BONE AND JOINT

MUSEUM CATALOGUE

Department of Pathology, University of Adelaide, 2004

BONE AND JOINT

INTRODUCTION

The pathology of bones and joints encompasses a very wide range of disorders, including metabolic, degenerative, traumatic, infective, inflammatory and neoplastic, some associated with high mortality, others affecting quality of life rather than duration. In orthopaedic units, the most common conditions that you are likely to encounter will be acute fractures and chronic degenerative and inflammatory diseases.

An understanding of bone and joint pathology will be made considerably easier if, in addition to having a good understanding of the relevant anatomy, including bone development and growth and types of joint, you have a good understanding of the normal histological structure of bone, cartilage and synovium and the physiology of bone formation and turnover.

Any comments on this catalogue are welcome. Please contact a member of the department.

HOW TO USE THIS CATALOGUE

This catalogue can be used as a tool to develop your knowledge, as well as provide an opportunity for revision.

It is divided into:

- Introduction and approach to specimens of bone and joint (pages 2-4).
- Index (pages 5-7). Examples of specific diagnoses can be found via the index.
- Core and classic disease processes of bones and joints (pages 8-31). This gives examples and discussion of core and/or classic diseases of bones and joints. These are the specimens that students should focus on being able to identify initially. However, it depends to some extent on what you have covered in lectures and practical classes or resource sessions as to what you should know. Some of the specimens and discussion are directed more towards clinical medical students.
- Main catalogue (pages 32-55). This section covers the specimens in numerical order. Questions and/or comments accompany some of the specimens to help you expand your knowledge. In order to fit more specimens in the museum, not all of the pots are in numerical order on the shelves, and large specimens are often found on the bottom shelves.

You might find it useful to work quietly with a few friends and to have a few textbooks handy (e.g. pathology, medical, anatomy). You will also find that you can learn some anatomy and clinicopathological correlation from the specimens and information given.

You do not have to examine every single specimen in the museum. However, just as in clinical practice, you will not become proficient in diagnosing a condition if you have only seen one case. Exposure to a variety of cases (specific diagnoses can be found via the index) to experience the variability in morphology will help your learning greatly. In general red and blue dots indicate basic and straightforward cases, whereas yellow dots indicate a more complex case. This is not a hard and fast rule, and you will find yellow dot specimens turning up in resource sessions/practical classes and even exams, if they represent classic pathology.

In general

- read the clinical information given
- look at the entire specimen, not just the front
- identify and orientate the organ or tissue (where possible)
- identify the abnormality and from your knowledge of pathology (which will come with time) look for relevant features to help you make the diagnosis. Of course to appreciate the abnormal you first need to have an appreciation of normal anatomy
- make a diagnosis or differential diagnosis using any clinical information given to you – it is often relevant – sometimes the diagnosis is only made with knowledge of the clinical features. Even when you know the diagnosis, attempt to identify relevant features in the specimen and understand why this is the diagnosis.
- attempt to correlate the pathological features with the clinical features (clinico-pathological correlation) i.e. explain how the pathological features have caused the patients symptoms and signs (when relevant)
- try to answer any questions presented yourself before reading the answers.

You may prefer to look at the specimen 'blind', without reading the clinical information given first.

Limits to diagnosis on macroscopic examination

In all cases a diagnosis is given, but it is important to realise that sometimes the final diagnosis was only made based on the clinical history and histological examination. In some cases the macroscopic appearance is classic and even without the history and histology you should be able to make the diagnosis from the appearance, in others, it might only be possible to give a list of differential diagnoses or a more general diagnosis.

Remember that some of these specimens are very old, and some of the investigations and treatments mentioned may be out of date.

BASIC APPROACH TO THE INTERPRETATION AND DESCRIPTION OF BONE AND JOINT PATHOLOGY SPECIMENS

Students are expected to be able to give a brief succinct description of relevant macroscopic features of a specimen using appropriate terminology, as well as to arrive at a diagnosis or differential diagnosis. Even if not asked for a description, identification of relevant features is helpful in the diagnostic process. Your descriptive skills will improve with practice. In any aspect of medicine, one needs to approach things in a systematic manner; otherwise important points may be omitted.

As with all specimens:

- Read the clinical history, it will often provide relevant information (although sometimes it is helpful to look at the specimen without any information and work out what is going on for yourself)
- Look at the front of the pot first (i.e. the one with the number and the dot) but make sure to look at the back and sides as well
- Identify the bones/joints and their orientation where possible

The next decisions to make are whether the specimen looks smaller (is it from a child?) or larger than normal, if the epiphyseal cartilaginous plate is still present and whether any abnormality present is focal or diffuse. To describe a specimen you need to be able to use the correct terminology to communicate the nature of the pathology that is present.

Focal lesion

These are probably the easiest and consist of single abnormalities that anyone can point to with confidence and say "This is the abnormality". Having identified the abnormality, you should then say where it is using appropriate anatomical terms and then describe it:

- Colour: what colour is it? Is it all one colour or is it many colours (variegated)? Does it look homogenous (all the same the whole way through)?
- Size: you can give a measurement but don't get too obsessive
- Shape
- Consistency: this is of course difficult when the specimen is in a pot and you are unable to touch it, and who would want to anyway? But even just by looking you can get some idea: Does it look solid? Does it look friable (as if it's falling to pieces?) or are there bits missing or greyish areas (altered blood) to suggest necrosis?
- Margins: the appearance of margins can be helpful in deciding if a lesion is likely to be benign or malignant. Are they well-defined or well-demarcated – i.e. is there a clear regular line between the lesion and the adjacent normal tissue – or irregular or even diffuse, where the line between the lesion and the adjacent normal tissue is harder, perhaps impossible, to trace? Malignant lesions typically have diffuse/irregular or infiltrative margins and benign tumours typically have well-defined margins. You won't be surprised to hear that there are exceptions to this rule: sometimes rapidly growing malignant tumours or metastases may have deceptively well-defined margins. On the other hand some benign lesions may have poorly defined edges. A bit of practice looking at specimens will make it easier to distinguish them.
- Site: the site (which bone and which part of the bone) of a lesion can give a hint to the diagnosis, as specific conditions tend to occur in specific bones and specific parts of the bone e.g. osteogenic sarcomas tend to arise in the metaphyses of long bones, most commonly around the knee

Multifocal

This means that there is more than one distinct lesion within the specimen. All the above comments regarding the description of focal lesions apply here as well. Metastases are typically multifocal or multiple. It is not possible to determine the site of the primary tumour and generally not possible to determine whether metastases are osteolytic or osteosclerotic from their macroscopic appearance.

Diffuse

These lesions can be hard to describe and in the case of bone pathology it raises the possibility of some kind of metabolic disorder.

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CORE AND CLASSIC DISEASE PROCESSES

BONE: ACHONDROPLASIA

CASE 4329

Clinical information
The specimen is from a male infant who died at the age of 3 months. During life swellings were noticed at the ends of the long bones and there was kyphosis and scoliosis of the spine. The chest was somewhat deformed, being flattened from before backward.

Describe the specimen
The specimens of the long bones show shafts that are shorter than normal for an infant of this age, causing the bone ends to appear enlarged. Bone formation can be seen in the cartilaginous epiphyses at the ends of the femora and tibiae and in the vertebrae at the back of the pot.

What is the diagnosis?
Achondroplasia

What is achondroplasia?
Achondroplasia is a genetically determined disease in which there is impaired endochondral ossification at the epiphyseal growth plates resulting in a failure of growth in the length of long bones. It is the most common cause of dwarfism. It is an autosomal dominant disorder, with approximately 80% of cases representing new mutations.
Patients typically have a point mutation in the gene that codes for FGF receptor 3, resulting in constant activation of this receptor and subsequent inhibition of chondrocyte proliferation at the growth plate. The epiphyses themselves grow relatively normally and hence appear relatively enlarged. There is also lack of development of the bones at the skull base that are formed in cartilage. Intra-membraneous ossification is unaffected so the cortices of the long bones and the bones of the skull vault grow normally. Affected persons have a trunk of relatively normal length and short limbs. They are usually intellectually and sexually normal with a normal life span though a female achondroplastic can rarely deliver a baby per vaginam because of the deformity of the pelvis. Some patients develop severe kyphoscoliosis.

Comment
This case could in fact represent a related condition known as thanatophoric dwarfism, also caused by a mutation in FGFR3, but different to that causing achondroplasia. Additional features include a small chest cavity and a bell shaped abdomen, with resultant respiratory insufficiency. Death occurs either at birth or soon after.

BONE: OSTEOPOROSIS

CASE 17441

Clinical information
The patient was an elderly man who had had numerous fractures, old and recent, in ribs and clavicles with collapse of several vertebral bodies.

Describe the specimen
The specimen is a sagittal section through a portion of the spinal column. The cortex of the vertebrae is thinned and there are large spaces between the trabeculae in the spongy bone. Several Schmorl's nodes are seen herniating into vertebral bodies.

What is the diagnosis?
Osteoporosis

What is osteoporosis, what types are there and how does it arise?
Osteoporosis refers to a reduction in normally mineralised bone mass resulting from resorption outweighing formation in normal bone remodelling. There is reduced thickness of the cortex and a reduction in the number and size of trabeculae. The disorder may be localised to a region or limb or generalised. Localised osteoporosis may arise in a limb from lack of use.
Generalised osteoporosis

- Primary osteoporosis refers to cases of uncertain pathogenesis. There is normally a progressive loss of bone mass from the 4th decade of life, women > men initially. Severe reduction in bone mass resulting in osteoporosis appears to be influenced by genetic factors, hormonal influences, calcium intake, exercise and cigarette smoking.
  Primary osteoporosis is subdivided further:
  - Postmenopausal: in postmenopausal women from increased osteoclast activity
  - Senile: in elderly males and females (>70 yrs) from attenuated osteoblast function
- Secondary osteoporosis mainly arises as a result of endocrine conditions (e.g. corticosteroid administration, excess endogenous cortisol, hypogonadism).

What are the complications of osteoporosis?
Osteoporosis is an important cause of morbidity in the elderly. The main problem is fracture of the weakened bone, particularly neck of femur, distal radius and vertebral bodies (crush fracture). Vertebral fractures can cause pain, loss of height and various deformities. Hospitalisation and lack of mobility as a result of fractures in the elderly can result in significant mortality and morbidity from pulmonary embolism and pneumonia.

BONE: RICKETS

CASE 11846

Clinical information
No clinical information is available.

Describe the specimen
The specimen consists of the wall of the right hemithorax. There is marked broadening of the costochondral junctions.

What is the diagnosis?
Rachitic rosary

What is rickets and how does it develop?
Rickets results from inadequate mineralization of newly formed bone matrix (osteoid) in children due to vitamin D deficiency, abnormalities in vitamin D metabolism or phosphate deficiency states. There is subsequent abnormal cartilage proliferation with hypertrophy and thickening of epiphyseal growth plates. Endochondral ossification proceeds very slowly. Affected children are often apathetic and short, with characteristic changes in teeth and bones (e.g. thickening of costochondral junctions, shortening and bowing) and fractures are frequent. Vitamin D deficiency may arise from e.g. inadequate sun exposure, dietary deficiency and defective intestinal absorption. Rickets is now rare in developed countries.

What is osteomalacia?
Osteomalacia is the equivalent condition (inadequate mineralization of newly formed bone matrix) that develops from similar deficiencies in adults, developing following closure of the growth plates. Osteoid is slow to mineralise. Patients may experience bone pain and pathological fractures.

BONE: PAGET DISEASE

CASE 50551/82

Clinical information
The patient was a man aged 75.

Describe the specimen
There are 2 specimens. One is of femur that has been sliced coronally. It shows bowing deformity, great cortical thickening and loss of fine trabecular structure. The other specimen of skull shows gross cortical thickening and loss of medullary spaces.

What is the diagnosis?
Paget disease of bone

What is Paget Disease of bone?
Paget Disease of bone is a chronic condition where there is disorganised bone remodelling resulting in thickened but weakened bones. It is most common in elderly Caucasian males. Its cause is unknown, however, there is some evidence that it could be viral in origin. The disease may be solitary or polyostotic, involving bones of the axial skeleton and long bones of the leg. There is an initial osteoclastic resorptive stage followed by a mixed stage with osteoblastic and osteoclastic activity, ending in a burnt out stage with thickened disorganised trabecular and cortical bone. Microscopically the bony lamellae demonstrate a characteristic mosaic pattern of cement lines.

What are the potential complications of Paget Disease?
- although the bone is thickened, pathological fractures may occur
- deformities of weight bearing bones may arise e.g. bowing
- bone remodelling may lead to narrowing of the foramina at the base of the skull, pressing on cranial nerves
- disorganisation of subchondral bone and bowing of bones can lead to secondary osteoarthritis
- blood flow is increased in diseased areas of bone. With extensive disease, high output cardiac failure may develop
- osteogenic sarcomas may arise in sites of disease

BONE: FRACTURE

CASE 13169

Clinical information
The injury occurred 3 weeks previously.

Describe the specimen
The specimen consists of the clavicle with an unreduced fracture at its midpoint. Old haemorrhage can be seen and surrounding the fracture is ill-defined osseofibrous tissue.

What is the diagnosis?
Fractured clavicle with surrounding callus

CASE 22705

Clinical information
This 43-year old man was a schizophrenic who suffered quadriplegia during a suicide attempt seven years before admission. The injury occurred at the C7 level. He had also had a total laryngectomy for carcinoma of the larynx in the past. He died following a respiratory infection.

Describe the specimen
The specimen is a longitudinal sagittal section of the lower cervical and upper thoracic spine showing wedging and considerable posterior protrusion of the body of C7. The spinal cord is compressed at the level of the injury.

What is the diagnosis?
Cervical fracture with cord compression

What complications may arise following fractures?
- haemorrhage
- soft tissue (muscles, tendons, ligaments etc) and nerve injury (stretching or tearing)
- bone marrow or fat embolism
- infection (particularly with open fractures)
- complications of treatment: related to surgery or plaster cast
- deep venous thrombosis (more so with leg fractures)
- deformities relating to impaired healing

What factors may delay healing of a fracture?
Local: movement of bone ends, poor alignment, poor blood supply, large haematoma, multiple bone fragments (i.e. comminuted fracture), infection, underlying bone disease.
Significant disruption of the periosteum or of the blood supply to the medullary cavity lead to impaired formation of external and internal callus respectively.
General: old age, poor nutrition, immunosuppression

What is a pathological fracture? What are some causes of pathological fracture?

A pathological fracture is one that occurs in diseased bone. It often requires less than normal stresses for fracturing.

Causes include

- osteoporosis
- primary (benign or malignant) or secondary bone tumours
- Paget Disease of bone
- osteitis fibrosa cystica (from hyperparathyroidism)
- osteogenesis imperfecta

Comment

It is also important that you know the mechanisms and their timing involved in the healing of a fracture, so that factors that can delay or prevent healing are recognised and treated.

BONE: AVASCULAR NECROSIS OF THE HEAD OF THE FEMUR WITH SECONDARY OSTEOARTHRITIS

CASE 19160/81

Clinical information
The patient was a man aged 29. He had undergone renal transplantation and was taking Prednisolone.

Describe the specimen
The specimen consists of the head of the femur that has collapsed and its articular cartilage is eroded.

What is the diagnosis?
Osteoarthritis of the head of the femur

Comment
This case has arisen following avascular necrosis of the head of the femur, probably caused by prednisolone.

What is the pathogenesis of this disease?
Necrosis of bone results from ischaemia of which there are a variety of causes including nitrogen embolism ('the bends'), thrombosis in sickle cell anaemia and vasculitis, and damage to blood vessels as a result of trauma or radiation. However, a number of cases are idiopathic (e.g. Legg –Calve-Perthes Disease in the femoral head in children) and others follow steroid therapy. Subchondral infarcts often collapse and predispose to secondary osteoarthritis.

BONE: SEQUESTRUM FOLLOWING OSTEOMYELITIS

CASE 18477/92

Clinical information
This patient developed osteomyelitis following plating of a fracture of the tibia.

Describe the specimen
The specimen consists of an irregular piece of the shaft of the tibia. The surface of the bone is irregularly eroded in a pattern reminiscent of white ants working on wood. Pus is visible in the medullary space. The screw holes from a previous plate are apparent.

What is the diagnosis?
Sequestrum following longstanding osteomyelitis

What are the important causes of osteomyelitis?
The main causative organisms include Staphylococcus aureus (most common overall), various Streptococci, various gram negatives including E. coli, Salmonella species (especially in patients with sickle cell disease) and Haemophilus influenzae. These will cause an acute suppurative osteomyelitis. Treponema pallidum (gummas in adults and congenital syphilitic bone lesions) and Mycobacterium tuberculosis will cause chronic infection.

What are the predisposing factors for osteomyelitis?
The organisms may be introduced via

- the haematogenous route from a septic focus elsewhere (e.g. skin, teeth) or following introduction via skin trauma or IV drug use.
- direct inoculation (open fractures, prosthetic material, penetrating wounds, surgery)
- contiguous spread of adjacent infection

What is the pathogenesis of osteomyelitis?
Bacteria penetrate blood vessels (often in the metaphyseal regions of the long bones, where there is high vascularity in children; vertebrae are another common site), proliferate and initiate a suppurative inflammatory response. Local blood flow is impaired and areas of bone become necrotic. Pus and bacteria can enter the vessels of the cortex and spread through the cortex to the periosteum, further compromising the blood supply and sometimes forming subperiosteal abscesses. Fragments of dead bone are called sequestra. Reactive new bone formation occurs in an attempt to wall off the infection.

What are the potential complications of osteomyelitis?

- septicaemia
- pathological fracture
- spread of infection via the periosteum into the adjacent joint -> septic arthritis, especially in children where the periosteum is more loosely attached
- spread of infection into the overlying soft tissues, even forming sinuses to the skin
- the disease may become chronic
- squamous cell carcinomas in the skin around a chronically draining sinus
- secondary amyloidosis in chronic cases

BONE: TUBERCULOUS OSTEOMYELITIS OF THE SPINE (POTT DISEASE)

CASE 6058

Clinical information
No clinical details are available.

Describe the specimen
The specimen consists of most of the thoracic spine that has been sectioned to show the vertebrae and spinal cord. There are ill-defined collections of pale caseous material in three consecutive vertebral bodies. Two are markedly affected and their weakness has caused them to collapse anteriorly resulting in a kyphotic deformity. Anterior to the collapsed vertebrae is part of a thick-walled cavity 1cm in diameter. This is continuous with the caseous material in a vertebral body through a defect in its periosteum. Note that the anterior end of an intervertebral disc is also involved. The spinal cord and the meninges appear normal.

What is the diagnosis?
Tuberculous osteomyelitis of the spine

Comment
The bone is a common site of extrapulmonary tuberculosis, the organisms gaining access via the blood stream. The spine is the most common site of skeletal involvement. Destruction of vertebrae may result in scoliotic and/or kyphotic deformities. Infection may erode through into soft tissues and compress the spinal cord or nerves or extend down into the psoas muscle.

BONE: OSTEOCHONDROMA

CASE 19314

Clinical information
The patient was a man aged 20. A large lump had been noted arising from the left iliac bone for 18 months.

Describe the specimen
The specimen consists of half an irregular bony and cartilaginous mass that measures 7cm in maximum dimension. The cut surface shows irregular cancellous bone covered by a thick irregular cartilaginous cap except at the base where it has been chiselled from the underlying bone.

What is the diagnosis?
Osteochondroma/exostosis

What is an osteochondroma?
Usually arising in children and adolescents, osteochondroma is a hamartoma of bone and is the most frequent benign bone tumour. They arise from the metaphysis of the bone, most commonly femur, tibia, humerus or pelvis. The lesions grow outwards from the bone. They may be single or multiple, the latter being associated with an autosomal dominant hereditary disease – multiple hereditary exostoses.

BONE: GIANT CELL TUMOUR

CASE 946

Clinical information
No clinical information is available.

Describe the specimen
The specimen comprises the lower femur. One condyle is greatly expanded by a partially cystic neoplasm. The articular cartilage has remained intact but the bony tissue of the condyle has almost completely disappeared. There is some ragged grey haemorrhagic solid tissue remaining lining the cavity.

What is the diagnosis?
Giant cell tumour

Comment
Giant cell tumour of bone is a locally aggressive neoplasm characterised by the presence of multinucleate giant cells of osteoclastic differentiation. It is, however, other mononuclear cells of mesenchymal origin within the lesion that are thought to be the neoplastic element. These tumours are usually located at the junction of the metaphysis and epiphysis of a long bone and are most commonly found around the knee. The lesion is generally lytic but well circumscribed, expanding rather than invading through the overlying cortex. The lesion is generally solid, often with areas of haemorrhage, but some times cystic degeneration occurs. Histology confirmed the diagnosis in this case, but the diagnosis can be suggested from the location and typical macroscopic features just described. These tumours are viewed as potentially malignant, as following simple curettage they often recur and a small proportion metastasise. Almost all cases of metastases have occurred following surgical intervention, suggesting that mechanical disruption may promote access of tumour cells to the blood stream.

BONE: OSTEOGENIC SARCOMA

CASE 957

Clinical information
No clinical information is available.

Describe the specimen
The specimen consists of the upper end of the tibia that has been sectioned longitudinally. The epiphyseal plate is visible. Within the metaphysis is a pale brown-grey, fleshy tumour which invades both into the medullary cavity, subperiosteally, raising the periosteum, and through the skin anteriorly. The cortical bone in the region of the tumour has been almost completely destroyed but the epiphyseal plate remains intact above.

What is the diagnosis?
Osteogenic sarcoma/osteosarcoma

Is this specimen from a child or adult? Why?
The specimen is from a child or teenager as the epiphyseal plate is still cartilaginous. (Ossification of most bones is completed between the ages of 17-24 years).

In what age group and where do these lesions usually arise?
Osteogenic sarcomas most commonly arise in adolescents and in males more often than females. They usually arise in the metaphyses of long bones, especially around the knee. The proximal humerus is the next most common site.

What are the risk factors for osteogenic sarcoma?
For most cases there are no known risk factors, although as with all tumours, genetic mutations are fundamental in the pathogenesis and many arise at sites of greatest bone growth and mitotic activity. Patients with hereditary retinoblastomas have a greatly increased incidence of osteosarcoma, related to mutations in the retinoblastoma gene, alterations in this gene also being found in many sporadic osteogenic sarcomas. Occasional cases arise in certain pre-existing bone lesions: older patients who develop osteogenic sarcoma often have underlying Paget Disease of bone or a history of radiation exposure to the area.

Comment
Osteogenic sarcoma is the most common primary malignant tumour of bone. Histologically it is diagnosed by the presence of malignant osteoblast like cells that form osteoid. The gross appearance of the tumour is highly variable. The tumour often invades through cortex, lifting the periosteum and triggering reactive subperiosteal bone formation, giving characteristic appearances on x-ray. The lung is a common site of metastases. It is a highly malignant tumour but recent developments in chemotherapy and limb sparing surgery have resulted in improved survival rates.

BONE: ENCHONDROMA

CASE 8091

Clinical information
The patient was a man aged 26 who had had lumps on his right arm and right hand since he was a baby. Similar lumps were present attached to a rib on the left side and in the 4th toe of his right foot. The 3rd and 4th fingers of his right hand were amputated because they were so deformed that they were useless and impeded the use of his other fingers and thumb.

Describe the specimen
The specimen consists of these fingers. The substance of the fingers is grossly distended and nodular. The cut surface of one of the tumours is pale with white flecks. The tumour appears well circumscribed.

What is the diagnosis?
Multiple enchondromas

Comment
Chondroma is a benign cartilaginous tumour that occurs most frequently in the small bones of the hands and feet. About 30% are multiple. Those arising within the medullary cavity are known as enchondromas. This patient may well have had Ollier Disease, a bone disease characterised by the development of multiple enchondromas that arise from proliferation of cartilage that does not ossify. The lesions in Ollier Disease frequently undergo malignant transformation.

BONE: CHONDROSARCOMA

CASE 20451

Clinical information
The patient was a man aged 49 whose illness began with pain in the right hip radiating to the foot, aggravated by standing and by abduction of the thigh. X-ray of the hip at this stage was said to be normal. Two and a half years later the disability was still present and x-ray showed abnormality. Biopsy revealed chondrosarcoma that was treated with radiotherapy. Two subsequent cordotomies were necessary to relieve pain and had some success. He died 3.5 years after the onset of the illness. At post-mortem widespread metastases were present.

Describe the specimen.
The specimen consists of a portion of the right hip and joint with the upper half of the right femur divided by a coronal cut. Fleshy lobulated and partly necrotic tumour involves the hip-bone and has invaded the joint capsule and joint space. It extends posteriorly as a large fleshy mass into the gluteal region. Patchy pale tumour appears also to be involving the femur.

What is the diagnosis?
Chondrosarcoma

Comment
Chondrosarcoma is a malignant neoplasm where the cells demonstrate cartilaginous differentiation. It is the second most common primary malignant bone tumour. There are a variety of different types that are subdivided according to their location and histological pattern. Most cases occur in middle-aged or elderly persons in the axial skeleton. Some arise from pre-existing benign cartilaginous lesions.

Macroscopically this lesion can only be said to be a malignant neoplasm, though even without the history, sarcoma or even chondrosarcoma could be suggested due to its location.

BONE: LEUKAEMIA

CASE 50086/84

Clinical information
The patient was a man aged 64 said to have chronic lymphocytic leukaemia.

Describe the specimen
There are 2 specimens, one of each femur sectioned coronally. In one specimen, a pathological fracture has occurred through the neck. The cortex in the region of the fracture is thinned. The medullary cavity is quite abnormal for a patient of this age, containing deep red tissue. The other specimen also shows the normal yellow marrow of the medullary cavity to largely be replaced by red marrow.

What is the diagnosis?
Pathological fracture in a femur involved by leukaemia.

What is red marrow and what is white/yellow or fatty marrow?
Red marrow is where there is active haemopoietic tissue. Nonetheless, histologically even in normal haemopoietic areas in the adult, approx. 50% of marrow is fat, 50% is haemopoietic tissue. White/yellow marrow is where there is no or minimal active haemopoiesis.

Where is red marrow normally present in adults?
In adults, red (haematopoietic) marrow is restricted to the bones of the skull, vertebral column, thoracic cage, girdle bones and the proximal femur and humerus.

Where is red marrow normally present in children?
In the medullary cavity of all bones. N.B. In the fetus, haematopoiesis occurs in the liver.

What conditions in adults may cause the red marrow to extend down into the long bones?
Haemopoietic cells of the red marrow can proliferate and replace the white or fatty marrow in a number of pathological states. This may happen, if for example, there is an abnormal proliferation of certain cells in the marrow (e.g. leukaemia and multiple myeloma) or in many different types of anaemia where the marrow undergoes hyperplasia in response to the increased demand for erythropoiesis. In some situations, all of the available marrow space may become active and haematopoiesis may also occur in the liver and spleen (extramedullary haematopoiesis).

BONE: MULTIPLE MYELOMA

CASE 10198

Clinical information
The patient presented with increasing lassitude and breathlessness, loss of weight, epistaxis and pallor. On admission he was anaemic and his serum protein was raised. His urine did not contain Bence-Jones protein. X-rays of the skull and long bones showed numerous well-defined osteolytic areas. A sternal marrow puncture showed relatively numerous pathological plasma cells.

Describe the specimen
The specimen shows the sternum, lower end of the femur and a piece of the skull. There are numerous fairly well-defined, greyish and yellow lytic tumour nodules scattered throughout the specimens.

What is the diagnosis?
Multiple myeloma (without the history, the differential diagnosis is metastatic tumour)

What is multiple myeloma?
Multiple myeloma is a malignant neoplastic process originating in the bone marrow, the cells having features of plasma cells. Lesions are multiple and generally confined to the bones, though in some cases extra-osseus lesions are also present. The skeletal lesions are typically osteolytic due to the cells producing a variety of cytokines that activate osteoclasts. The neoplastic cells make complete (usually IgG) and/or incomplete monoclonal immunoglobulins that can be detected in the serum (M protein).

What is Bence Jones protein?
Bence Jones protein is the name given to monoclonal light chains present in the urine (having been filtered through the glomerulus), present in up to 75% of cases of multiple myeloma.

What are the potential complications of multiple myeloma?
Skeleton
- pathological fractures
- extensive osteolysis -> hypercalcaemia

Blood
- neoplastic cell proliferation in marrow can cause anaemia or pancytopenia

Immunity and immunoglobulins
- impaired humoral immunity -> susceptible to infection, especially bacterial
- increased immunoglobulin may -> hyperviscosity syndrome
- immunoglobulin light chains (usually lambda) can deposit in tissues -> primary amyloid

Hypercalcemia
- neurologic manifestations, polyuria, constipation etc
- renal stones
- calcium deposition in tissues

Kidney
- hypercalcemia -> renal stones and calcium deposition (nephrocalcinosis)
- amyloid
- infection
- cast (Bence Jones protein) nephropathy
- neoplastic infiltration

Comment

Multiple myeloma usually arises in middle-aged-elderly persons. Death is usually secondary to infection or renal failure.

Other plasma cell lesions include solitary plasmacytoma (in bone or soft tissues). These may also cause a monoclonal gammopathy, as may plasmacytoid lymphoma (Waldenstrom's macroglobulinaemia). There is also a
monoclonal gammopathy of undetermined significance.

BONE: METASTATIC CARCINOMA

CASE 50186/92

Clinical information

The patient was a man aged 72 who presented initially with prostate carcinoma in 1987 and was treated with transurethral prostatectomy and local radiotherapy. He was admitted in June 1992 with development of an incomplete quadriplegia secondary to infiltration of the odontoid process by metastatic carcinoma with atlanto-axial subluxation. In addition virtually every level of the vertebral column was infiltrated by metastatic carcinoma.

Describe the specimen

There are 2 specimens of vertebral column. The cancellous bone of the vertebral bodies contains patchy deposits of pale tumour with surrounding congestion. In some areas the normal trabecular pattern is lost and the bone appears dense. In 2 areas in the longer specimen, the intervertebral discs herniate into the weakened vertebral body.

What is the diagnosis?

Metastatic prostate carcinoma (one cannot tell that it is from prostate by the macroscopic appearance)

What tumours commonly metastasise to bone?

Carcinomas metastasise to bone much more readily than sarcomas. In adults, more than 80% of bone metastases originate in breast, lung, prostate, kidney or thyroid.

In which bones do metastases normally occur?

Most metastases are in the axial skeleton (skull, ribs, spine, sacrum). The metaphyses of long bones may also be involved. Metastases are preferentially situated in the medullary cavity. Prostate metastases are commonly found in the lower vertebral column due to the many communications between the prostatic venous plexus and the vertebral veins.

Which metastases are typically osteosclerotic and which osteolytic?

Prostate (and neuroendocrine carcinoma) metastases are typically osteosclerotic, as are a proportion of breast metastases. Some produce a mixed pattern and others tend to be osteolytic, acting by secreting substances that activate osteoclasts.

JOINT: SUPPURATIVE ARTHRITIS

CASE 12803

Clinical information
The patient was a man aged 64 who was a known chronic alcoholic and who had an infected right shoulder joint after an old arthrodesis. A discharging sinus was present on the tip of the shoulder. He died from bronchopneumonia and pulmonary infarction.

Describe the specimen
The specimen consists of an opened shoulder joint. A ragged cavity originally filled with pus is present. It has shaggy necrotic walls. The joint is completely disorganised and the bone ends are eroded.

What is the diagnosis?
Suppurative arthritis of the shoulder joint

What are the predisposing factors for suppurative arthritis?
Organisms can enter the joint via open wounds, contiguous spread from adjacent osteomyelitis or soft tissue infection, or via the bloodstream. Conditions that may be associated with a bacteraemia include septic skin lesions, abrasions, oropharyngeal infections and IV drug use. Normal joints may be affected but predisposing joint conditions include prosthetic joints, arthritis and trauma.

What are the main causes of suppurative arthritis?
The main causative organisms include Staphylococcus aureus (most common overall), various Streptococci, Haemophilus influenzae, various Gram negative bacilli and gonococcus.

What are the complications of suppurative arthritis?
Rapid diagnosis of suppurative arthritis is important as it can cause rapid joint destruction and permanent deformities.

What symptoms and signs is a patient with suppurative arthritis likely to have?
An acutely painful, hot, swollen and tender joint in which movement will be painful (usually a single joint). The patient will generally be febrile. Gonococcal arthritis may run a more subacute course.

Comment
Tuberculosis may also cause an arthritis, but it is not suppurative.

JOINT: OSTEOARTHRITIS

CASE 6207

Clinical information
No clinical information is available.

Describe the specimen
The specimen is of a knee joint that has been opened from the front with the patella reflected superiorly. There is marked osteophytic lipping of the patella and the femoral condyles. The lateral condyles of the femur and the tibia show bare eburnated bone with little residual articular cartilage.

What is the diagnosis?
Osteoarthritis of the knee

CASE 1303

Clinical information
No clinical information is available.

Describe the specimen
The specimen consists of the macerated cervical spine. There is marked osteophytic lipping of many parts of the vertebrae with bony fusion anteriorly between the bodies of C6 and C7 and C7 and T1 and between the arches of C7 and T1 posteriorly.

What is the diagnosis?
Cervical osteoarthritis

What is the pathogenesis of osteoarthritis and what are its risk factors?
Despite the name, osteoarthritis is not an inflammatory joint disease. It essentially results from wear and tear within a joint. Many cases are age related. Genetic influences are also important and gender affects distribution. Joints with pre-existing abnormalities such as rheumatoid arthritis, gout, following trauma or of congenital origin are particularly predisposed and disease often occurs at a younger age in these cases (secondary osteoarthritis).
Increased loads on the cartilage result in chondrocyte damage. Initially chondrocytes proliferate and produce more matrix but this is biochemically altered with greater water content and reduced proteoglycan content compared to normal. Progressive degradation results in cracks developing (fibrillation) in the cartilage that can extend into subchondral bone. Portions of cartilage can be dislodged. Eventually the subchondral bone becomes exposed and forms the new joint surface. Cartilage fibrillation initiates osteoblastic activity with thickening of the subchondral bone. Communications between the joint cavity and underlying bone can result in synovial fluid being forced into the bone to form bone ‘cysts’. At the edge of the joint, mesenchymal stem cells differentiate into osteoblasts and chondroblasts to form new bone (osteophytes) in an attempt to form new articular surface.

What morphological changes occur in osteoarthritis?

Cartilage:

- Proliferation of chondrocytes and initial increase in matrix
- Fibrillation
- Erosion with narrowing of the joint space

Underlying bone

- Microfractures
- Sclerosis
- 'Cyst' formation
- Outgrowths of new bone – osteophytes – at edge
- Exposure of sub-articular bone to joint cavity (eburnation)

Joint capsule and synovium

- Mild secondary chronic inflammation

JOINT: RHEUMATOID ARTHRITIS

CASE 50595/82

Clinical information

The patient was a man aged 67.

Describe the specimen

The specimen consists of part of the elbow joint with ulna and radius. There is marked villous proliferation of the synovium. The articular cartilage of the ulna has been destroyed and the surface is irregular and pitted.

What is the diagnosis?

Rheumatoid arthritis of the elbow joint

CASE 16760

Clinical information

The patient was a woman aged 63 who had had rheumatoid arthritis for 30 years, now said to be burnt out. She died from cardiac failure.

Describe the specimen

The specimen consists of a longitudinal slice through the left knee joint. The joint is completely obliterated by dense fibrous adhesions that bind all three bones together. The cortical bone is thinned.

What is the diagnosis?

Fibrous ankylosis of the knee joint

What histological changes occur in and around the joints in rheumatoid arthritis?

Synovium and joint space

- hyperplastic synovium thrown into folds (villi) with increased vascularity and containing lymphoid follicles with germinal centres and many plasma cells and lymphocytes
- granulation tissue (pannus) and ultimately fibrous tissue forms in the joint between exposed bone ends resulting in ankylosis. The fibrous tissue may eventually ossify.
- synovial fluid: fibrin and neutrophils in synovial fluid when active

Cartilage and bone

- erosion and fibrillation of cartilage
- secondary osteoarthritic changes: osteophyte formation, sclerosis, bone cysts etc
- localised osteoporosis

Tendons: inflammation

What extra-articular manifestations can occur in rheumatoid arthritis?

- rheumatoid nodules: areas of fibrinoid necrosis surrounded by granulomatous inflammation, usually in subcutaneous tissue but can occur virtually anywhere e.g. lungs, cardiac valves, myocardium
- systemic manifestations: fever, fatigue, anaemia
- blood vessels: small vessel vasculitis, aortitis
- lung: chronic inflammation, fibrosis, rheumatoid nodules, pleuritis
- splenomegaly and lymphadenopathy
- ocular manifestations
- secondary amyloid

JOINT: CHRONIC TOPHACEOUS GOUT OF THE FINGER

CASE 14163

Clinical information
The patient was a man aged 74 who had had chronic tophaceous gout for 20 years. He contracted an infection in the terminal pulp space of an involved finger that was amputated.

Describe the specimen
The specimen consists of a finger. A large rounded mass 4cm in diameter is present on the dorsal aspect of the proximal phalanx. A smaller mass lies on the medial side of the middle phalanx. There is patchy ulceration at the finger-tip.

What is the diagnosis?
Chronic tophaceous gout of the finger (the diagnosis cannot readily be made from the macroscopic appearance)

What is a tophus?
A tophus is a deposit of urate crystals in periarticular soft tissue, cartilage or tendon. The crystals initiate a foreign body type granulomatous inflammatory reaction.

What other problems may arise in a patient with gout or hyperuricaemia?
- Acute arthritis – acute inflammation in a joint due to deposition of sodium urate crystals
- Secondary osteoarthritis in joints damaged by gouty arthritis
- Renal problems
    - Acute urate nephropathy from the deposition of crystals in the tubules that can precipitate acute renal failure. Tends to occur in patients with leukaemias and lymphomas undergoing chemotherapy resulting in excessive nucleic acid breakdown
    - Chronic urate nephropathy from more insidious deposition of urate in the tubules and interstitial tissues of the kidney which induces chronic granulomatous inflammation, tubular atrophy and interstitial scarring, ultimately leading to chronic renal failure
    - Uric acid stones