Chondrosarcoma: An overview

Ali Najefi
ST6
BTU Teaching 19/04/2018

Introduction

- Definitions
- Epidemiology
- Types
- Radiology
- Histology
- Treatment
- Prognosis
- Future directions
What is a Chondrosarcoma?

- Chondrosarcoma is a malignant tumor of bone that is characterized by the production of cartilage matrix by tumor cells
- Diverse histopathology and clinical behavior
- Categorised together in the WHO classification as atypical cartilaginous tumour/chondrosarcoma grade I.

Table 1: Classification of malignant primary bone tumours (adapted from WHO classification [14])

<table>
<thead>
<tr>
<th>Chondrogenic tumours</th>
<th>1. Atypical cartilaginous tumour/chondrosarcoma (grade I)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2. Chondrosarcoma (grades II/III)</td>
</tr>
<tr>
<td></td>
<td>3. Dedifferentiated chondrosarcoma</td>
</tr>
<tr>
<td></td>
<td>4. Mesenchymal chondrosarcoma</td>
</tr>
<tr>
<td></td>
<td>5. Clear cell chondrosarcoma</td>
</tr>
<tr>
<td>Osteogenic tumours</td>
<td>1. Low-grade central osteosarcoma</td>
</tr>
<tr>
<td></td>
<td>2. Conventional (high-grade) osteosarcoma (chondroblastic fibroblastic osteoblastic)</td>
</tr>
<tr>
<td></td>
<td>3. Telangiectatic osteosarcoma</td>
</tr>
<tr>
<td></td>
<td>4. Small cell osteosarcoma</td>
</tr>
<tr>
<td></td>
<td>5. Secondary osteosarcoma</td>
</tr>
<tr>
<td></td>
<td>6. Parosteal osteosarcoma</td>
</tr>
<tr>
<td></td>
<td>7. Periosteal osteosarcoma</td>
</tr>
<tr>
<td></td>
<td>8. High-grade surface osteosarcoma</td>
</tr>
<tr>
<td>Notochordal tumours</td>
<td>Chordoma</td>
</tr>
<tr>
<td>Vascular tumours</td>
<td>1. Epithelioid haemangioendothelioma</td>
</tr>
<tr>
<td></td>
<td>2. Angiosarcoma</td>
</tr>
<tr>
<td>Other malignant mesenchymal tumours</td>
<td>Fibrosarcoma, Liposarcoma etc.</td>
</tr>
<tr>
<td>Miscellaneous tumours</td>
<td>1. Ewing sarcoma</td>
</tr>
<tr>
<td></td>
<td>2. Adenaltihoma</td>
</tr>
<tr>
<td></td>
<td>3. Undifferentiated high-grade pleomorphic sarcoma of bone</td>
</tr>
</tbody>
</table>
WHO classification

CARTILAGE TUMOURS
Osteochondroma 9210/0*
Chondroma 9220/0
Enchondroma 9220/0
Periosteal chondroma 9221/0
Multiple chondromatosis 9220/1
Chondroblastoma 9230/0
Chondromyxoid fibroma 9241/0
Chondrosarcoma 9220/3
  Central, primary, and secondary 9220/3
  Peripheral 9221/3
  Dedifferentiated 9243/3
  Mesenchymal 9240/3
  Clear cell 9242/3

Epidemiology

- 9% of all bone tumours
- UK age standardised rates report 0.19/100,000 population
- 2nd most common primary malignancy of bone (non-haematological)
- Primary and Secondary
  - Primary peaks around 30-60 years of age
  - Secondary between 25-45 years of age
- Slightly higher incidence in males
- No Race Predilection
- 100-120 new cases per year in the UK
Location - Primary

- Pelvis
- Proximal Femur
- Proximal Humerus

- Can occur in ribs and scapula

- Although rare in hand, most common primary malignancy of bone here.

Location – Secondary (Peripheral)

Secondary lesions occur at sites of benign cartilage lesions

- Multiple enchondromas
  - Ollier disease – 25% by age 40
  - Maffucci - higher
- Multiple Hereditary Exostoses
  - Around 5% lifetime risk
  - 1% risk for solitary enchondromas (Referral bias – true incidence unknown)
Secondary Chondrosarcoma

Associated with
• Enchondromas
• Osteochondromas
• Synovial chondromatosis
• Chondromyxoid fibroma
• Periosteal chondroma
• Chondroblastoma
• Previous radiation treatment
• Fibrous dysplasia
Types of Primary Chondrosarcoma

- Conventional (90%)
  - Central or peripheral
- Clear Cell
- Mesenchymal
- Dedifferentiated

Clear Cell CS

- Slow growing
- Epiphyseal (especially proximal femur)
- Locally recurrent tumour
- It is often confused with chondroblastoma or GCT.
- Metastases occur only after multiple local recurrences.
- Primary treatment is wide excision.
- Systemic therapy is not required.
Mesenchymal CS

- High grade
- Predilection for flat bones; long tubular bones are rarely affected.
- It tends to occur in younger individuals and has high rates of metastatic potential.
- The 10-year survival rate is 28%.
- This entity responds favorably to radiotherapy.
- Treatment is surgical removal combined with adjuvant chemotherapy.
- Radiotherapy is recommended if the tumor cannot be completely removed.

Dedifferentiated CS

- Approximately 10% of chondrosarcomas may be dedifferentiated into a fibrosarcoma or osteosarcoma.
- This occurs in older individuals and is highly fatal.
- Surgical treatment is wide excision
- Adjuvant therapy is warranted.
Clinical Features

- Increasing Pain
- Palpable mass
- Slow growing – symptoms may be present for many years
- Pain without pathological fracture – differentiates enchondroma and chondrosarcoma

Radiographic Appearance

- Margin/pattern of bone destruction
- Presence/type of matrix mineralization
- Cortical response
- Soft-tissue mass
- Presence/type of periosteal reaction

- The site of the lesion and age of the patient must be considered
Radiographic appearance

- Arises in the medullary cavity
- Irregular matrix calcification.
- The pattern of calcification has been described as “punctate,” “popcorn,” or “comma shaped.”
- More aggressive appearance than enchondroma
  - Bone destruction,
  - Cortical erosions,
  - Periosteal reaction
  - Soft-tissue mass.

Radiographic appearance

- CT can be helpful to show endosteal erosions
- MRI shows soft tissue component
- Size of the cartilaginous cap of an osteochondroma with CT or MRI
  - >2 cm in a skeletally mature patient
Enchondroma

Juxtacortical chondroma

Fig. 11.7a-c. Juxtacortical chondroma: Radiographs (a,b) and computed tomography (c) show a saucer-like juxtacortical lesion separated by a thick sclerotic rim from the medullary cavity.
Osteochondroma

Chondromyxoid fibroma
Grade 2 Chondrosarcoma

- Plain film demonstrates a large, lobulated, ill-defined lesion centered in the distal femoral metaphysis. There is endosteal scalloping and periosteal thickening. Central supply and "ring and arc" calcifications are apparent and are typical of cartilaginous matrix. Small radiolucent areas are seen at the periphery of the lesion.

Chondrosarcoma
Chondrosarcoma
Dedifferentiated CS

Fig. 10.22. Dedifferentiated chondrosarcoma. Radiograph shows a lytic lesion with a dense chondrogenic calcification centrally in the medullary cavity of the distal diaphyseal tibiae and an adjacent ill-defined lytic lesion with a pathologic fracture in the cortex.
Histology

- Grade I, II, or III.
- The aggressiveness predicted by histologic grade.
- Grading system is based on three parameters
  - Cellularity
  - Degree of nuclear atypia
  - Mitotic activity.

Enneking Staging

Table 2: Enneking staging.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Grade</th>
<th>Tumour</th>
<th>Metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>G1 low grade</td>
<td>T1 cortex intact (intra-compartmental)</td>
<td>M0</td>
</tr>
<tr>
<td>IB</td>
<td>G1 low grade</td>
<td>T2 cortex breached with soft tissue extension</td>
<td>M0</td>
</tr>
<tr>
<td>IIA</td>
<td>G2 high grade</td>
<td>T1 cortex intact</td>
<td>M0</td>
</tr>
<tr>
<td>IIB</td>
<td>G2 high grade</td>
<td>T2 cortex breached with soft tissue extension</td>
<td>M0</td>
</tr>
<tr>
<td>IIIA</td>
<td>G1 or G2</td>
<td>T1</td>
<td>M1</td>
</tr>
<tr>
<td>IIIB</td>
<td>G1 or G2</td>
<td>T2</td>
<td>M1</td>
</tr>
</tbody>
</table>
Histology Grade 1

- Very similar to enchondroma.
- Cellularity is higher, and there is mild cellular pleomorphism.
- The nuclei are small but often show open chromatin pattern and small nucleoli.
- Binucleated cells are frequent.
- Mitoses are very rare.

Grade 1 chondrosarcomas are locally aggressive and prone to recurrences, but usually do not metastasize.
Histology Grade 2

- The cellularity is higher than in Grade 1 tumors.
- Characteristic findings are moderate cellular pleomorphism, plump nuclei, frequent bi-nucleated cells, and occasional bizarre cells.
- Mitoses are rare.
- Foci of myxoid change may be seen.

Unlike Grade 1 tumors, about 10% to 15% of Grade 2 chondrosarcomas produce metastases.

Histology Grade 3

- Characteristic findings are
  - high cellularity
  - Marked cellular pleomorphism
  - High N/C ratio
  - Many bizarre cells
  - Frequent mitoses

These are high grade tumors with significant metastatic potential.
Management

Low-grade

• Extended curettage with the use of intraoperative adjuvant treatments (phenol, cement, cryotherapy).
• Low-grade peripheral chondrosarcomas (arising from osteochondromas) should be surgically excised, aiming to excise the tumour with a covering of normal tissue over it.
• Those with soft-tissue extension should be treated similar to high-grade lesions.
High Grade

- Wide or radical resection or amputation.
- Endoprosthesis
- The local recurrence rate after intraoperative tumor contamination is high.
- Pulmonary metastases can be treated with surgical resection if possible.

Chemotherapy

- No role in the treatment of conventional chondrosarcoma
- Frequently used for treatment of dedifferentiated and mesenchymal chondrosarcomas.
- Recent evidence suggests that mesenchymal chondrosarcoma may be responsive to chemotherapy and may be considered for adjuvant or neoadjuvant therapy
Radiotherapy

- Limited role
- Unresectable or inoperable
- Inadequate margins
- Axial skeleton and pelvic or shoulder girdle, or both, can be controlled by radiation therapy.
- Chondrosarcomas of the facial bones and skull are successfully treated with combination of radiotherapy.
- Mesenchymal Chondrosarcoma

Prognosis

- Depends mostly on the size, grade, and location of the lesion.
- If incomplete resection (usually because of its size or location), local recurrence is likely.
- Low-grade lesions have a greater than 90% 10-year survival rate.
- High-grade conventional chondrosarcoma are reported to have a 20% to 40% 10-year survival rate.
- The 5-year survival rate is less than 15% for patients with dedifferentiated chondrosarcoma, with most deaths occurring in the first 2 years.
Future directions

Future directions

• The identification of IDH1 and IDH2 mutations in chondrosarcoma has led these to be targeted with new, specific agents, although the effectiveness and future role of such agents are unclear.
  • *Amary MF, Bacsí K, Maggiani F, et al: IDH1 and IDH2 mutations are frequent events in central chondrosarcoma and central and periosteal chondromas but not in other mesenchymal tumours. J Pathol 224:334-343, 2011*
  • Identification of Mesenchymal chondrosarcoma is supported by identification of an HEY1- NCOA2 fusion, which can occur in both bone and soft tissue. Adjuvant chemotherapy may provide a survival advantage.

Summary

• Older age group
• Central or peripheral
• Multiple types
• Can be difficult to distinguish from benign cartilage tumours
• Matrix calcification, aggressive appearance
• Surgery is mainstay of treatment
• Mesenchymal chondrosarcoma responds to CT/RT
Thank You

- Campbells 13th edition, 2017
- Sarcomas of the Soft Tissue and Bone, Martin M. Malawer, Lee J. Helman, and Brian O’Sullivan, 2008
- Imaging of Bone tumours and tumour like lesions, Baerth, Knaut. Springer.