Bone: Giant cell tumour

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Identity

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.
Alias
Osteoclastoma; Giant cell tumour of bone

**Clinics and pathology**

**Disease**
Locally destructive, benign and 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 hyperpara-thyreoism should be considered, which may look histologically identical. Although defined as a benign lesion, adjacent soft tissue invasion, angio-vascular invasion and pulmonary metastases (1%) may occur.

**Phenotype / cell stem origin**
Not yet determined.

**Embryonic origin**
Mesoderm.

**Etiology**
The exact origin is still unknown, but data obtained from ultrastructural analyses and cell cultures, 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, patholog-ical 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.

**Pathology**
A mixture of four components can be distinguished:
- spindled-shaped and rounded mononuclear cells,
- osteoclastic-type giant cells and small blood vessels. The spindle-shaped mononuclear cells are regarded as neoplastic on results from electron microscopy and cell cultures. The origin of this cell type is still unknown, but it 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) and low histological grade giant cell tumours. As mentioned earlier, this tumour can histological be graded into 3 grades according to Jaffe (1940) or into 4 grades (Netherlands Committee on Bone Tumours). According to the latter grading system, grade 1 en 2 are considered as being benign, grade 3 as borderline malignant and grade 4 as malignant tumours. Grade 4 tumours show histological overlap with malignant fibrous hystiocytoma of bone. Although many authors are sceptic about grading giant cell tumours, this shows a good correlation with clinical outcome.

In that time no adjuvant chirurgical treatment, like cryosurgery or phenol additive was used. Now-adays the usefulness of grading in relation to recurrences is highly influenced by more effective surgical adjuvant techniques. According to literature still 20% of the giant cell tumours will recur, despite of these new surgical techniques. Together with the risk of developing pulmonal metastases, grading of giant cell tumours is in our view still valuable. In this grading system mitosis, pleiomorphism of the spindled mononuclear cells, giant cells and the individual size of the giant cells will be taken into account. Most important is the mitotic activity. When mitoses are occasional observed the risk of developing recurrences and pulmonal metastases is negligible. If more than 1 mitosis is present per 1 high power field, patients are significantly at risk for developing recidives and pulmonal metastases (23%). Grade 2 tumours do have the highest prevalency (grade 1: 4%, grade 2: 88%, grade 3: 5%, grade 4: 3%).
Mixture of three cellular components composes 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.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Ground pattern cells</th>
<th>Giant Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>• No atypia</td>
<td>• Numerous</td>
</tr>
<tr>
<td></td>
<td>• Rare mitotic figure</td>
<td>• Large sized</td>
</tr>
<tr>
<td>II</td>
<td>• Little polymorphism</td>
<td>• Less numerous</td>
</tr>
<tr>
<td></td>
<td>• Regular mitotic figures, but less than 1 mitosis / hpf (250 μm)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>• Atypia</td>
<td>• Less numerous</td>
</tr>
<tr>
<td></td>
<td>• More than 1 mitosis / hpf (250 μm)</td>
<td>• Smaller sized</td>
</tr>
<tr>
<td>IV</td>
<td>• Sarcomatous dedifferentiation</td>
<td>• Small amount</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Small sized</td>
</tr>
</tbody>
</table>

Table: Grading of giant cell tumours according to the Netherlands Committee on Bone Tumors.

**Treatment**
Surgical intervention is the only treatment of choice. Mostly a curettage followed by local adjuvant cryosurgery or phenol instillation is sufficient to eradicate this lesion and to save the joint. The use of polymethylmethacrylate for filling the cavity after curettage additively decreases the percentage of recurrences. An added advantage of using cement is that recurrences are detected sooner. Sometimes ‘en bloc’ resection is needed to be curative. Pulmonal metastases are treated by local excision.

**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%.

**Cytogenetics**
Note
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


Reid R, Banerjee SS, Sciot R. Giant cell tumour Pathology and genetics of tumours of soft tissue and bone (WHO 2002)


This article should be referenced as such: