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Case Report

Diagnostic and Management Challenges in Chondrosarcoma: A Case-Based Expert Review

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Abstract

This case-based expert review from ORTHOBIT 2025 Congress (Tehran, Iran) highlights the practical challenge of distinguishing between enchondroma/atypical cartilaginous tumor (ACT) (low-grade) and higher-grade chondrosarcoma (CS). A 57-year-old woman presented with 4 months of shoulder pain. Magnetic resonance imaging (MRI) revealed a proximal humeral metaphyseal intramedullary cartilaginous lesion with a focal cortical breach and a small extraosseous component. The core needle biopsy (CNB) suggested enchondroma, and the patient underwent extended curettage, cementation, and plate fixation. Final pathology upgraded the lesion to central CS, grade 2, prompting resection and reconstruction using a proximal humeral megaprosthesis. At 3 years, she was pain-free, recurrence-free, The Musculoskeletal Tumor Society Score (MSTS) 26/30, with moderate range of motion (ROM) limitation, and radiographic superior prosthetic migration without major complications. This case emphasizes the importance of radiology-pathology correlation and planning for possible diagnostic upgrading in borderline cartilaginous tumors.

Keywords: Chondrosarcoma; Bone Neoplasms; Magnetic Resonance Imaging; Biopsy

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Background

Chondrosarcomas (CSs) are malignant cartilaginous tumors that exhibit a wide range of aggressiveness. As the second most common bone sarcoma after osteosarcoma, they account for a significant proportion of bone tumor-related morbidity and mortality (1). The diagnostic overlap between benign enchondromas and atypical cartilaginous tumors (ACTs)/low-grade CS often leads to uncertainty, especially when lesions are incidentally discovered. Proper classification is essential because the treatment approach and prognosis vary significantly across grades and subtypes. Errors in diagnosis or under-treatment of axial or high-grade lesions can result in recurrence, metastasis, or unnecessary morbidity. This case-based article is drawn from an expert panel discussion at the ORTHOBIT 2025 Congress (Tehran, Iran) and explores the diagnostic and therapeutic complexities associated with CS.

In this manuscript, we used the World Health Organization (WHO, 2020) terminology for central conventional cartilaginous tumors. An atypical cartilaginous tumor (ACT) refers to lesions in the appendicular skeleton (long bones) that are histologically equivalent to grade 1 conventional CS but are designated ACT to reflect intermediate behavior. For the axial skeleton (pelvis/spine), the term conventional CS, grade 1, is retained, and ACT is not used. Higher-grade disease is termed conventional CS, grade 2, or grade 3 (2).

The index case was selected from the authors' clinical practice because it exemplifies diagnostic uncertainty at the interface of enchondroma, ACT, and CS1 and was considered suitable for discussion at the ORTHOBIT 2025. Clinical, imaging, and histopathological data were reviewed in institutional multidisciplinary meetings, in which attending professors and subspecialty experts contributed their experience and opinions; the manuscript's conclusions reflect collective expert judgment arising from these discussions. To contextualize the panel insights, the authors performed a targeted literature search of PubMed and Embase, focusing on the diagnostic criteria, biopsy accuracy, imaging modalities, and management strategies for cartilaginous tumors. Only de-identified patient information was presented, and written informed consent for the publication of anonymized case details and images was obtained. Institutional review requirements were followed in accordance with the local policy.

Case Report

A 57-year-old woman was referred with progressive left shoulder pain for four months, localized to the anterior and lateral shoulder. Pain limited the active range of motion (ROM), whereas passive ROM was preserved, suggesting pain inhibition rather than true mechanical stiffness. No constitutional symptoms were reported. Plain radiographs of the left shoulder (Figure 1A) revealed an abnormality in the proximal humerus, prompting further evaluation.

Magnetic resonance imaging (MRI) revealed a lobulated intramedullary lesion centered in the proximal humerus, predominantly involving the metaphysis with extension toward the adjacent proximal segment (metaphyseal-proximal diaphyseal region). The lesion was measured [Anteroposterior (AP) × Medio-Lateral (ML) × Caudo-Cranial (CC): 4 × 3 × 7 mm). It showed low signal intensity on T1-weighted sequences and high signal on T2-weighted sequences, with internal low-signal foci on T2 consistent with chondroid mineralization/calcification (Figure 1B-C). A focal cortical breakthrough was noted with a small extraosseous/soft-tissue component (Figure 1D).

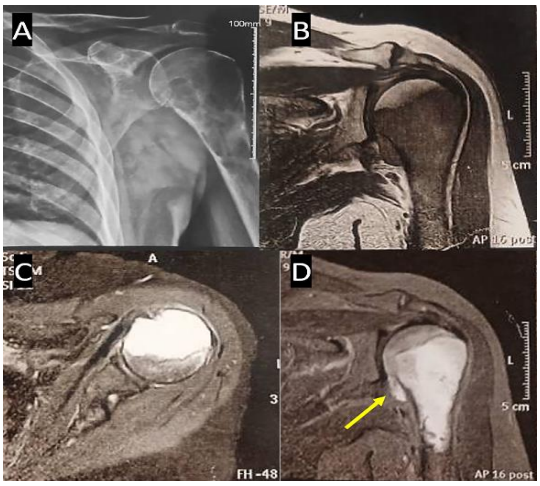

Figure 1. Proximal humerus lesion. (A) Radiograph showing abnormality. (B, C) Magnetic resonance imaging (MRI): lobulated intramedullary lesion, metaphysis involved, measuring 4x3x7cm (AP x ML x CC), low T1, high T2 signal with chondroid mineralization. (D) MRI: focal cortical breakthrough with soft-tissue component.

A core needle biopsy was performed on the patient. Histopathological examination revealed a cartilaginous lesion without cytological atypia, and the initial diagnosis was enchondroma/ACT. Given the biopsy results and the lack of additional abnormal findings on clinical assessment, the patient underwent surgical treatment.

The patient underwent extended intralesional curettage of the lesion, followed by defect filling with polymethylmethacrylate (PMMA) cement and prophylactic internal fixation using an anatomic proximal humerus plate (Figure 2 A-B).

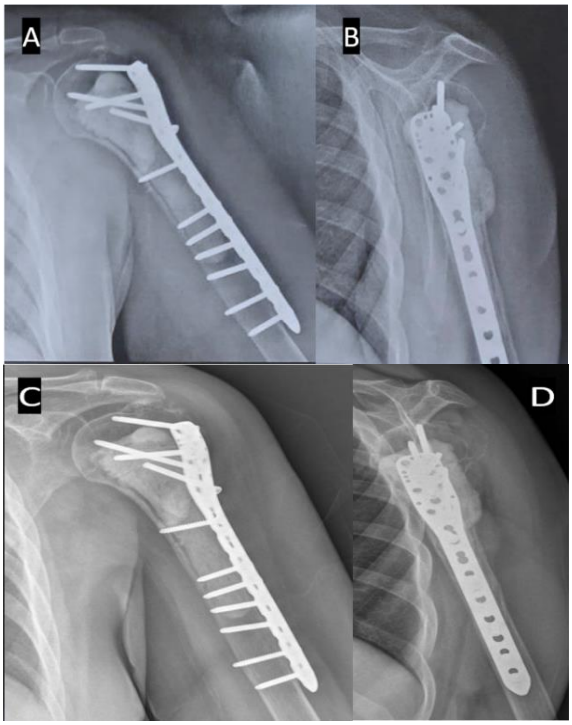

Figure 2. Proximal humerus lesion management. (A, B) Post-intralesional curettage, polymethylmethacrylate (PMMA) cementation, and internal fixation with anatomic proximal humerus plate. (C, D) Two-month postoperative radiographs revealing progressive periprosthetic lucency and radiographic evidence suggestive of local recurrence at the lateral and posterior proximal humerus.

Representative curettage material was sent for a definitive histopathological evaluation.

Final Pathology and Escalation of Treatment: Contrary to the core needle biopsy CNB diagnosis, the final pathology report of the curettage specimen revealed CS, grade 2. Postoperative radiographs at 2 months (Figure 2 C-D) were obtained during the reassessment and planning.

In view of the intermediate-grade diagnosis (grade 2) and the preoperative MRI finding of cortical breach with a small soft-tissue component, the patient was subsequently treated with oncologic resection and reconstruction with a proximal humerus tumor endoprosthesis (MUTARS® Proximal Humerus) (Figure 3 A-B).

At 3 years postoperatively, the patient remained free of local recurrence, as determined by clinical assessment and surveillance imaging. She reported no pain and had no postoperative complications (including infection, instability episodes, neurovascular deficit, or reoperation). Functionally, she had a moderate reduction in shoulder ROM but was able to perform activities of daily living independently and return to her routine work. Her functional outcome was favorable, with an Musculoskeletal Tumor Society Score (MSTS) of approximately 26/30. Follow-up radiographs demonstrated superior migration of the proximal humeral megaprosthesis (Figure 3 C), consistent with the mechanical/soft-tissue balance around the shoulder. Given her satisfactory function and the absence of symptoms, this was managed with ongoing observation.

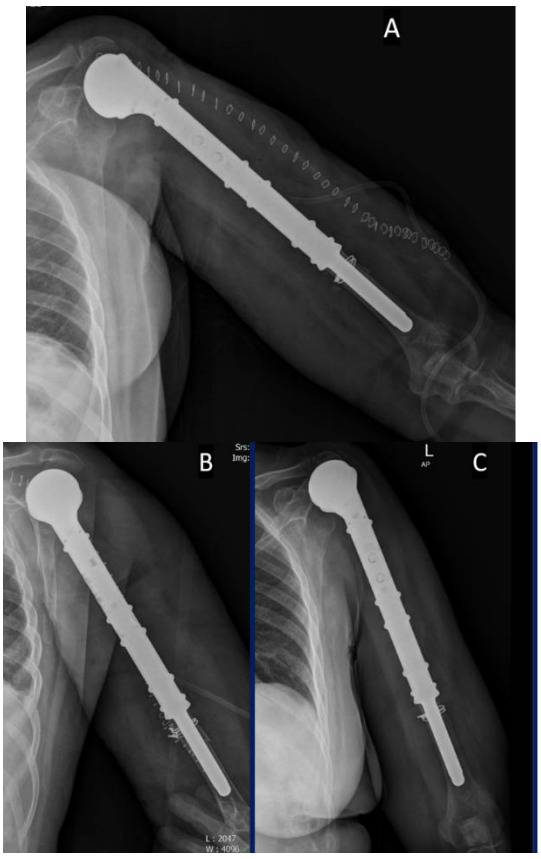

Figure 3. . Wide resection and reconstructio and postoperative follow-up. (A, B) Post-resection and reconstruction with MUTARS® Proximal Humerus endoprosthesis. (C) Follow-up radiograph at 3 years demonstrates superior migration of the proximal humeral megaprosthesis, managed with ongoing observation due to satisfactory function and absence of symptoms.

This case is described in a completely anonymized manner, with no patient identifiers included. Approval from the Institutional Review Board (IRB) was not necessary or was waived for a single retrospective case report at our institution. Formal written consent for publication was obtained.

Review of the Evidence

Classification and Epidemiology: The 2013 and 2020 WHO updates refined the taxonomy of cartilaginous tumors, renaming grade I CS in the appendicular skeleton as an ACT to reflect its intermediate behavior, while retaining CS1 for axial sites, given their higher risk profile (3, 4). The 2020 classification further divides CS into eight subtypes: central conventional (grade 1 vs. 2-3), secondary peripheral (grade 1 vs. 2-3), periosteal, dedifferentiated, mesenchymal, and clear cell, each with distinct biological potentials (2). The incidence is approximately 2-4 per million per year, with a mean age at diagnosis of 51 years and a slight male predominance (5, 6). Emerging data from Iran suggest a younger presentation and poorer outcomes relative to global cohorts (7).

Key Diagnostic Challenges: Distinguishing benign enchondromas, ACTs, and low-grade CS remains difficult because of overlapping radiologic and histological features. Expert panels emphasize that neither hypercellularity nor myxoid change alone reliably indicates malignancy (8, 9); context –including lesion size, location, and symptoms –is crucial. ACT and grade I CS may be indistinguishable on core biopsy, necessitating integrated clinical-radiologic-pathologic review. When imaging is equivocal, dynamic gadolinium-enhanced MRI, positron emission tomography-computed tomography (PET-CT), and, if uncertainty persists, image-guided biopsy are recommended to establish definitive grading (10, 11). The role of biopsy in the diagnostic evaluation of suspected low-grade CS remains highly contentious within the orthopedic oncology community (6). Current practice patterns demonstrate significant heterogeneity, with some clinicians advocating for imaging-based diagnosis and proceeding directly to definitive management, while others consider tissue sampling an essential medico-legal safeguard against potential misdiagnosis (8). This divergence in clinical approach reflects the inherent limitations of both diagnostic modalities: imaging may lack sufficient specificity to reliably distinguish low-grade CS from benign cartilaginous lesions, while biopsy procedures carry risks of sampling error, tumor seeding, and diagnostic ambiguity due to overlapping histological features between enchondroma and low-grade CS (12, 13).

When biopsy is pursued, evidence suggests that diagnostic accuracy may be optimized through several technical considerations: employment of image-guided sampling techniques, incorporation of MRI signal characteristics into procedural planning, acquisition of multiple tissue samples to minimize sampling bias, and provision of comprehensive clinical history and imaging findings to the examining pathologist (14-16). However, it must be acknowledged that even under optimal conditions, histopathological differentiation between benign and low-grade malignant cartilaginous tumors can remain challenging, and the clinical significance of this diagnostic uncertainty in treatment decision-making warrants further investigation (17, 18).

Radiologic Features of Malignancy: On radiographs and cross-sectional imaging, features favoring CS over enchondroma include (19-22):

- Endosteal scalloping involving > 2/3 of cortical thickness
- Cortical expansion or breakthrough with ill-defined margins
- Popcorn or “ring-and-arc” calcifications within the matrix
- Septonodular (multilobular) enhancement on MRI
- Entrapped fat clefts (“fat-fringe” sign) are indicative of ACT but are absent in higher-grade lesions.

Alhumaid et al. underscored the added value of evaluating marrow edema, soft-tissue extension, and trapped fat to differentiate ACT from high-grade CS on MRI, though they advocated multimodal imaging for optimal accuracy (23).

Management Strategies: Treatment is grade- and site-specific (1, 24).

- ACT (appendicular sites): Extended intralesional curettage with adjuvants (e.g., high-speed burr, phenol) offers low recurrence and superior function versus wide resection, with comparable oncologic safety.
- CS 1 (axial sites): Wide en bloc excision is advised given higher recurrence and metastatic risk.
- High-grade (CS 2-3) and dedifferentiated variants: En bloc resection is mandatory; chemotherapy is reserved for mesenchymal or dedifferentiated subtypes per National Comprehensive Cancer Network (NCCN)/ European Society for Medical Oncology (ESMO) guidelines, while conventional CS shows limited chemo- or radio-sensitivity.

Chen et al.’s meta-analysis found no difference in local recurrence or metastasis between curettage and resection for ACT –even in large (T2) lesions –supporting less invasive surgery when properly selected (25).

Survival and Prognosis: Prognosis correlates closely with grade and subtype. Five-year survival exceeds 90% for ACT/CS1 and secondary CSs; it falls to 75% for CS 2 and 30% for CS 3. Presence of metastases at diagnosis portends a 5-year survival of just 28% (median Overal Survival: 14 months). Dedifferentiated CS carries the worst outlook (0-24 percent 5-year survival), while mesenchymal, clear cell, and juxtacortical subtypes range from 50% to > 90% depending on age and location (1).

Evolving Evidence and Controversies: Despite clear WHO guidance, real-world practice shows variability: national registry data reveal a trend toward wider resections for borderline ACTs despite lack of level I evidence. Advanced imaging modalities and multidisciplinary tumor boards are increasingly relied upon to refine preoperative grading and guide personalized treatment decisions.

The advent of liquid biopsy technologies has transformed cancer treatment across various tumor types (26), with CSs recently becoming a key area of research in this rapidly advancing domain (27). The analysis of circulating tumor deoxyribonucleic acid (ctDNA) is emerging as a particularly promising non-invasive biomarker platform for managing CS, with potential uses in the initial diagnosis, monitoring of the disease during treatment, and prognostic stratification (28). Early studies on ctDNA detection in patients with CS have shown promising results, indicating the feasibility of identifying tumor-specific genetic changes in blood samples (29). Although liquid biopsy holds promise in musculoskeletal oncology, its application in central cartilaginous tumors is

still in the exploratory phase. Current evidence lacks validated thresholds for clinical decisions, positioning it as a tool for future research rather than for immediate clinical application. Management should continue to rely on established clinicoradiologic-pathologic correlations. Liquid biopsy methods may help address clinical challenges in CS management, such as diagnostic difficulties in complex locations, monitoring of treatment response, and assessment of progression risk. However, larger prospective studies with standardized methods and extended follow-up are necessary to confirm the utility of ctDNA analysis before it can be implemented clinically (30).

Discussion

This case underscores how a cartilaginous lesion of the proximal humerus can appear indolent on initial workup yet still warrant escalation in diagnostic concern. Radiographs were unrevealing, computed tomography (CT) showed no periosteal reaction or obvious cortical defect, MRI demonstrated a multilobular intramedullary lesion without clear extraosseous extension, and scintigraphy showed only mild uptake (not markedly greater than the anterior iliac crest). However, multidisciplinary re-review identified subtle endosteal scalloping and morphology that were not fully reconciled with a simple enchondroma, shifting the working diagnosis toward an ACT/grade-1 CS spectrum lesion.

A case-specific challenge is managing uncertainty when multiple borderline signals converge. Pain, mild tracer uptake, and limited scalloping are each nonspecific in isolation; together, they increase the likelihood that the lesion is clinically relevant and potentially more aggressive than its initial description. The panel's focus was, therefore, on deliberate radiology-pathology correlation and aligning the diagnostic pathway with the treatment decision that would change the management. If tissue sampling is pursued, it should be planned with imaging guidance and explicit communication of radiologic concerns, recognizing that even optimal sampling may not fully resolve borderline grading.

Because the lesion was appendicular (proximal humerus) and, on reviewed imaging, lacked a soft-tissue mass or frank cortical breakthrough, the management logic favored a function-preserving strategy consistent with ACT-spectrum disease. In practice, this means intralesional excision with extended curettage and high-speed burring, use of local adjuvants and defect filling per institutional protocol, and generous sampling for definitive histology at the time of the surgery. Patients should be counseled that classification at this boundary carries uncertainty and that the operative plan and follow-up strategy are designed to minimize both undertreatment and overtreatment. If the final pathology or interval imaging suggests higher-grade biology, escalation to oncologic resection should be reconsidered.

The three pitfalls highlighted by this presentation are particularly relevant: 1) over-reassurance from normal radiographs in symptomatic patients, 2) under-recognition of subtle cortical involvement on CT/MRI, and 3) siloed decision-making based on imaging-only or histology-only conclusions. A practical approach for similar cases includes senior musculoskeletal radiology review with explicit assessment of cortical involvement, multidisciplinary discussion before definitive surgery, and a surveillance plan with predefined triggers for re-evaluation such as progression of pain, interval growth, increasing cortical involvement, or development of extraosseous extension.

Conclusion

CS diagnosis and management require integrated clinical, radiological, and pathological assessments to minimize misclassification and optimize outcomes. Distinguishing between enchondroma, ACT, and low-grade CS remains challenging because imaging and histology often overlap; therefore, multidisciplinary tumor board review and targeted use of advanced imaging and image-guided biopsy can improve diagnostic confidence. Treatment must be individualized according to the grade and site. Extended intralesional curettage with adjuvants is an appropriate limb-sparing option for selected appendicular ACTs, whereas axial or higher-grade lesions generally require wide en bloc resection. Emerging biomarkers, such as ctDNA, show promise for non-invasive monitoring but require prospective validation before routine use. Vigilant radiographic-pathologic correlation and shared decision-making are essential to balance oncologic control with functional preservation.

Conflict of Interest

The authors declare no conflict of interest in this study.

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