Malignant Cartilage Tumors
Chondrosarcoma

James C. Wittig, MD
Orthopedic Oncologist
Sarcoma Surgeon
www.TumorSurgery.org
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

**Grade**
- Grade 1 (30%)
- Grade 2 (40%)
- Grade 3 (30%)
- Dedifferentiated (8%)
- Clear Cell (4%)
- Mesenchymal (1%)
Conventional Chondrosarcoma
Conventional Chondrosarcoma

Clinical Presentation

• **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:**
  - Peak incidence between 50-70 years of age
  - Uncommon before the age of 40

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

- **Metaphysis or diaphysis**
  - Rarely, they arise in the epiphysis
- **Calcifications** have a distinctive “Ring and Arc”-like pattern
- **Low-grade chondrosarcomas**
  - Uniformly calcified
  - Well-defined margins
- **High-grade chondrosarcomas**
  - Large non-calcified areas
  - Irregular, ill-defined margins
  - Often extend into soft tissues
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
- Cortical Thickening
- Endosteal Erosion
Plain X-ray: Chondrosarcoma of Femur

- Permeative lesion greater than 5 cm
- Calcifications in lesion
- Deep endosteal scalloping
- Expansion
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
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
Long Bone 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:**
  - >5cm (CT/MRI)
- **Bone Scan:** => ASIS 82%
- **Endosteal scallopping 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?**
  - *AIC = Anterior Iliac Crest*
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 Metacarpal of Hand

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

- Intermediate Signal
- Soft Tissue Mass
- High Signal on T2
- T2 Weighted image
Bone Scan: Chondrosarcoma of Metacarpal
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 Intralesional 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
- Intralesional 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
- Tumor in Medullary Canal
- Cortical Thickening
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

T1 Image

T2 Image
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 arise from osteochondromas
  - Scapula, ribs, pelvis and proximal femur
- Most are low grade and cured by wide excision
- Dedifferentiation possible
Osteochondroma vs. Secondary Chondrosarcoma

- 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
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
Plain X-ray: Secondary Chondrosarcoma of Proximal Femur
MRI: Secondary Chondrosarcoma of Proximal Femur: Thick Cartilage Cap (>2cm)
CT and MRI: Secondary Chondrosarcoma of Proximal Femur

Base of Osteochondroma
Microscopic Pathology

- Broad spectrum of microscopic appearances that depends on Grade
- Entrapment of pre-existing trabeculae by chondrosarcoma is important for distinguishing low grade chondrosarcoma from enchondroma (The chondrosarcoma surrounds pre-existing trabeculae)
Microscopic Pathology

- Three Grade System
- I, II, III
- Cellularity, myxoid change, nuclear pleomorphism, multinucleated lacunae and mitoses increase as go from Grade I to III
Conventional Chondrosarcoma

Grade I (Low Grade Chondrosarcoma)

- Similar microscopic features to Enchondroma
- Require clinical and radiographic data to support diagnosis
- Relatively low cellularity
- Mitotic figures not typically present
- **Bone Entrapment of pre-existing trabeculae is important**
- More than occasional double nuclei
Entrapment of Trabeculae by Chondrosarcoma
Chondrosarcoma surrounds the trabeculae
This is a feature of malignancy
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
Grade II Chondrosarcoma
Microscopic Pathology: Grade II Chondrosarcoma

Hypercellular

Cells are crowded

Binucleated cells common
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
- Cells may have stellate/spindle appearance with myxoid chondroid matrix
- Presence of mitotic figures
Grade III Chondrosarcoma of Pelvis
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
Biological Behavior

• 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 Chondrosarcomas grow locally in an aggressive manner. They metastasize in up to 33% of cases. Most commonly metastasize to the lungs and
  • Grade III Chondrosarcomas 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 wide en bloc/radical resection although amputation may be needed for large tumors.
  - No Chemotherapy and No Radiation (except in rare circumstances of spine or large pelvic tumors)
Dedifferentiated Chondrosarcoma
General Information

- Dedifferentiated chondrosarcoma consists of a low grade malignant hyaline cartilage tumor associated with a high-grade nonchondroid spindle sarcoma. The two components are juxtaposed with abrupt clear demarcation line.
  - Sarcoma is most commonly an MFH, osteosarcoma or fibrosarcoma.
  - Extremely aggressive tumor with a high metastatic rate and dismal prognosis.
  - 50% arise from a secondary chondrosarcoma.
Clinical Presentation

• **Age:**
  • Most patients are older than 50

• **Sites:**
  • Pelvis, proximal femur, proximal humerus, distal femur, ribs
Radiographic Presentation

- Radiology emulates pathology: Biphasic Tumor
  - One region low grade chondrosarcoma
  - Second more aggressive area with bone destruction, lysis of calcification, soft tissue mass
  - Cortical permeation and a soft tissue mass in 70% of cases
- Characteristically abrupt transition between chondroid tumor and dedifferentiated, lytic component
Plain X-Ray: Dedifferentiated Chondrosarcoma of Proximal Tibia

- Low Grade Cartilaginous Area
- Heavily Calcified
- Aggressive Lytic Area (Dedifferentiated Sarcomatous Component)
- Cortical Destruction
- Soft Tissue Mass without Calcification
Plain X-ray: Dedifferentiated Chondrosarcoma of Humerus

- Low Grade Cartilage Component
- Stippled Calcifications
- Aggressive Dedifferentiated Sarcomatous Component
- Lysis, Cortical Destruction
- Soft Tissue Mass without Calcification
Plain X-ray/CT: Dedifferentiated Chondrosarcoma of Proximal Humerus

- Lytic, Dedifferentiated Component
- Low Grade Cartilage Component
- Heavily Calcified
- Soft Tissue Extension on CT
- Ring and Arc Calcifications
Plain X-ray: Dedifferentiated Chondrosarcoma of Proximal Femur

- Heavily Mineralized Low Grade Cartilage Component
- High Grade, Lytic Dedifferentiated Sarcoma Component
- Cortical Destruction
- Soft Tissue Extension
- Cortical Thickening
- Heavily Mineralized Low Grade Cartilage Component
CT Scan: Dedifferentiated Chondrosarcoma of Proximal Femur

Chondroid Calcification

Cortical Destruction and Soft Tissue Extension
MRI: Dedifferentiated Chondrosarcoma of Proximal Femur

Cortical Destruction and Soft Tissue Extension
Microscopic Pathology

• Chondrosarcoma component is often grade I (Low Grade Hyaline Type Cartilage)

• Dedifferentiated component: high grade spindle cell sarcoma

• Sharp and distinct junction. There are no dedifferentiated areas admixed in the middle of the cartilaginous areas
Microscopic Pathology: Dedifferentiated Chondrosarcoma

Low Grade Cartilage Component

High Grade Malignant Spindle Cell Component
Microscopic Pathology: Dedifferentiated Chondrosarcoma

Low Grade Cartilage Component

Dedifferentiated Component
Microscopic Pathology: Dedifferentiated Chondrosarcoma

Low Grade Cartilage Component

Dedifferentiated Component
Dedifferentiated Chondrosarcoma: High Power View of Dedifferentiated High Grade Pleomorphic Spindle Cell Component

Malignant Fibrous Histiocytoma with Storiform Pattern
Treatment & Prognosis

- Wide/Radical limb sparing resection whenever feasible
- Amputation may be necessary for large tumors
- Chemotherapy may be considered for high grade dedifferentiated component but is controversial and no clear cut benefit has ever been demonstrated
- 90% of patients are dead of metastatic disease within 2 years
Clear Cell Chondrosarcoma
General Information

- Malignant low to intermediate grade tumor
- Comprised of neoplastic chondrocytes
  - Abundant, clear cytoplasm
  - Little intervening matrix
- Foci of conventional chondrosarcoma may be present
- Approximately 15% rate of metastases primarily to the lungs
Clinical Presentation

• **Age:**
  - 20 years to 40 years of age

• **Sites:**
  - Epiphyses of long bones (rarely metaphysis or diaphysis)
  - Proximal femur, proximal humerus, distal femur, proximal tibia
Radiographic Presentation

- Osteolytic, expansile epiphyseal lesion
- May have focal calcifications
- Often a sharp interface between tumor and surrounding bone
  - Sclerotic rim is uncommon
- Overlying cortex is usually thin, but intact
- Rarely an associated soft tissue component
MRI: Clear Cell Chondrosarcoma of Proximal Femur

T1: Intermediate Signal

T2: High Signal
Plain X-ray: Clear Cell Chondrosarcoma of Proximal Femur
Clear Cell Chondrosarcoma Radiography

- Fine marginal sclerosis
- Calcified matrix
- Purely Lytic
Microscopic Pathology

- Large clear cells with abundant cytoplasm, sharp cell border
- Nuclei are more pleomorphic than chondroblastoma (less uniform compared to chondroblastoma)
- Special stains- S-100-positive, P.A.S-positive
- Heavy glycogen production accounts for the clear appearance of the cytoplasm
- May have small deposits of uncalcified or calcified osteoid
Microscopic Pathology: Clear Cell Chondrosarcoma

- Clear Cells
- Osteoid Production
Microscopic Pathology: Clear Cell Chondrosarcoma

Clear Cytoplasm
Microscopic Pathology: Clear Cell Chondrosarcoma

Clear Cytoplasm

Giant Cells
Microscopic Pathology: Clear Cell Chondrosarcoma
Treatment & Prognosis

- Wide resection
- Simple excision or curettage
  - 80% risk of local recurrence
- Amputation always a possible back up
- No chemo or radiation
Mesenchymal Chondrosarcoma
General Information

- High grade malignant, cartilage-forming tumor
- Noncartilaginous small, round, oval, or spindle shaped cells with islands of malignant cartilage dispersed throughout noncartilaginous component of tumor
- Tumor frequently has a hemangiopericytoma-like appearance
- Metastasizes to the lungs and lymph nodes
- May have chondroid matrix calcification
Clinical Presentation

• **Age:**
  - 10 to 40

• **Sites:**
  - Arises in bone and soft tissue (1/3 of cases arise from soft tissue)
  - Femur, ribs, spine, maxilla, mandible, and pelvis
Plain X-ray: Mesenchymal Chondrosarcoma of Fibula Shaft

- Permeative Lesion
- Indistinct Border
- Cortical destruction
- Soft Tissue Extension
- Stippled Calcifications
Plain X-ray: Mesenchymal Chondrosarcoma from Proximal Humerus
Plain Radiograph of an Extraskeletal Mesenchymal Chondrosarcoma

Heavily Calcified
Microscopic Pathology

• Neoplastic cells may be small, round, oval, or spindle shaped
  • Undifferentiated mesenchymal cells similar to Ewing sarcoma
• Low grade islands of cartilage scattered throughout the mesenchymal cells
  • Usually only a small part of lesion
• Lesions are vascular and often have large, anastomosing vessels that impart hemangiopericytoma-like pattern
• Similar chromosomal translocation as Ewing sarcoma t(11;22)
Microscopic Pathology: Mesenchymal Chondrosarcoma

Mesenchymal Small Round Blue Cell Component

Cartilaginous Component
Microscopic Pathology: Mesenchymal Chondrosarcoma
Microscopic Pathology: Mesenchymal Chondrosarcoma
Microscopic Pathology: Mesenchymal Chondrosarcoma

Mesenchymal (Small Round Blue Cell) Component

Large Nuclei; No Cytoplasm; No Matrix

Collagen Deposition
Microscopic Pathology: Mesenchymal Chondrosarcoma

Mesenchymal (Small Round Blue Cell) Component

Hemangiopericytoma-like Pattern of Blood Vessels

Large Staghorn Blood Vessels
Differential Diagnosis

- Ewing Sarcoma
- Small Cell Osteosarcoma
- Dedifferentiated Chondrosarcoma
Biological Behavior

- High metastatic and local recurrence rates
  - Metastasizes primarily to lungs, other bones, lymph nodes and viscera
  - 70% mortality
Treatment & Prognosis

• Surgery and chemotherapy. Radiation is used in selected cases, particularly extraskeletal mesenchymal chondrosarcomas.
Juxtacortical (Periosteal) Chondrosarcoma
Juxtacortical Chondrosarcoma

• Definition: A malignant, subperiosteal cartilaginous tumor that lacks osteoid production and erodes the underlying cortical bone (periosteal chondrosarcoma)

• Age: 80% are >20 years old vs periosteal osteosarcoma and periosteal chondroma

• Clinical: Painless, mass or swelling; 1/3 of patients have pain (pain rarely exceeds swelling)
Juxtacortical/Periosteal

- Similar to juxtacortical chondroma except larger and grows aggressively
- Periosteal lesion – cortical erosion
- Chondroid matrix calcification
- Similar to periosteal osteosarcoma however no hair on end periosteal reaction
- Larger soft tissue mass/size (>3-4cm)
- Intramedullary canal spared
Juxtacortical Chondrosarcoma

• Most Common Locations:
  • Femur
  • Humerus
  • Pelvis
  • Rib or foot
Radiographic Presentation

- **Radiology:**
  - Metaphyseal
  - Cortical erosion with sclerotic underlying cortex (saucer shaped defect)
  - Matrix calcification
  - Triangular sclerotic spur at margin of tumor
  - >5cm in diameter; average size: 11 cm (vs periosteal chondroma that is usually <5cm)
  - No hair on end periosteal reaction (vs. chondroblastic osteosarcoma)
  - Intramedullary canal is spared
Plain X-ray: Periosteal Chondrosarcoma of Distal Femur

- Erosion of Outer Cortex
- Cortical Thickening at Periphery of Lesion
Juxtacortical Chondrosarcoma

• **Prognosis:**
  - 80-90% long term survival

• **Treatment:**
  - Wide Limb Sparing Resection whenever feasible
  - No Chemotherapy and radiation
Thank You!