Conventional Chondrosarcoma

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General Information

- Malignant mesenchymal tumor of cartilaginous differentiation.
- Conventional Chondrosarcoma is the most common type of chondrosarcoma (malignant cartilage tumor)
- Neoplastic cells form **hyaline type cartilage or chondroid type tissue** (Chondroid Matrix) but not osteoid
- If lesion arises de novo, it is a primary chondrosarcoma
- If superimposed on a preexisting benign neoplasm, it is considered a secondary chondrosarcoma
- Central chondrosarcomas arise from an intramedullary location. They may grow, destroy the cortex and form a soft tissue component.
- Peripheral chondrosarcomas extend outward from the cortex of the bone and can invade the medullary cavity. Peripheral chondrosarcomas most commonly arise from preexisting osteochondromas.
- Juxtacortical chondrosarcomas arise from the inner layer of the periosteum on the surface of the bone. It is technically considered a peripheral chondrosarcoma.
Chondrosarcoma

- Heterogeneous group of tumors with varying biological behavior depending on grade, size and location
  - Cartilage tumors can have similar histology and behave differently depending on location. For instance a histologically benign appearing cartilage tumor in the pelvis will behave aggressively as a low grade chondrosarcoma. Likewise, a histologically more aggressive hypercellular cartilage tumor localized in a phalanx of a digit may behave in an indolent, non aggressive or benign manner.

- There are low (grade I), intermediate (grade II) and high grade (grade III) types of conventional chondrosarcoma.

- Low grade lesions are slow growing and rarely metastasize. Low grade chondrosarcomas can be difficult to differentiate from benign tumors histologically. Clinical features and radiographic studies are important to help differentiate. Low grade chondrosarcomas can dedifferentiate into high grade sarcomas and higher grade chondrosarcomas over a prolonged period of time. These higher grade sarcomas readily metastasize and are associated with a poor prognosis.

- High grade lesions grow aggressively locally and metastasize readily. They are more easily differentiated from low grade and benign cartilage tumors.

- Chondrosarcomas most commonly arise from bone but can also arise from soft tissue. They are the most common bone sarcoma in adults and the second most common bone sarcoma overall after osteosarcoma. Most malignant cartilage tumors are low to intermediate grade tumors.
Classification of Cartilage Tumors

- **Benign**
  - Enchondroma
  - Osteochondroma
  - Chondroblastoma
  - Chondromyxofibroma

- **Malignant**
  - Conventional Intramedullary
    - Grade 1 (Low Grade)
    - Grade 2 (Intermediate Grade)
    - Grade 3 (High Grade)
  - Dedifferentiated
  - Clear Cell
  - Mesenchymal
    - Intramedullary
    - Extraskeletal
  - Secondary
    - Osteochondroma or Enchondroma
  - Periosteal/Juxtacortical
  - Extraskeletal (Soft Tissue)
Classification

Chondrosarcoma

Primary (90%)
- Arising de novo in normal bone
  - Central Intramedullary (99%)
    - Conventional (85-90%)
      - Grade 1 (30%)
      - Grade 2 (40%)
      - Grade 3 (30%)
    - Dedifferentiated (8%)
    - Clear Cell (4%)
    - Mesenchymal (1%)
  - Peripheral (1%)
    - Periosteal C.S

Secondary (10%)
- Arising from pre existing conditions of bone
  - Enchondroma
  - Osteochondroma
  - Ollier’s, Maffucci’s
  - Fibrous Dysplasia
  - Paget’s
  - Chondroblastoma
  - Radiation induced
  - Mesenchymal (1%)
Clinical Presentation
Conventional Chondrosarcoma

- **Signs/Symptoms:**
  - Pain, with or without mass
  - Pathological fracture is rare

- **Prevalence:**
  - 2 to 1 male predilection
  - Most common bone sarcoma in adult population
  - Second most common primary sarcoma of bone
  - 20% of all primary malignant bone sarcomas

- **Age:**
  - All ages but peak incidence between 50-70 years of age
  - Uncommon before the age of 40
  - Primary chondrosarcoma most common between fifth and seventh decade
  - Secondary chondrosarcoma most common between fourth and fifth decade

- **Sites:**
  - Most common sites: Proximal femur, Distal femur, Proximal Humerus, Pelvis, Scapula, Ribs
  - Spine and craniofacial bones are rare sites
Radiographic Presentation

- Conventional chondrosarcomas primarily occur in the **metaphysis** or **diaphysis**
  - Rarely, they arise in the **epiphysis**
- Peripheral chondrosarcomas form a mass that extends from surface of bone
- Calcifications have a distinctive “Ring and Arc”-like pattern
  - Due to lobular growth of cartilage and enchondral ossification around the perimeter
- Low-grade chondrosarcomas
  - Uniformly calcified
  - Well-defined margins
- High-grade chondrosarcomas
  - Large non-calcified areas
  - Irregular, ill-defined margins
  - Often extend into soft tissues

[Image of an X-ray with an arrow pointing to calcifications]
Conventional Intramedullary Chondrosarcoma

Radiographic Presentation

- May be Geographic to Permeative depending on Grade
- Deep endosteal scalloping
- Cortical thickening/Periosteal reaction
- Cortical destruction and soft tissue mass variable
  - Benign cartilage tumors never have a soft tissue component
- Chondroid matrix (78% by x-ray; 94% by CT)
  - Calcifications in a ring and arc-like manner
  - Stippled calcifications
  - CT is useful for evaluating subtle calcification
- MRI – similar to muscle in T1W
  - Lobulated high intensity T2W images
  - Matrix Calcification – Low intensity
  - Best test for evaluating intramedullary extent and soft tissue extension
Conventional Intramedullary Chondrosarcoma

Radiological Features of Malignancy

- Bone contour in the affected area may be expanded
- Cortical thickening
- Endosteal scalloping
- New areas of lysis adjacent to calcified areas
- Cortical destruction and soft tissue extension in higher grade lesions; extension into soft tissues is definitive
Plain X-ray: Chondrosarcoma of Proximal Femur

Permeative Lesion greater than 5cm
Deep Endosteal Scalloping
Cortical Thickening
Calcifications
Plain X-ray: Chondrosarcoma of Femur

- Permeative lesion greater than 5 cm
- Calcifications in lesion
- Deep endosteal scalloping
Plain X-ray: Chondrosarcoma of Proximal Femur

Permeative Lesion

Calcifications

Calcified Area

Lysis next to Well Calcified Area

Deep endosteal Erosion

Cortical Destruction

Periosteal Reaction

Cortical Thickening
Radiologic Differentiation of Chondrosarcomatous Lesions

- Aggressive chondroid lesion with soft tissue mass
  - High grade conventional chondrosarcoma
  - Dedifferentiated chondrosarcoma
  - Mesenchymal chondrosarcoma
- Large fluid component bone or soft tissue (Myxoid chondrosarcoma)
- Change in appearance or foci of more aggressive nature (Dedifferentiated chondrosarcoma)
  - Lysis or cortical destruction adjacent to well calcified area
Diagnostic Dilemma: Long Bone Enchondroma vs. Chondrosarcoma

- **Enchondroma**
  - Common in hand/foot
  - Common in long bones (1.7% femora)
  - Rare in axial skeleton
  - Rare in pelvis
  - Never has an associated soft tissue component

- **Chondrosarcoma**
  - Common in axial skeleton
  - Common in long bones
  - Rare in hand/foot
  - May or may not have an associated soft tissue mass
  - Low grade chondrosarcomas do not often have an associated soft tissue mass and are most difficult to differentiate from an enchondroma
**Clinicoradiological Aspects:**

- **Age** <50; Pain not attributable to lesion
- **Size:**
  - <5cm (CT/MRI)
- **Bone Scan** =/< ASIS* 79%
- **Majority in diaphysis**
- **Endosteal scalloping depth** <2/3 cortex (90-95%)
- **No cortical thickening**
- **No periosteal reaction**
- **NO cortical destruction**
- **NO soft tissue mass**
- **MRI peripheral enhancement?**
  - *AIC = Anterior Iliac Crest*
Long Bone Chondrosarcoma

- **Clinicoradiological Aspects:**
  - Age > 50; Pain attributable to lesion
  - Size:
    - > 5 cm (CT/MRI)
  - Bone Scan =/> ASIS 82%
  - Endosteal scalloping depth > 2/3 cortex (75-90%)
  - Cortical Thickening (47%)
  - Periosteal Reaction (51%)
  - Soft Tissue Mass (Variable; May not have a soft tissue mass)
  - Epiphyseal Extension (majority metaphysis)
  - MRI peripheral and septal enhancement?
Grade I Chondrosarcoma

- Calcifications in ring and arc-like manner; stippled calcifications
- Mild bony expansion
- >5cm
- Endosteal scalloping > 2/3 cortical thickness
Grade I Chondrosarcoma

Subtle Cortical Thickening and Periosteal Reaction

Ring and Arc Calcifications
Grade I Chondrosarcoma
T1 Weighted MRI

Periosteal Reaction
Cortical Thickening
MRI Low Grade Chondrosarcoma
Endosteal Scalloping

Endosteal Scalloping >2/3 Cortical Thickness
CT Scan: Grade I Chondrosarcoma

Stippled Calcifications
Bony Expansion
Cortical Thickening
CT Scan Axial Section
Grade I Chondrosarcoma

- Subtle Cortical Thickening
- Calcifications
CT Scan: Grade I Chondrosarcoma
Plain X-Ray/Bone Scan: Grade I Chondrosarcoma of Proximal Humerus

X-rays look identical to Enchondroma

Uptake Hotter than ASIS
Plain X-Ray: Grade I Chondrosarcoma of Femoral Neck

Lesion with Epiphyseal Extension

Sclerosis

Calcifications
MRI: Grade I Chondrosarcoma of Proximal Femur

T1 Weighted Image

T2 Weighted Image
CT Scan: Grade I Chondrosarcoma of Femoral Neck
Plain X-Ray: Grade I Chondrosarcoma of Metacarpal of Hand

- Stippled Calcifications
- Cortex Destroyed
- Soft Tissue Component
MRI: Grade I Chondrosarcoma of Hand

- High Signal on T2
- Intermediate Signal
- Soft Tissue Mass

T1 Weighted Image

T2 Weighted image
Bone Scan: Chondrosarcoma of Metacarpal
Gross Specimen: Chondrosarcoma of Metacarpal
Low Grade Chondrosarcoma

Cortical Erosion

Lesion > 5cm

Calcifications
Grade I Chondrosarcoma of Proximal Humerus
Plain X-rays: Grade II Chondrosarcoma of Acetabulum
CT Scan: Grade II Chondrosarcoma of Acetabulum

- Lytic Lesion
- Surrounding Sclerosis
- Subtle Intrallesional Calcification
- Pelvic Location Places Lesion in Category of Chondrosarcoma
MRI: Grade II Chondrosarcoma of Acetabulum
High Signal on T2 may be misinterpreted as a cyst
Plain X-rays: Grade II Chondrosarcoma of Proximal Humerus

Calcifications

Subtle Periosteal Reaction  Soft Tissue Component  Intrallesional Calcifications
Plain X-ray: Grade II Chondrosarcoma of Proximal Humerus

- Permeative Lesion
- Periosteal Reaction
- Calcifications
CT Scan: Grade II Chondrosarcoma of Proximal Humerus

- Soft Tissue Component
- Cortical Thickening
- Tumor in Medullary Canal
MRI: Grade II Chondrosarcoma of Proximal Humerus

Soft Tissue Component Indicative of Chondrosarcoma

T1 Weighted Image
Cartilage Grows in Lobular Manner

T2 Weighted Image
Cartilage is High signal on T2
Plain X-Ray and Bone Scan
Grade II Chondrosarcoma of Proximal Femur

- Permeative Lesion >5cm
- Hotter than ASIS on bone Scan
- Deep Endosteal Scalloping
- Cortical Thickening
- Areas of Lysis
MRI: grade II Chondrosarcoma of Proximal Femur
MRI: Grade II Chondrosarcoma of Proximal Femur

Soft Tissue Component not detected on X-ray
Plain Xray: Grade II Chondrosarcoma of Proximal Femur
Plain X-ray: Grade III Conventional Chondrosarcoma of Pelvis

Lytic Lesion of Pelvis

Cortical Destruction
Secondary Chondrosarcoma

- Secondary Chondrosarcomas arise from a pre-existing lesion such as an osteochondroma or enchondroma
- Most commonly secondary chondrosarcomas arise from osteochondromas
- Most secondary chondrosarcomas are low grade and cured by wide excision
- Secondary chondrosarcomas can also dedifferentiate into high grade spindle cell sarcomas or become higher grade lesions if left untreated for prolonged periods of time
- Secondary chondrosarcomas are more likely to occur in setting of multiple hereditary exostoses and enchondromatosis. Osteochondromas that arise from the scapula, ribs and pelvis and proximal femur are the most likely to undergo malignant change or dedifferentiate.
Osteochondroma vs. Secondary Chondrosarcoma

- The cartilaginous cap deserves the most attention when differentiating a benign osteochondroma from a secondary chondrosarcoma that arose from a pre-existing osteochondroma.

- In adults, the cartilaginous cap regresses and becomes thin due to enchondral ossification of the majority of the cap.

- Malignant transformation is suggested by:
  - Cartilaginous cap thickness greater than 2cm
  - Cortical destruction
  - Backgrowth of the cartilaginous cap into the stalk or medullary canal
  - Lysis of calcifications in cap
Osteochondroma: Cartilage Cap

- **Radiographs**
  - Chondroid Calcification in cap
  - Increasing destruction or change in appearance is worrisome for malignancy

- **MRI**: Best test for evaluating thickness of cap and surrounding bursa
  - Intermediate T1W Images
  - High Intensity T2W Images because of fluid content
Osteochondroma: Cartilage Cap

■ CT
  ■ The cap will appear as soft tissue with calcification
  ■ Peripheral stippled calcifications suggest malignancy or lysis adjacent to well calcified area
  ■ Can be difficult to distinguish from muscle

■ Cap thickness
  ■ Benign < 1.5 cm (0.1 – 3.0 cm; Avg. 0.6 – 0.9 cm)
  ■ Malignant > 1.5 cm (1.5 – 12 cm; Ave. 6 cm)
Plain X-ray: Secondary Chondrosarcoma of Pelvis

Calcifications
Secondary Chondrosarcoma of Pelvis

- Stalk of Osteochondroma
- Thick Cap
- Peripheral Calcifications
MRI and CT: Secondary Chondrosarcoma

Thick Cartilage Cap
Specimen Radiograph: Secondary Chondrosarcoma of Pelvis

- Stalk of Osteochondroma
- Thick Cartilage Cap
MRI: Secondary Chondrosarcoma of Proximal Femur: Thick Cartilage Cap (>2cm)
CT and MRI: Secondary Chondrosarcoma of Proximal Femur

Base of Osteochondroma
Gross Pathology

- Likely to have the consistency of hyaline cartilage
  - Translucent, blue-gray to white
- Lobular pattern is usually seen
- Yellow, chalky deposits of calcium
- Cystic areas with mucoid material frequent
- Hemorrhagic necrosis sometimes found especially Grade III tumors
- May have soft tissue component

![Tibia with Gross Pathology Features](image)
Gross Specimen: Chondrosarcoma of Acetabulum
Gross Specimen: Chondrosarcoma of Proximal Humerus
Entrapment of Trabeculae by Chondrosarcoma

Chondrosarcoma surrounds the trabeculae

This is a feature of malignancy
Microscopic Pathology

- Broad spectrum of microscopic appearances
- General appearance
  - Irregularly shaped lobules of cartilage
    - Vary in size and abut one another
    - May be separated by fibrous bands, cleft-like spaces, or narrow bands of bone
    - Cellularity may be greater at the edges of the lobules
  - Chondrocytes often arranged in clusters
    - Normal, slightly enlarged, or overtly enlarged nuclei
    - Mononuclear or multinucleated
    - Binucleated, trinucleated cells common
    - Mitotic figures present
  - Distribution of mitotic figures is highly uneven
  - Matrix varies from mature hyaline cartilage to myxoid stroma
  - Entrapment of pre-existing trabeculae by chondrosarcoma is important for distinguishing low grade chondrosarcoma from enchondroma (The chondrosarcoma surrounds pre-existing trabeculae)
Microscopic Pathology

- **Microscopic Grading**
  - **3-Grade system**
    - **Grade 1**
      - Chondrocytes with small, dense nuclei
      - Few multinucleated cells
      - Chondroid stroma
      - Sparse myxoid area
    - **Grade 2**
      - Less matrix
      - More cellular
      - Especially prominent at periphery of lobules
      - Necrosis
        - Small, microscopic foci to completely necrotic lobules
    - **Grade 3**
      - Greater cellularity and nuclear pleomorphism
      - Chondroid matrix sparse
      - Intercellular material myxoid
      - Neoplastic chondrocytes arranged in cords and clumps
      - Individual cells are stellate or grossly irregular
      - Foci of necrosis are frequently extensive
  - Individual lesions may have areas of different grades
Conventional Chondrosarcoma

Grade I (Low Grade Chondrosarcoma)

- Similar microscopic features to Enchondroma
- Require clinical and radiographic data to support diagnosis
- Hypercellularity, plump cells, prominent nucleoli, nuclear pleomorphism
- Mitotic figures not typically present
- Bone Entrapment of pre-existing trabeculae is important
- More than occasional double nuclei
- Continuous growth with infiltrative growth pattern
- Rare metastatic spread
Microscopic Pathology: Grade I Chondrosarcoma
Microscopic Pathology: Grade I Chondrosarcoma

Entrapment of Pre-existing Trabeculae of Bone
Microscopic Pathology: Grade I Chondrosarcoma
Conventional Chondrosarcoma

**Grade II (Intermediate Grade Chondrosarcoma)**

- Increased cellularity evenly distributed in a cartilaginous matrix
- Plump cartilage cells with enlarged nuclei and distinct nucleoli, greater nuclear pleomorphism
- Frequent binucleated, trinucleated cells
- Occasional mitotic figures
- Foci of Myxoid change
- Greater potential of local recurrence
- Metastatic rate 10-15%
Grade II Chondrosarcoma
Microscopic Pathology: Grade II Chondrosarcoma

Hypercellular
Cells are crowded
Binucleated cells common
Microscopic Pathology: Grade II Chondrosarcoma
Microscopic Pathology: Grade II Chondrosarcoma

Trinucleated Cells

Binucleated Cells
Microscopic Pathology: Grade II Chondrosarcoma
Microscopic Pathology: Grade II
Chondrosarcoma and Bony Entrapment

Bony Trabeculae
**Conventional Chondrosarcoma**

**Grade III (High Grade Chondrosarcoma)**

- Higher cellularity and greater degree of cellular pleomorphism
- Hyaline cartilage matrix is sparse
- Marked nuclear pleomorphism
- Cells may have stellate/spindle appearance with myxoid chondroid matrix
- May have myxoid areas
- Prominent nuclear atypia
- Presence of mitotic figures
- Locally highly aggressive
- Metastatic rate over 50%
Grade III Chondrosarcoma of Pelvis
Microscopic Pathology: Grade III Chondrosarcoma
Microscopic Pathology: Grade III Chondrosarcoma

Hypercellular

Chondroid Area
Microscopic Pathology: Grade III Chondrosarcoma

- Spindle/Stellate Appearance to Cells in Areas
- Mitotic Figure
- Cell in Lacunae
- Signet Ring Configuration
- Pleomorphism
Microscopic Pathology: Grade III Chondrosarcoma
Microscopic Pathology: Grade III Chondrosarcoma
Microscopic Pathology: Grade III Chondrosarcoma
Differential Diagnosis

- Grade I chondrosarcoma vs. enchondroma
- Chondroblastic osteosarcoma
The biological behavior is related to grade:

- **Grade I Chondrosarcoma** rarely metastasize and grow slowly. They may dedifferentiate to high grade sarcomas such as osteosarcoma, MFH, and fibrosarcoma.

- **Grade II Chondrosarcoma** grow locally in an aggressive manner. They metastasize in up to 33% of cases. Most commonly metastasize to the lungs.

- **Grade III Chondrosarcoma** grow locally in an aggressive manner and metastasize in up to 70% of cases. Most commonly metastasize to the lungs.
Treatment

Surgery is the main treatment. Most patients can be treated with a limb sparing resection although amputation may be needed for large tumors. Chemotherapy has little role in treatment of chondrosarcomas. It may be considered for grade III and dedifferentiated chondrosarcomas although its use is controversial. Radiation has little role in treatment of chondrosarcomas. It may be considered for treating microscopic disease following surgical removal of large tumors especially of the pelvis and spine when wide resection is not feasible.

- Wide/Radical En bloc Resection
  - Preferred treatment for Grade II and III Tumors

- Curettage can be considered for grade I chondrosarcomas
  - High recurrence rate for grade II and III chondrosarcomas
Amputation for a Large Chondrosarcoma of the Hand Metacarpal
Prognosis

- Depends on 2 major factors
  - Stage
  - Histological grade
- ~70% of grade 3 tumors metastasize even if a wide surgical margin is achieved
  - Metastases are uncommon in grade 1 tumors
  - 10-33% of grade 2 tumors metastasize
- Prognosis of grade 1 and 2 tumors governed by resectability and location
- Patients who present with metastatic disease have a dismal prognosis
- Local recurrences or metastases usually occur within 5 years
- Death rate is very high
  - Especially if tumor is in difficult location or grade 3