Lumbar Chordoma: A Primary Bone Tumor

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INTRODUCTION

- Primary malignant bone tumor of embryonic notochord remnants
- 1-4% of primary bone tumors, <0.1 per 100,000
- Location: Sacral (50%), Skull base (35%), Vertebral column (15%)
- Classic, chondroid (5-15%), and dedifferentiated (5%) variants
- Most commonly in late middle age (50s to 60s)
- Low-grade, slow growing tumor
- But locally aggressive, high rate of local recurrence (20% in 1st year)
- Local recurrence is most important predictor of mortality
- Metastasis only occurs very late in disease
- Median survival of about 6 years, less than 12 months with mets
- 5 year survival of 70%, 10 year survival of 40%
- Primary therapy- aggressive surgical resection (if possible)
- New targeted therapies currently under investigation

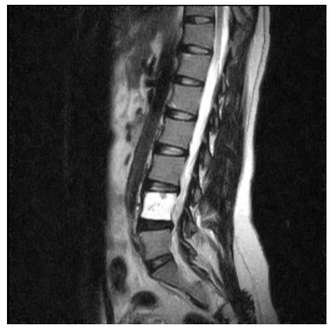
Patient Presentation

32 year old with non-specific low back pain and radiculopathy
No other clinical findings

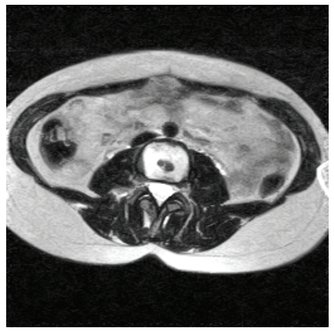
Common Findings

- Often clinically silent until late in disease
- Insidious onset of pain is most common initial symptom
  May exist for 14-24 months prior to diagnosis
- Neurologic deficits can occur based on location

Radiological Imaging



T2 Sagittal MRI of Spine



Axial MRI of L4 Spine

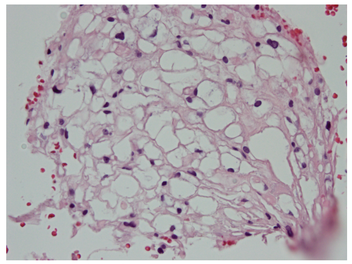
- Hyperintense bony lesion replacing the L4 vertebral body
- No involvement of posterior spinal elements
- Relatively non-aggressive appearance

Pathology and Immunohistochemistry

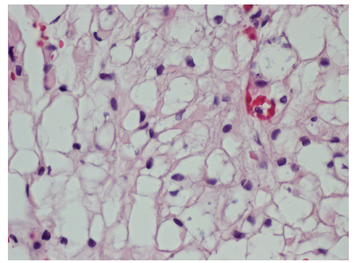
Gross Appearance

- Purple to Gray
- Cystic and gelatinous
- Focal hemorrhage
- Often encapsulated

CT-guided Needle Core Biopsy

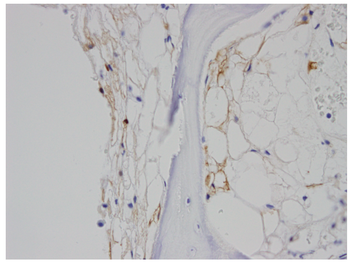


H&E Stain Low Power

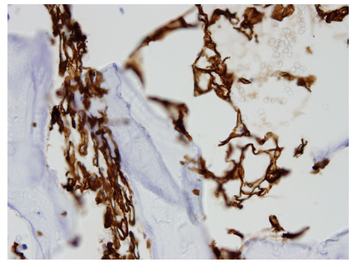


H&E Stain High Power

Classic Chordoma Low-grade tumor of epitheloid cells with bubbly, pale cytoplasmic vacuoles termed physaliferous cells. Lobules separated by fibrous bands in a myxoid stroma. Moderate atypia and mitotic count.



Weak S-100 Positive Staining



Strong CK19 Positive Staining

Immunohistochemical Markers

- Strong positive staining for cytokeratin 19 (epithelial marker)
- Weakly positive staining for S-100 protein
- Positive staining for epithelial membrane antigen (EMA)
- Positive staining for Brachyury (transcription factor)
- Negative staining for D2-40, GFAP, CD10, CD20, CD138

Histopathologic Variants

Chondroid Chordoma- hyaline or myxoid cartilage, better prognosis
Dedifferentiated Chordoma- high-grade spindle cells, poor prognosis

Histopathologic Differential Diagnosis

Chrondrosarcoma- cartilage, negative CK19, EMA, Brachyury staining
Multiple myeloma, myxopapillary ependymoma, chordoid meningioma

Treatment

Current Gold Standard Treatment

En-bloc surgical resection with wide margins + post-operative XRT
Extent of initial resection is most important factor in opportunity for cure
Local recurrence of tumor is marker for treatment failure

Key Treatment Obstacles and Issues

- Vital neurological structures surround resection field
  May limit radical resection to preserve neurological function
  Total en-bloc resection is possible in less than 50% of spine lesions
- Resistant to traditional radiation doses (40-60 Gy)
  Stand-alone radiotherapy has proven ineffective; adjuvant only
  Delivery of higher doses is limited by low tolerance of spinal cord
- Insensitive to conventional chemotherapy (slow growing tumor)
  Limits management of microscopic residual and metastatic disease
- Most tumors eventually recur despite optimal treatment
  Complex retreatment is plagued with high morbidity and toxicity

Future Directions

Proton or Heavy Particle Radiation Therapy

Deliver higher dose radiation with minimal injury to surrounding tissues
No exit dose and potential radiobiologic effects
Evidence suggests improved local control and lower recurrence
Significant construction and operational expense of hadrons

Molecular Targeted Therapy

Overexpress receptor tyrosine kinases PDGF, EGFR, KIT, c-MET
Investigational anti-tumor treatment with TK inhibitors
Clinical response from Imatinib treatment in advanced disease
Stable disease with symptomatic improvement
Erlotinib, Gefitinib, Cetuximab (EGFRi) and Sunitinib (PDGFi, VEGFi)

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