Bone: Giant cell tumour of bone

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Abstract

Review on giant cell tumor of bone, with data on clinics, histopathology and genetics

Keywords

Giant cell tumor of bone; Bone neoplasm; H3F3A

Identity

Other names
Osteoclastoma

Phylum
Bones; Giant cell tumors (Osteoclastoma)
A characteristic well-defined eccentric, lytic subchondral lesion involving the epiphysis and metaphysis. The borders are well defined and usually not sclerotic. Pathologic fracture is present in 5-10% of giant cell tumours. Dynamic MRI shows a fast uptake and a slow wash out of contrast.

**Classification**

Giant cell tumor of bone is a locally aggressive primary bone neoplasm.

**Clinics and pathology**

**Disease**
Locally destructive, mono-ostotic tumoral lesion, typically presenting in the meta-epiphysis of long tubular bones with predilection for the knee region of skeletally mature patients (more than 95% of the patients is older than 25 years). Poly-ostotic lesions are exceptionally rare, counting for less than 1% of all cases. In these cases especially brown tumour of hyperparathyreoidism should be considered, which may look histologically identical. Although defined as a benign lesion, adjacent soft tissue invasion, angiovascular invasion and pulmonary metastases (1%) may occur.

**Phenotype / cell stem origin**
Primitive mesenchymal stromal cell.

**Embryonic origin**
Mesoderm.

**Etiology**
The exact origin is still unknown, but data obtained from ultrastructural analyses and cell cultures, as well as novel molecular data, suggest that the stromal cell, or mononuclear spindle cell, is neoplastic. The mononuclear rounded cells and the osteoclastic giant cells are seen as reactive. Therefore, some suggest that stromal cell tumour is a better name, because this fits more precisely the concept of the mononuclear spindled cell (stromal cell) as neoplastic.

**Epidemiology**
This tumour represents 8% of all primary and approximately 20% of benign primary bone tumours. Mostly affecting adults in the third, fourth and fifth decade of life (72%). It is very rarely seen under the age of 10 years (1,3%). There is a slight female predominance (male/female ratio: 46,6%/53,4%).

**Clinics**
Pain of several weeks to months duration and a constantly expanding mass on X-ray, primary in the epiphysis, leading to cortex destruction, pathological fracture and soft tissue invasion. Finally ulceration of the skin occurs if not threatened. A pathological fracture could occasionally be the first sign of this tumour.
Mixture of three cellular components composites the tumour: tumoral spindle shaped mononuclear cells, reactive rounded mononuclear cells and diffusely scattered osteoclast type giant cells. Note that mitoses are strictly limited to the first cell type.

Pathology

A mixture of four components can be distinguished: spindle-shaped and rounded mononuclear cells, osteoclastic-type giant cells and small blood vessels.

The spindle-shaped mononuclear cells are regarded as neoplastic. This cell type is thought to arise from the primitive mesenchymal stromal cell. Conventional mitotic figures are restricted to mononuclear cells. If atypical forms or strong nuclear atypia is noted, a secondary sarcomatous malignancy is almost always present. Secondary changes may be present like osteoid deposits, foci of fibrosis, collections of foamy cells or cystic degeneration. Secondary aneurysmal bone cyst formation is present in 6.5% of the cases. Mostly this is restricted to younger patients (median of 14 years). In the 2013 WHO classification, grading of histopathological features of GCTB is not considered predictive for clinical behaviour including risk for recurrent or metastatic disease. Originally, giant cell tumors of bone were histologically graded into 3 grades according to Jaffe (1940) or into 4 grades (Netherlands Committee on Bone Tumours).

Evolution

Non-treatment always leads to destruction of cortical bone, to soft tissue invasion and finally to ulceration of the skin. Local recurrences can occur following proper treatment, mostly indicating less radical initial resection.

Prognosis

Good, despite of recurrences and pulmonary metastases. In general much is depending on the surgical technique and expertise in combination with the histological grade of this tumour. Although pulmonary metastases may occur in rare cases, angiovascular invasion does not have any significant influence on its prognosis. The mortality rate due to giant cell tumour is about 4%.

Genetics

A specific driver mutation in the histone 3.3 gene H3F3A (p.Gly34) was recently identified in approximately 92% of giant cell tumours of bone. H3F3A mutation detection can be used as a diagnostic tool for the distinction of giant cell tumor of bone from other giant cell-containing tumors. A subset of the mutations can be easily detected using a G34W mutation specific antibody.

Cytogenetics

No recurrent chromosomal structural or numeric aberrations of importance have been detected yet.

When confronted with a rearrangement, especially concerning 16q22 or 17p3, an associated aneurysmal bone cyst should be excluded.

Cytogenetics Morphological

The most frequent chromosomal anomaly is telomeric association. Comparing telomere length of giant cell tumours to this of leukocytes of the same patient, a reduction has been demonstrated. Most
commonly affected telomeres are 11p, 13p, 14p, 15p, 19q, 20q and 21p.

References


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