Osteochondroma

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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

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Contents

SOFT TISSUE TUMOURS

WHO Classification of Soft Tissue Tumours 9

1 Adipocytic tumours 19
Lipoma 20
Lipomatosis 23
Lipomatosis of nerve 24
Lipoblastoma / Lipoblastomatosis 26
Angiolipoma 28
Myolipoma of soft tissue 29
Chondroid lipoma 30
Spindle cell lipoma / Pleomorphic lipoma 31
Hibernoma 33
Atypical lipomatous tumour / Well differentiated liposarcoma 35
Dedifferentiated liposarcoma 38
Myxoid liposarcoma 40
Pleomorphic liposarcoma 44
Mixed-type liposarcoma 46

2 Fibroblastic / Myofibroblastic tumours 47
Nodular fasciitis 48
Proliferative fasciitis and proliferative myositis 50
Myositis ossificans and fibroosseous pseudotumour of digits 52
Ischaemic fasciitis 55
Elastofibroma 56
Fibrous hamartoma of infancy 58
Myofibroma / Myofibromatosis 59
Fibromatosis colli 61
Juvenile hyaline fibromatosis 63
Inclusion body fibromatosis 64
Fibroma of tendon sheath 66
Desmoplastic fibroblastoma 67
Mammary-type myofibroblastoma 68
Calcifying aponeurotic fibroma 69
Angiomyofibroblastoma 71
Cellular angiofibroma 73
Nuchal-type fibroma 75
Gardner fibroma 76
Calcifying fibrous tumour 77
Giant cell angiofibroma 79
Superficial fibromatoses 81
Desmoid-type fibromatoses 83
Lipofibromatosis 85
Extrapleural solitary fibrous tumour and haemangiopericytoma 86
Inflammatory myofibroblastic tumour 91
Low grade myofibroblastic sarcoma 94
Myxoinflammatory fibroblastic sarcoma 96
Infantile fibrosarcoma 98
Adult fibrosarcoma 100
Myxofibrosarcoma 102
Low grade fibromyxoid sarcoma 104
Sclerosing epithelioid fibrosarcoma 106

3 So-called fibrohistiocytic tumours 109
Giant cell tumour of tendon sheath 110
Diffuse-type giant cell tumour 112
Deep benign fibrous histiocytoma 114
Plexiform fibrohistiocytic tumour 116
Giant cell tumour of soft tissue 118
Pleomorphic malignant fibrous histiocytoma / Undifferentiated high grade pleomorphic sarcoma 120
Giant cell malignant fibrous histiocytoma / Undifferentiated pleomorphic sarcoma with giant cells 123
Inflammatory malignant fibrous histiocytoma / Undifferentiated pleomorphic sarcoma with prominent inflammation 125

4 Smooth muscle tumours 127
Angioleiomyoma 128
Leiomyoma of deep soft tissue 130
Leiomyosarcoma 131

5 Pericytic (perivascular) tumours 135
Glomus tumours 136
Myopericytoma 138

6 Skeletal muscle tumours 141
Rhabdomyoma 142
Embryonal rhabdomyosarcoma 146
Alveolar rhabdomyosarcoma 150
Pleomorphic rhabdomyosarcoma 153

7 Vascular tumours 155
Haemangiomas 156
Epithelioid haemangioma 159
Angiomatosis 161
Lymphangioma 162
Kaposiform haemangioendothelioma 163
Retiform haemangioendothelioma 165
Papillary intralymphatic angioendothelioma 167
Composite haemangioendothelioma 168
Kaposi sarcoma 170
Other intermediate vascular neoplasms 173
Epithelioid haemangioendothelioma 173
Angiosarcoma of soft tissue 175

8 Chondro-osseous tumours 179
Soft tissue chondroma 180
Extraskeletal osteosarcoma 182

9 Tumours of uncertain differentiation 185
Intramuscular myxoma 186
Juxta-articular myxoma 188
Deep 'aggressive' angiomyxoma 189
Pleomorphic hyalinizing angiectatic tumour of soft parts 191
Ectopic hamartomatous thymoma 192
Angiomatoid fibrous histiocytoma 194
Ossifying fibromyxoid tumour 196
Mixed tumour / Myoepithelioma / Parachordoma 198
Synovial sarcoma 200
Epithelioid sarcoma 205
Alveolar soft part sarcoma 208
Clear cell sarcoma of soft tissue 211
Extraskeletal myxoid chondrosarcoma 213
Malignant mesenchymoma 215
Desmoplastic small round cell tumour 216
Extrarenal rhabdoid tumour 219
Neoplasms with perivascular epithelioid cell differentiation (PEComas) 221
Intimal sarcoma 223

BONE TUMOURS

WHO Classification of Bone Tumours 225

10 Cartilage tumours 233
Osteochondroma 234
Chondromas 237
Chondroblastoma 241
Chondromyxoid fibroma 243
Synovial chondromatosis 246
Chondrosarcoma 247
Dedifferentiated chondrosarcoma 252
Mesenchymal chondrosarcoma 255
Clear cell chondrosarcoma 257

11 Osteogenic tumours 259
Osteoid osteoma 260
Osteoblastoma 262
Conventional osteosarcoma 264
Telangiectatic osteosarcoma 271
Small cell osteosarcoma 273
Low grade central osteosarcoma 275
Secondary osteosarcoma 277
Parosteal osteosarcoma 279
Periosteal osteosarcoma 282
High grade surface osteosarcoma 284

12 Fibrogenic tumours 287
Desmoplastic fibroma of bone 288
Fibrosarcoma of bone 289

13 Fibrohistiocytic tumours 291
Benign fibrous histiocytoma of bone 292
Malignant fibrous histiocytoma of bone 294

14 Ewing sarcoma / Primitive neuroectodermal tumour 297
Ewing tumour / PNET 298

15 Haematopoietic tumours 301
Plasma cell myeloma 302
Malignant lymphoma 306

16 Giant cell tumours 309
Giant cell tumour 310
Malignancy in giant cell tumour 313

17 Notochordal tumours 315
Chordoma 316

18 Vascular tumours 319
Haemangioma and related lesions 320
Angiosarcoma 322

19 Myogenic, lipogenic, neural, and epithelial tumours 325
Leiomyoma of bone 326
Leiomyosarcoma of bone 327
Lipoma of bone 328
Liposarcoma of bone 330
Schwannoma 331
Adamantinoma 332
Metastases involving bone 334

20 Tumours of undefined neoplastic nature 337
Aneurysmal bone cyst 338
Simple bone cyst 340
Fibrous dysplasia 341
Osteofibrous dysplasia 343
Langerhans cell histiocytosis 345
Erdheim-Chester disease 347
Chest wall hamartoma 348

21 Congenital and inherited syndromes 349
Familial adenomatous polyposis 352
Beckwith-Wiedemann syndrome 354
Enchondromatosis: Ollier disease and Maffucci syndrome 356
McCune-Albright syndrome 357
Multiple osteochondromas 360
Retinoblastoma syndrome 363
Rothmund-Thomson syndrome 365
Werner syndrome 366

Contributors 369
Source of charts and photographs 374
References 376
Subject index 420

Osteochondroma

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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. Inheri-tance 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 physeal plate or herniation of the plate in the metaphysis {415,988, 1457,1464,1718}.

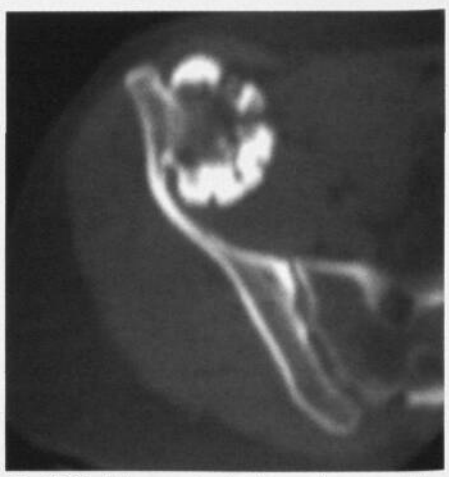

Fig. 10.01 A large ostechondroma is seen at the upper ilium extending into the false pelvis.

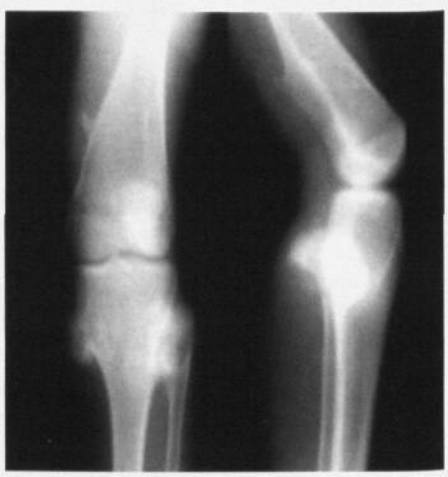

Fig. 10.02 A patient with multiple osteochondromas. The limb shows shape and modeling defects.

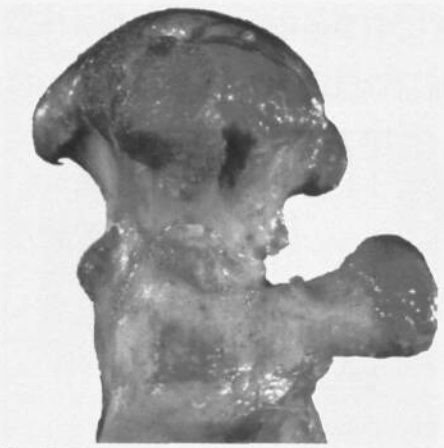

Fig. 10.03 Outer aspect and cut section of osteochondroma of the upper fibula demonstrating the continuity of the cortex and marrow cavity of the osteochondroma with that of the underlying bone.

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

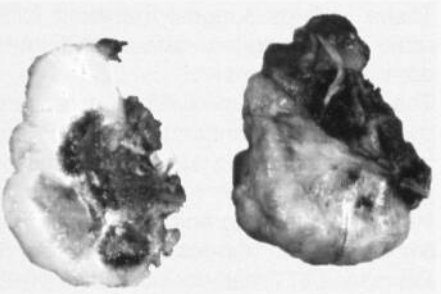

Fig. 10.04 Osteochondroma cut surface and outer surface showing the bony stalk and the overlying cartilage cap.

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.

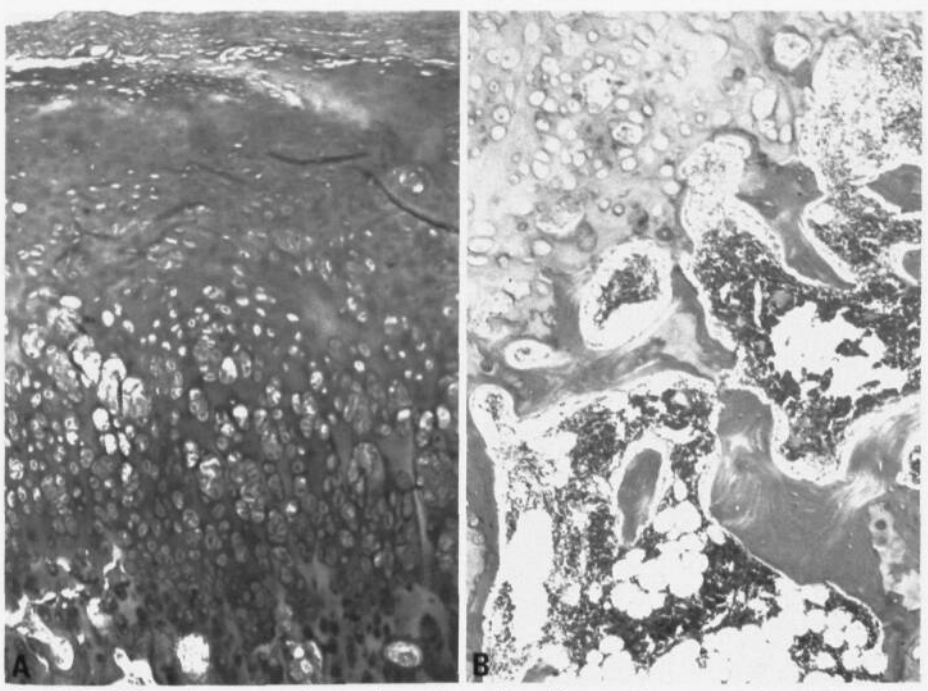

Fig. 10.05 **A** Osteochondroma, showing the outer perichondrium, cartilage cap and underlying stalk. Variable amount of endochondral ossification occurs at the bone/cartilage interface. **B** Endochondral ossification is often seen at the base of the osteochondroma. This is a normal feature and should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

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}.

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 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}.

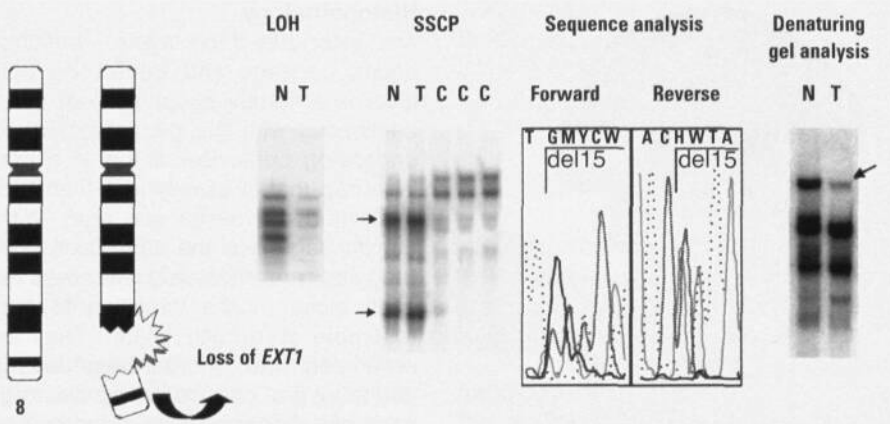

Fig. 10.06 Chromosomal band 8q24 rearrangement in sporadic osteochondroma (on the left). LOH at 8q24 in a patient with multiple exostoses is demonstrated by microsatellite analysis (D8S198). SSCP mutation analysis *reveals aberrant bands (indicated by arrows) in both normal (N) and osteochondroma (T) 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).

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.