Pseudotumors of bone and bone lesions mimicking tumours

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Abstract

We review entities that have historically been thought to be pseudotumors or mimics of bone tumours. We discuss tumifactive amyloid deposits, the brown tumours of hyperparathyroidism, the various types of cysts that can be seen in bone, Nora lesion, subungual exostosis, haemophilic pseudotumors, non-ossifying fibroma, fibrous dysplasia, osteofibrous dysplasia, Paget disease, tophaceous gout and pseudogout.

Keywords amyloid; bone cysts; brown tumour; fibrous dysplasia; gout; haemophilic pseudotumors; hyperparathyroidism; intraosseous ganglion; non-ossifying fibroma; Nora lesion; osteofibrous dysplasia; Paget disease; pseudogout; pseudotumors

Pseudotumors of bone and bone lesions mimicking tumours

Several diseases in various organs that have historically been considered to be pseudotumors have recently been found to have clonality or other consistent molecular evidence of being neoplastic. This is also true of bone lesions. This review will consider some of the conditions that fall into the category that have historically been considered pseudotumors.

1 Amyloid tumour
2 Brown tumour
3 Bone cysts
4 Nora lesion (bizarre parosteal osteochondromatous proliferation)
5 Subungual exostosis
6 Non-ossifying fibroma (Metaphyseal fibrous defect)
7 Fibrous dysplasia
8 Osteofibrous dysplasia
9 Paget disease
10 Tophaceous gout and pseudogout
11 Hemophillic pseudotumor
12 Trauma related conditions (stress fracture and myostitis ossificans)
13 Gorham disease

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Amyloid tumour of bone

Amyloidosis is a term used to designate a group of different diseases that have in common, the deposition of fibrillar proteins arranged in beta-pleated sheets. Amyloidosis involving the bone can form radiologically identified lesions (tumifactive amyloid) but is similar to amyloidosis elsewhere; the proteins can be highlighted by stains such as Congo red, crystal violet and thioflavin-T or thioflavin-S. Various causes of amyloid deposition are similar to other organs including monoclonal gammopathy, hereditary amyloidosis and chronic infections. Osseous amyloid deposits composed primarily of beta-2 microglobulin have also been described in chronic haemodialysis patients. More recently, structurally altered transthyretin has been identified as a cause of amyloidosis and localized amyloid deposits associated with apolipoproetin A1 produced by chondrocytes have been described in knee menisci.[1]

Brown tumour

As also discussed in the article on metabolic bone disease in this journal, brown tumours are space-occupying lesions of bone that are seen in the setting of long-term hyperparathyroidism. They occur in bone that has been physically damaged during the course of the disease and consist of aggregates of mononuclear cells varying from spindle-shaped to polyhedral that contain variable numbers of osteoclast-like giant cells. The background is often hemorrhagic and the lesion often contains noticeable deposits of hemosiderin derived from the haemorrhage, which is the reason that the tissue appears brown grossly. These lesions resemble giant cell tumours of bone histologically, however, they usually are not located at the ends of bone and the patients usually have clinical derangements of calcium and phosphate. A notable exception are patients that have normocalcemic hyperparathyroidism, in which case the parathyroid hyperfunction may be proven by assaying patient sera for parathyroid hormone levels. Despite the fact that these lesions cause geographic bone destruction and may be confused with neoplasms, they regress spontaneously if the hyperparathyroidism is cured (Figures 1–4).

Practice points

- Hyperparathyroidism should be considered as a differential in lesions with giant cells such as giant cell tumour especially if the X-ray appearance is not typical for a giant cell tumour.

Bone cysts

There are four kinds of cysts that can be seen in bone. The most common ones include the simple (or unicameral) cyst, aneurysmal (or multiloculated) bone cyst, intraosseous ganglion, and epidermal inclusion cyst.

Unicameral (Simple) bone cyst

Unicameral bone cysts are seen in children and young adults. They most commonly occur in the long tubular bones, especially the humerus and femur. Less often, flat bones (such as the ilium) and short tubular bones (such as the calcaneus) can also be

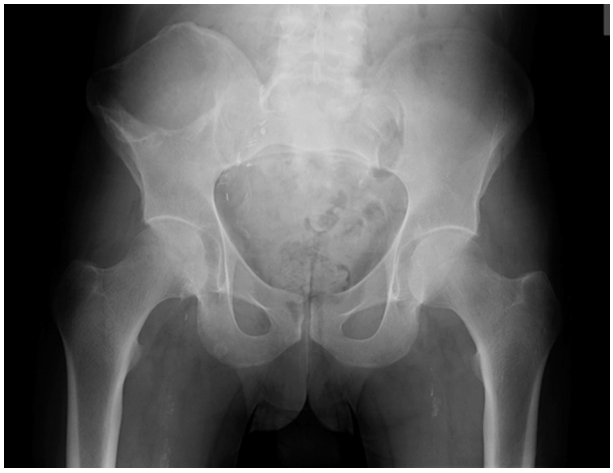

Figure 1 This is a plain film of a brown tumour of the ilium. The lesion is large but has well defined geographic margins.

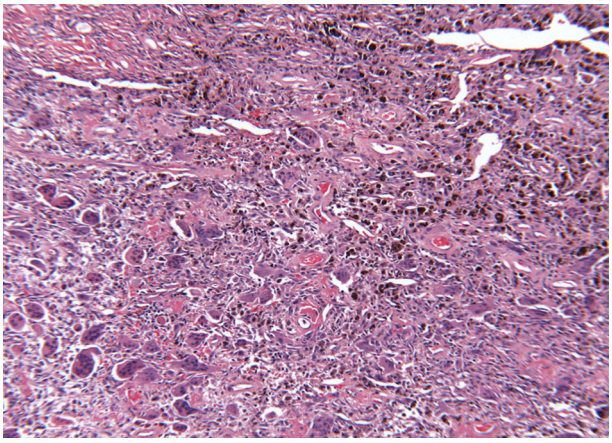

Figure 3 Histological exam showed prominent hemosiderin (brown-black pigment seen at the top-right), mononuclear spindle shaped cells and a sprinkling of giant cells (bottom left).

involved. They are usually asymptomatic until there is a spontaneous fracture, however, there may be stiffness or they may be incidentally discovered in asymptomatic individuals. They are lined by a flattened cell layer that is not epithelial, and are intramedullary in location. They may be unilocular or they may have several locules that are filled with clear or straw coloured fluid; the fluid may appear bloody if there has been a prior fracture.

Simple cysts are central, symmetrical, radiolucent, and extend from the metaphyseal side of the growth plate toward the diaphysis. The overlying cortex may be thinned and there may appear to be expansion of the bone, but the bone in simple cyst is almost never wider than the growth plate unless there has been prior fracture and remodelling (Figure 4A). Plain radiographs and CT scans sometimes show a fragment of bone within the cyst (the fallen leaf); this implies that the cyst contents are fluid. Magnetic resonance imaging studies demonstrate the presence of fluid within the cyst cavity (Figure 4B). The maintenance of fluid pressure in the intact cyst plays a role in the enlargement and propagation of the cyst away from the growth plate as the bone grows. If the cyst is separated from the growth plate in a skeletally immature individual, it is sometimes referred to as "inactive." The natural course of simple cyst is to heal, especially after fractures; however, surgical management may be required to prevent pathological fracture; often this is in the form of intralesional steroid injection or curettage.

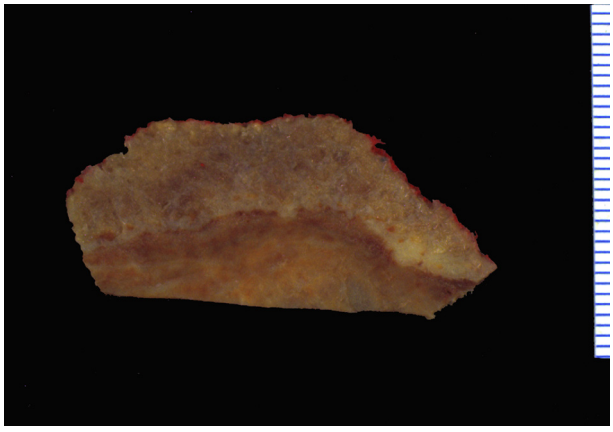

Figure 2 The resection specimen shows again the sharply demarcated margins between the yellow-brown lesional tissue (brown tumour) seen at the bottom of the picture and the whitish normal bone above.

The histological diagnosis of simple cyst is one of exclusion, and the histological findings may be scanty or incomplete, especially without correlation with the images. Curetted material from simple cyst shows fibrovascular tissue with occasional cases showing granulation tissue or a peculiar cementum-like material. Occasionally, a thin fibrous tissue lined by a layer of flattened cells is discerned (Figure 5).

Aneurysmal bone cyst

A primary aneurysmal bone cyst is a locally destructive but benign multilocular lesion that grossly resembles a blood-filled sponge and is mainly seen in children and young adults (Figure 6). It can affect any bone, but most commonly involved are the femur, tibia, humerus and the posterior elements of the vertebrae. Radiologically, these are expansile, often eccentric intramedullary metaphyseal lesions that can sometimes be associated with cortical breakthrough (Figure 7). Often, there is cortical thinning overlying the bony expansion, rendering the bone external to the lesion somewhat egg-shell like. MRI shows fluid–fluid levels in water sensitive pulse sequences. In the healing phase, there may be bone matrix appreciated within the cyst.

Histologically, aneurysmal bone cysts do not have diagnostic cells, but rather consist of a range of findings. In general, the tissue appears quite vascular and will contain a mixture of vessels ranging from capillary sized to very large sinusoidal spaces. The blood-filled spaces are lined by fibrous septae (Figure 8). While immunohistochemistry has demonstrated the presence of some endothelial cells lining some of the vascular spaces, it is generally accepted that many of the vascular spaces in aneurysmal bone cyst are not endothelialized. The septal walls usually contain a cellular spindle cell proliferation that can be very mitotically active. The septae lack smooth muscle, but may contain varying quantities of osteoid, calcifications, chondroid and multinucleated giant cells (Figure 9). The fibroblastic cells lack atypia; atypical mitoses should not be seen. Significant

