



Universiteit
Leiden
The Netherlands

Osteochondroma

Bovée, J.V.M.G.; Khurana, J.; Abdul-Karim, F.

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World Health Organization Classification of Tumours

WHO



OMS

International Agency for Research on Cancer (IARC)

Pathology and Genetics of Tumours of Soft Tissue and Bone

Edited by

Christopher D.M. Fletcher

K. Krishnan Unni

Fredrik Mertens

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Osteochondroma

J. Khurana
F. Abdul-Karim
J.V.M.G. Bovée

Definition

Osteochondroma is 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.

ICD-O codes

Osteochondroma	9210/0
Osteochondromatosis NOS	9210/1

Synonyms

Osteochondroma:

Osteochondromatous exostosis, solitary osteochondroma.

Multiple osteochondromas:

Hereditary osteochondromatosis, hereditary deforming osteochondromatosis, hereditary chondrodysplasia, diaphyseal aclasis, metaphyseal aclasis, hereditary multiple exostoses.

Epidemiology

Solitary osteochondroma

Osteochondroma may be the most common bone tumour [988,1875,2155]. The reported incidence, 35% of benign and 8% of all bone tumours, probably is an underestimate as the majority are asymptomatic and not clinically apparent [2155]. Most reported cases have been in the first 3 decades with no known sex predilection.

Multiple osteochondromas

Approximately 15% of patients (of all osteochondromas) have multiple lesions [2155], with an incidence up to 1:50,000 in some series [1887]. The age of patients with multiple lesions is similar to those with solitary osteochondromas and there is also no sex predilection. Inheritance is autosomal dominant.

Sites of involvement

Osteochondromas generally arise in bones preformed by cartilage. The most common site of involvement is the metaphyseal region of distal femur, upper humerus, upper tibia and fibula [2155].

Involvement of flat bones is less common with the ilium and scapula accounting for most of the cases.

Clinical features

Signs and symptoms

Many, if not most lesions, are asymptomatic and found incidentally. In symptomatic cases, the symptoms are often related to the size and location of the lesion. The most common presentation is that of a hard mass of long-standing duration. Some cases present with symptoms related to secondary complications such as mechanical obstruction, nerve impingement, bursa forming over the osteochondroma, pseudoaneurysm of an overlying vessel, infarction of the osteochondroma or fracture of the stalk of the lesion [131,188,470,988,1072,1468,1681,1875,2119,2152,2155].

Increasing pain and/or growing mass may be a manifestation of malignant transformation of osteochondromas. It is estimated to be less than 1% in patients with solitary and approximately 1-3% in patients with multiple osteochondromas. Higher incidences, some up to 20% of malignant transformation in multiple osteochondromas have been reported because of case selection and variable criteria used [211,1131,1875,2155,2206].

Imaging

Solitary osteochondromas may be pedunculated or sessile lesions. The characteristic feature is a projection of the cortex in continuity with the underlying bone. Irregular calcification is often seen. Excessive cartilage type flocculent calcification should raise the suspicion of malignant transformation. CT scan or MRI images typically show continuity of the marrow space into the lesion. These modalities may also predict the thickness of the cartilage cap [464,775,2285]. A thick cap raises the suspicion of malignant transformation. Osteochondromas grow away from the site of active growth, most likely due to forces from adjacent tendons and muscles.

Multiple osteochondromas are similar to the solitary ones but are generally associated with remodeling defects of bone. Many are flat and cauliflower shaped.

Aetiology

The aetiology is not known. Based on the resemblance of the cartilage cap to the growth plate, several hypotheses have been offered. These include the possibility of breakage, rotation and aberrant growth of the physal plate or herniation of the plate in the metaphysis [415,988,1457,1464,1718].

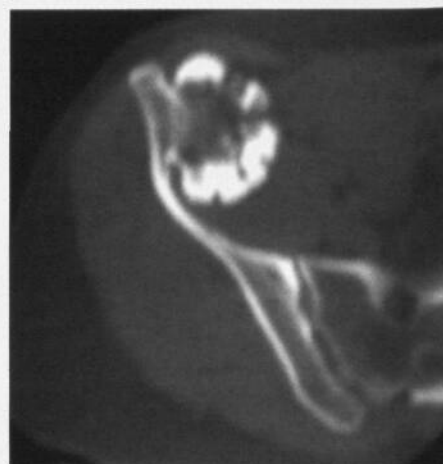


Fig. 10.01 A large osteochondroma is seen at the upper ilium extending into the false pelvis.



Fig. 10.02 A patient with multiple osteochondromas. The limb shows shape and modeling defects.



Fig. 10.03 Outer aspect and cut section of osteochondroma of the upper fibula demonstrating the continuity of the cortex and marrow cavity of the osteochondroma with that of the underlying bone.

Macroscopy

An osteochondroma may be sessile or pedunculated. The cortex and medullary cavity extend into the lesion. The cartilage cap is usually thin (and decreases in thickness with age). A thick and irregular cap (greater than 2 cm) may be indicative of malignant transformation.

Histopathology

The lesion has three layers – perichondrium, cartilage and bone. The outer layer is a fibrous perichondrium that is continuous with the periosteum of the underlying bone. Below this is a cartilage cap that is usually less than 2 cm thick (and decreases with age). Within the cartilage cap the superficial chondrocytes are clustered, whereas the ones close to the transition to bone resemble a growth plate. They are organised into chords and undergo endochondral ossification similar to the zone of provisional mineralization. Loss of the architecture of cartilage, wide fibrous bands, myxoid change, increased chondrocyte cellularity, mitotic activity, significant chondrocyte atypia and necrosis are all features that may indicate secondary malignant transformation. Fractures within a stalk may elicit a focal fibroblastic response.

Surface chondrosarcomas differ from osteochondromas by the absence of a stalk and the presence of lobular masses of cartilage that permeate and infiltrate the soft-tissues [1366]. Parosteal osteosarcoma may have a zone of typical cartilage simulating a "cap". They are, however, radiographically and

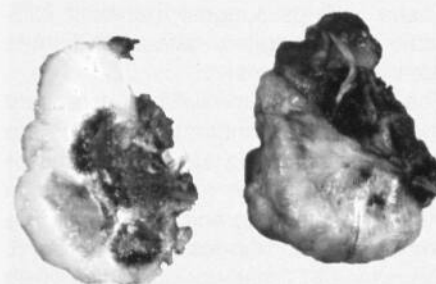


Fig. 10.04 Osteochondroma cut surface and outer surface showing the bony stalk and the overlying cartilage cap.

microscopically different from an osteochondroma. The characteristic fibroblastic proliferation and cytological atypia is not observed in an osteochondroma.

Bunions and osteophytes are bony growths (often without a cartilage cap) that have no marrow cavity or sometimes a poorly developed one that is not continuous with the medullary canal of the underlying bone. Exostoses that arise in the cranio-facial and jaw bones are sometimes called tori (sing. torus). These are usually osseous proliferations that are reactive to an irritant. A similar traumatic aetiology is most likely responsible for the subungual exostosis and the so-called aural meatal exostosis. Bizarre parosteal osteochondromatous proliferation (Nora's lesion) is a disorganized mass of bone, cartilage and fibrous tissue. Trevor disease (Dysplasia Epiphysealis Hemimelica) is a non-hereditary skeletal dysplasia that resembles an epiphyseal osteochondroma.

Genetics

It was long debated whether osteochondroma was a developmental disorder or a true neoplasm. Cytogenetic aberrations involving 8q22-24.1, where the *EXT1* gene is located, have been found in ten out of 30 sporadic and in 1 out of 13 hereditary osteochondromas [264, 1430]. Moreover, DNA flow cytometry of the cartilaginous cap demonstrated aneuploidy (DNA index range 0.88-1.17) in four of 10 osteochondromas [238]. LOH detected by microsatellite analysis using DNA isolated from the cartilaginous cap was found almost exclusively at the *EXT1* locus in 3 of 8 sporadic and 2 of six hereditary osteochondromas [238]. Fluorescence in situ hybridization revealed loss of the 8q24.1 locus in 27 of 34 (79%) osteochondromas [645].

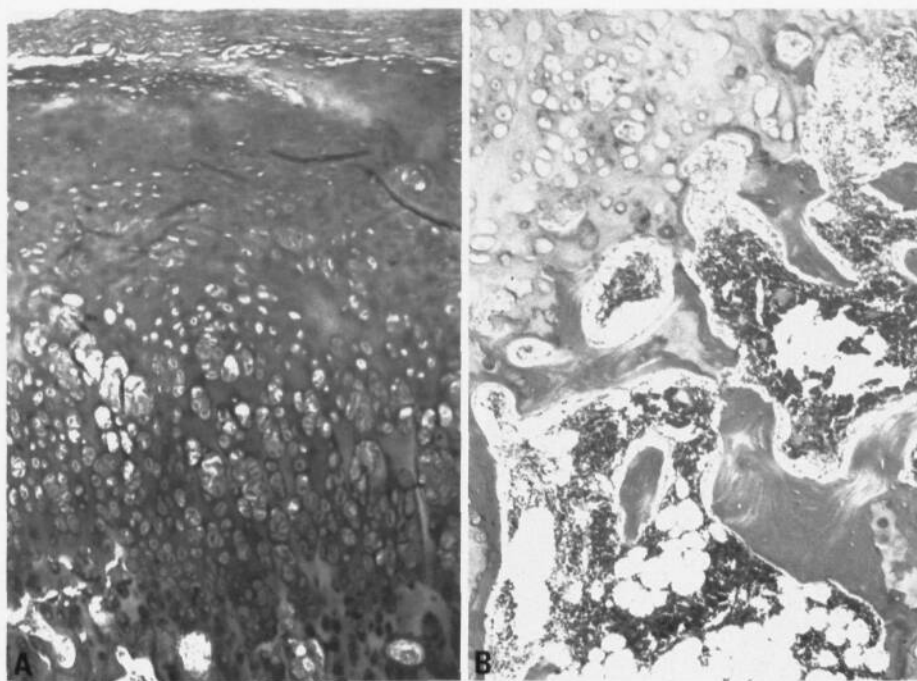


Fig. 10.05 **A** Osteochondroma, showing the outer perichondrium, cartilage cap and underlying stalk. Variable amount of endochondral ossification occurs at the bone/cartilage interface. **B** Endochondral ossification is often seen at the base of the osteochondroma. This is a normal feature and should not be interpreted as a malignancy invading into the stalk.

These findings suggest that both sporadic and hereditary osteochondromas are true neoplasms.

The *EXT* genes, involved in hereditary multiple osteochondromas (HMO), are hypothesised to be tumour suppressor genes. Most of the mutations found in HMO patients are predicted to result in a truncated or non-functional protein. Germline *EXT1* mutations combined with loss of the remaining wild type allele was demonstrated in three osteochondromas of two HMO patients [238]. One sporadic osteochondroma was described to harbour a deletion of one *EXT1* gene combined with an inactivating mutation in the other *EXT1* gene [168]. Although second mutations have been demonstrated in the minority of cases so far, these findings strongly suggest that inactivation of both copies of an *EXT* gene in a cartilaginous cell of the growth plate is required for osteochondroma formation in both hereditary and sporadic cases. Indeed, diminished levels of the *EXT1* and *EXT2* proteins [168] and of their putative downstream effectors (Ihh/PTHrP and FGF signalling pathway, see chapter 21) [241] were

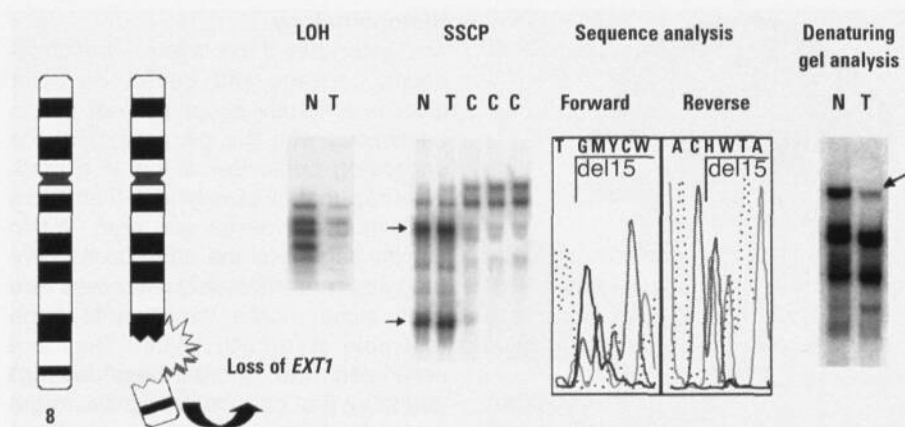


Fig. 10.06 Chromosomal band 8q24 rearrangement in sporadic osteochondroma (on the left). LOH at 8q24 in a patient with multiple exostoses is demonstrated by microsatellite analysis (D8S198). SSCP mutation analysis reveals aberrant bands (indicated by arrows) in both normal (N) and osteochondroma (T) DNA. Sequence analysis reveals a constitutional 15 bp deletion. The PCR fragment containing the mutation is run on a denaturing gel, illustrating loss of the wild-type allele (arrow).

demonstrated in both sporadic and hereditary osteochondroma chondrocytes [168]. Moreover, *EXT* mutations were described to induce cytoskeletal abnormalities (altered actin distribution) in osteochondroma chondrocytes [168, 169, 1237].

Prognostic factors

Excision of the osteochondroma is usually curative. Recurrence is seen with incomplete removal, however, multiple recurrences or recurrence in a well excised lesion should raise the suspicion of malignancy.