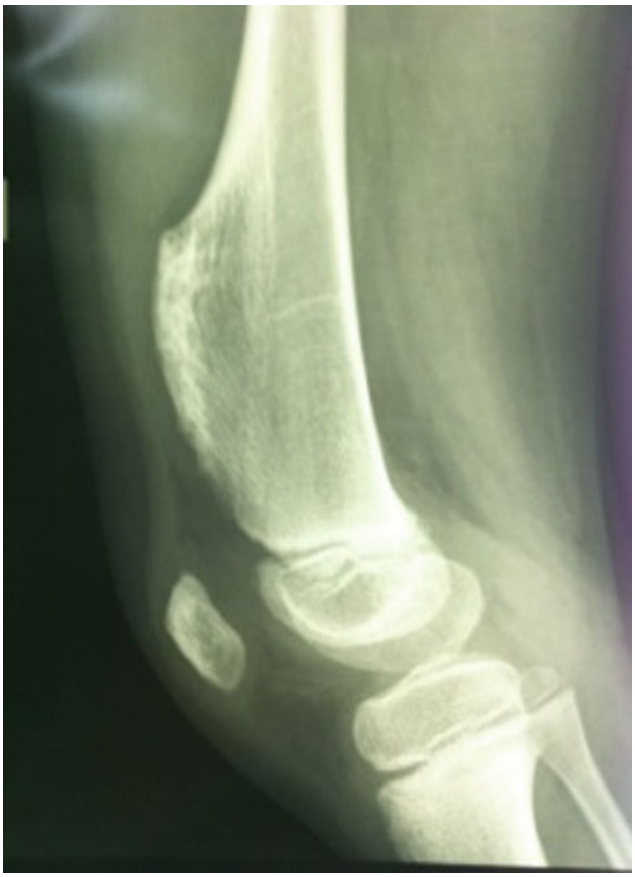

Fig. 6.9 Cesil osteochondroma

The radiographic appearance of a solitary osteochondroma is highly suggestive and usually sufficient for the correct diagnosis (Fig. 6.9). Typically it is characterized by an osseous protuberance (pedunculated or sessile) arising from the external surface of a metaphysis of a long tubular bone. The medullary cavity of the lesion should be continuous with the medulla of the affected bone. These slow-growing lesions will classically point away from the nearest joint and towards the diaphysis. In HMO the metaphysis of the tubular bone is usually widened due to failure of normal tubulation. The surface of an osteochondroma expands in a mushroom shape to form the cartilage cap. The tip of the osteochondroma may not be visible on plain radiographs. A large and poorly defined cartilaginous cap that contains irregular calcification is worrisome for malignant transformation.

Other Imaging Techniques

Although radiographs may be enough for the diagnosis of an osteochondroma of the extremities both CT scans and MR imaging have an important role in the evaluation of a lesion in areas where the anatomy is more complex (i.e., the pelvis and spine). In addition, a CT scan is helpful to examine the medullary continuity between the lesion and the host bone. This feature is important in order to differentiate a benign osteochondroma from juxtacortical lesions like peripheral chondrosarcoma and periosteal chondromas.

MR imaging has a definitive role in evaluating the cartilaginous cap of an osteochondroma. The high signal intensity on T2 weighted images allows measurements of the cartilaginous cap of an osteochondroma supplying additional information about the likelihood of sarcoma transformation.

Differential Diagnosis

Benign lesions:

- Subungueal exostosis: Usually found on the distal phalanx of the great toe (Fig. 6.10).
- Bizarre parosteal osteochondromatous proliferation (Nora's lesion).

The medullary portion of the exostosis is not directly in continuity with the medulla of the host bone. Usually involve small bones of the hands and feet.

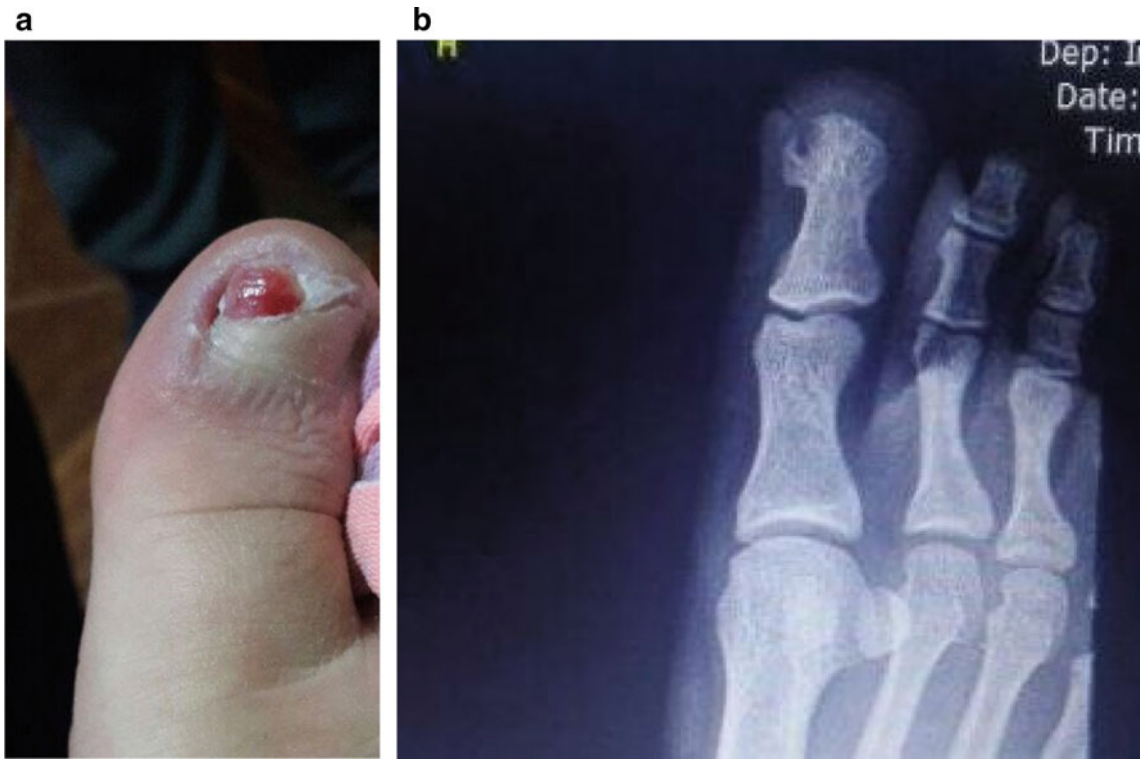

Fig. 6.10 Subungual exostosis: **a** clinical aspect **b** radiological aspect

– Metachondromatosis:

Autosomal dominant disorder characterized by multiple osteochondromas and intraosseous enchondromas mainly involving the digits. Unlike HMO rarely the multiple lesions cause lower limb deformities.

– Langer–Giedion syndrome – trichorhinophalangeal syndrome, type 2

Combined features of multiple exostoses with those of trichorhinophalangeal syndrome. Patients have a wide spectrum of mental retardation and deformities of the craniofacial bones and digits.

– Potcki–Shaffer syndrome

Patients present multiple exostosis, enlarged parietal foramina, craniofacial abnormalities and congenital deformities of the hand. Mental retardation may be present.

Malignant lesions:

– Parosteal osteosarcoma (Fig. 6.11)

Osteosarcoma of the surface of bone that radiographically has the appearance of a heavily mineralized mass. Most

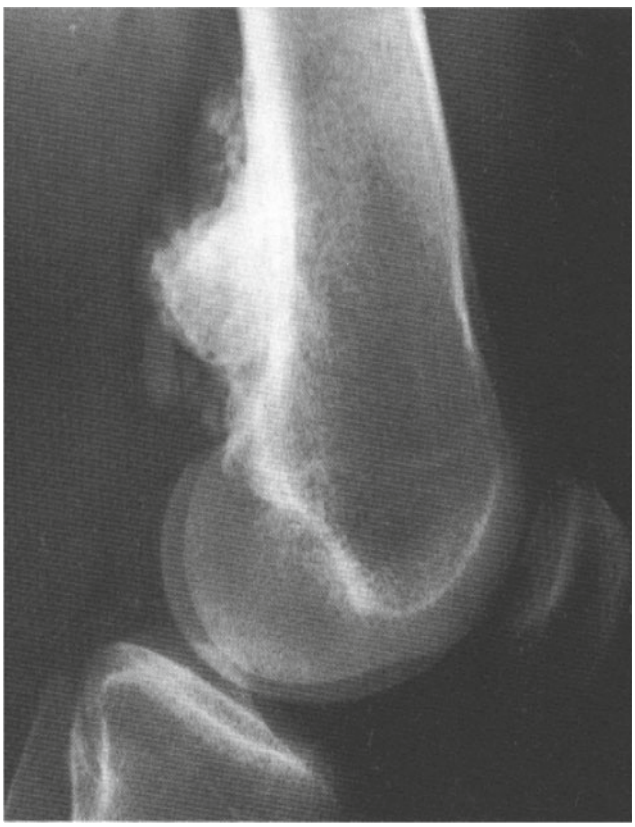

Fig. 6.11 Parosteal osteosarcoma

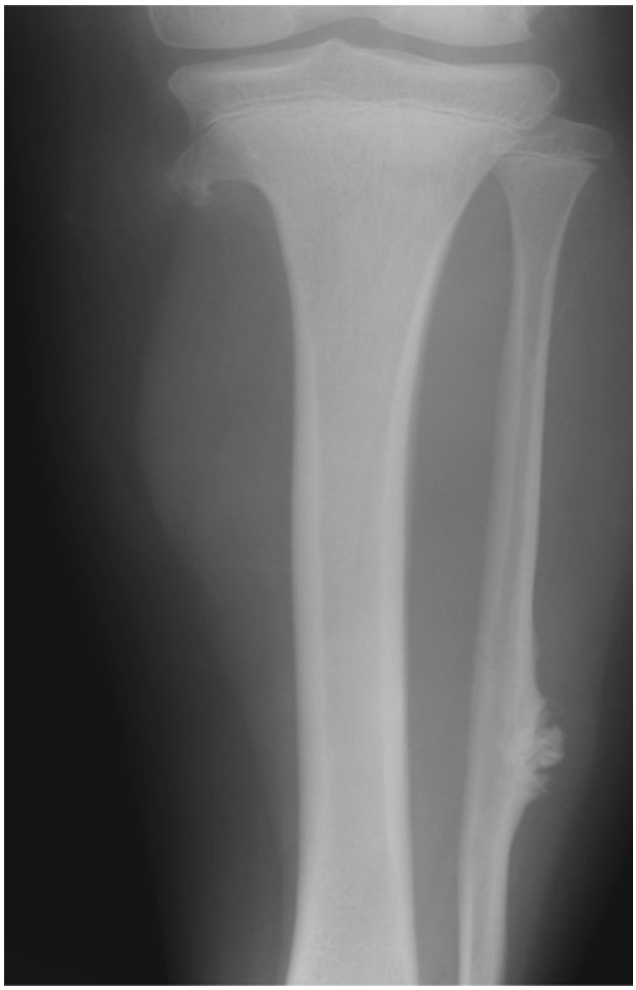

Fig. 6.12 Periosteal chondrosarcoma

commonly involves the posterior cortex of the metaphysis of the distal femur.

– Periosteal chondrosarcoma (Fig. 6.12)

Predominantly chondroblastic located on the surface of bone soft tissue invasion and without medullary involvement.

– Chondrosarcoma arising in an osteochondroma.

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