

Multidisciplinary Intervention for a Craniovertebral Junction Chondromyxoid Fibroma with Mutant-Pattern P53 Expression and Myogenic Differentiation: A Case Report

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Case Report

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Abstract

This article reports an extremely rare case of chondromyxoid fibroma (CMF) occurring in the craniovertebral junction (CVJ, C1 level epidural space). The patient presented with high cervical cord compression and occipital neuralgia. Multimodal imaging evaluation revealed an expansive, hypovascular mass involving the C1 appendages. Relying on preoperative 3D planning, intraoperative multimodal neuromonitoring, and precision osteotomy via an ultrasonic bone scalpel, a safe and total resection of the tumor was achieved. This approach successfully decompressed the spinal cord while maximally preserving cervical mobility, thereby avoiding prophylactic internal fixation and fusion. Pathology and immunohistochemistry confirmed the lesion as CMF, exhibiting exceptionally rare myogenic differentiation (SMA+, focal Desmin+). Notably, the tumor demonstrated an abnormal elevation of the Ki-67 index (5%) and a null-pattern mutant P53 expression. This aberrant immunophenotype strongly suggests genomic instability (such as potential TP53 nonsense mutations or large deletions), indicating a micro-trend toward borderline or malignant transformation and higher local invasive potential. This case not only expands the differential diagnostic spectrum for extradural masses in the CVJ region but also provides valuable clinical evidence for the surgical intervention of complex spinal mesenchymal tumors, the rigorous surveillance of high-risk subtypes, and translational medical explorations regarding targeted and proton therapies.

1. Clinical Data

1.1 Basic Information—A 48-year-old male was admitted in July 2025 with a primary complaint of “intermittent neck pain accompanied by dizziness and gait instability.” The patient had been in good physical and psychological health previously, without any history of surgery or familial genetic disorders.

1.2 Physical Examination: Cervical physiological curvature was preserved. Skin color and temperature were normal. There was no tenderness or percussion pain over the cervical spinous processes or interspinous spaces. Cervical range of motion was within normal limits. The patient experienced left-sided occipital neuralgia (more pronounced at night) and numbness in the occipital and diaphragmatic regions. An inverse Lhermitte’s sign was positive. Muscle strength in all four limbs was Grade 5. Bilateral Achilles and patellar tendon reflexes were hyperactive, while other pathological reflexes were not elicited.

1.3 Ancillary Examinations: Preoperative Cervical CT: Demonstrated a calcified nodule on the left side of the spinal canal at the C1 level with compression of the medulla oblongata; an MRI was recommended (Fig. 1). Cervical MRI: Revealed abnormal signals on the left side of the spinal canal and paravertebral region at C1. The spinal cord was compressed with signs of local degeneration. A benign space-occupying lesion (likely a schwannoma) was considered (Fig. 2). Cervical CT Angiography (CTA): Identified a calcified nodular lesion within the spinal canal at C1, with a soft tissue plaque in the left paravertebral area, spinal cord compression, and dilated adjacent veins. Digital Subtraction Angiography (DSA): Confirmed dilated veins surrounding the left-sided plaque (Fig. 3).

1.4 Surgical Procedure and Postoperative Course: A 10 cm longitudinal incision was centered at T1. Using a neurosurgical ultrasonic bone scalpel, the lower margin of the foramen magnum and the posterior arch of C1 were precisely removed. Upon exposure, the dura mater was intact with no cerebrospinal fluid leakage. The mass was located in the epidural space within the spinal canal (Fig. 4). After meticulous dissection, the tumor was resected and submitted for pathology. Internal fixation and fusion were not performed as the lateral mass destruction did not meet the criteria for spinal instability. **Pathological Findings:** Macroscopic examination revealed a cluster of grayish-brown tissue measuring 0.8 cm × 0.8 cm × 0.8 cm, consistent with chondromyxoid fibroma (Fig. 5). Immunohistochemistry: CKP(-); Vimentin(+); S-100(-); SMA(+); Desmin (focal+); CD34(-); P53 (exhibiting a fully negative null-pattern mutant expression, suggesting a possible nonsense mutation); Ki-67 (index: 5%) (Fig. 6). On postoperative day 3, the patient was able to ambulate independently with a cervical collar. Dizziness and gait instability were significantly improved. Follow-up MRI at 1 and 4 months showed postoperative changes with the complete resolution of abnormal signals (Fig. 7). The patient reported full symptomatic relief and postoperative course was uneventful.

1.5 Patient Assessment: The patient reported a good postoperative recovery, with both neck pain and gait instability alleviated after surgery. At the 3-month follow-up, the patient stated that they experienced no abnormalities during normal activities and were fully capable of performing activities of daily living (ADLs) and physical labor.

2. Discussion

2.1 Embryological Origin Hypotheses and Anatomical Paradox of CVJ-CMF

Chondromyxoid fibroma (CMF) is a rare benign bone tumor typically occurring in the metaphyses of long bones in the lower extremities; its occurrence in the axial skeleton (spine) accounts for less than 1% of cases. Cases involving the atlas (C1) and presenting with epidural compression are extremely rare in the literature and are frequently misdiagnosed [1-2]. As the core hub of the craniovertebral junction, C1 develops from the complex fusion of sclerotomes. Given that this tumor was epidural and involved the C1 appendages, we hypothesize that it may originate from undifferentiated mesenchymal progenitor cells remaining in the CVJ region during the embryonic period. Due to the relatively wide spinal canal at C1 (providing significant compensatory space), these slow-growing tumors often remain occult in the early stages. The onset of occipital neuralgia and high cervical cord compression symptoms typically signifies that the tumor has breached the cortex and is exerting a significant mass effect on the cervicomedullary junction [3]. This case disrupts the diagnostic paradigm in neurosurgery where "extradural masses in the CVJ region are primarily schwannomas, meningiomas, or chordomas," emphasizing that rare chondrogenic tumors must be included in the differential diagnosis when encountering lesions with calcification and bone destruction in this area.

2.2 Multimodal Imaging Features: From Morphology to Hemodynamics

The anatomical relationships of the CVJ are exceptionally complex. The imaging findings in this case presented a characteristic "trinity" of clues essential for preoperative assessment.

(1) CT Correlation with Pathological Matrix: Preoperative CT showed typical osteolytic bone destruction of the C1 appendages with "stippled" or "patchy" internal calcifications. Pathologically, this corresponds to the chondroid matrix and focal dystrophic calcification within the CMF. Unlike the extensive bone invasion seen in chordomas, this CMF exhibited expansive growth without a significant periosteal reaction, reflecting its relatively indolent biological nature ^[1]. Precision CT, supplemented by 3D-CTA reconstruction, clearly visualized the anatomical proximity to the bilateral vertebral arteries (V3 segment) ^[4], providing a "roadmap" for avoiding vascular injury during en bloc resection.

(2) MRI "Myxoid Trap" and Enhancement Patterns: MRI is indispensable for identifying soft tissue components. This tumor exhibited a distinct, well-circumscribed lobulated hyperintensity on T2-weighted imaging (T2WI) ^[5]. This signal, related to high water content in the myxoid matrix, can easily be confused with cystic schwannomas or chordomas in the CVJ region ^[6]. The key differentiator is the enhancement pattern: this case showed focal, patchy, and peripheral enhancement, unlike the homogeneous enhancement of schwannomas or the "honeycomb" enhancement of chordomas. This pattern reflects the alternating distribution of fibrous septa and myxochondroid nodules.

(3) Hemodynamic Significance: DSA and CTA provided vital evidence of the benign nature. The lesion was markedly hypovascular, lacking pathological tumor blush or major feeders from the carotid or vertebral systems. This ruled out hypervascular hemangioblastomas or metastatic renal cell carcinoma and excluded the need for preoperative embolization. DSA also confirmed the patency of dural sinuses and internal jugular veins, critical for predicting intraoperative bleeding and planning the decompression path.

2.3 Deep Reconstruction of Immunophenotype: Myogenic Differentiation and Pluripotency

Accurate pathological and immunohistochemical subtyping is the core of diagnosis. The double-negative expression of S-100 and CKP in this case was critical "exclusive" evidence against schwannoma and chordoma ^[7]. Uniquely, the tumor showed aberrant SMA(+) and Desmin (focal+) expression. Typical CMF features pure chondroid, myxoid, or fibrous differentiation; myogenic marker positivity is exceptionally rare. This phenotypic heterogeneity suggests that primitive mesenchymal cells in the CVJ have the potential for multidirectional differentiation into myofibroblasts, explaining why some tumors in this region exhibit higher local invasiveness and matrix remodeling capacity than appendicular CMF ^[8].

2.4 Genomic Instability: Clinical Implications of Ki-67 and P53 Mutations

Although classified as benign (Grade I) by the WHO, this case showed concerning immunophenotypic traits. The Ki-67 index in normal CMF is usually well below 2%; here, it rose to 5%. More importantly, the null-pattern P53 expression is a reliable surrogate for TP53 nonsense mutations or large deletions,

leading to total loss of tumor suppressor function^[9]. This molecular event, rare in benign bone tumors, strongly suggests the lesion is "borderline" or has a microscopic trend toward malignant transformation. Such patients must be treated as a "high-risk subtype" requiring stringent radiological follow-up.

2.5 Microsurgical Strategy: Balancing En Bloc Resection and Functional Preservation

In C1 surgery, pursuing oncological wide margins is often impractical due to proximity to the dens, medulla, and V3 segments of the vertebral artery. We employed a strategy of "maximal safe resection combined with minimally invasive neural decompression"^[10]. Multimodal monitoring (SEP/MEP) was the baseline safeguard. While lateral mass resection often requires fusion, the use of an ultrasonic bone scalpel allowed for precise osteotomy that preserved uninvaded articular facet structures. As biomechanical assessments did not indicate instability, we avoided prophylactic internal fixation, thereby preserving the patient's cervical mobility.

2.6 Translational Medicine Outlook: Proton Therapy and Targeted Intervention

Given CMF's resistance to conventional radiotherapy and the risk of radiation-induced medullary injury, new paradigms are needed for cases with R1/R2 resection or high-risk mutations (like this case's high Ki-67 and P53 mutation):

- ▣ Proton Beam Therapy: Utilizing the Bragg peak effect allows for high-dose conformal radiation to the tumor bed while protecting the medulla and vertebral arteries. This should be the preferred adjuvant intervention for residual CVJ-CMF^[11].
- ▣ GRM1-Targeted Therapy: Recent studies indicate that GRM1 gene rearrangement and overexpression are characteristic driver events in CMF. Targeting the MAPK/PI3K pathway via glutamate receptor antagonists (e.g., riluzole derivatives) offers promising translational prospects for refractory cases^[12]. (Table 1 summarizes the comparison with previous cases).

2.7 Limitations

Due to patient compliance, only 4-month follow-up imaging is available, limiting conclusions on long-term recurrence. Additionally, while P53 null-expression suggested a nonsense mutation, NGS was not performed to identify the specific TP53 mutation site. Future high-risk CMF cases should prioritize molecular pathology to reveal invasive mechanisms.

Intraspinal extradural tumors should not be reflexively diagnosed as schwannomas or chordomas. For rare CVJ-CMF, complete resection with minimal morbidity is a challenge. The success of this case—leveraging preoperative 3D spatial rehearsal and intraoperative "millimeter-level" ultrasonic osteotomy—serves as a multidisciplinary team (MDT) model integrating molecular pathology, advanced imaging, and modern radiotherapy.

Declarations

Data Availability Statement

All data presented in this study are included within the article. For further inquiries, please contact the corresponding author.

Ethics approval and consent to participate

This study describes a single case report and does not constitute a clinical trial or interventional research study. According to the institutional policy, formal ethics committee approval was not required. Written informed consent for participation in the study was obtained from the patient's legal guardians.

Consent for publication

Written informed consent has been obtained from the patient and their family for the publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Author Contributions

K.S and S.P drafted the initial manuscript; Y.Y participated in data collection. B.Y participated in the final review and revision of the article. All authors participated in manuscript revision. All authors contributed to the article and approved the submitted version.

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Conflict of Interest Disclosure

The authors declare no conflicts of interest.

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Clinical trial number

not applicable.

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Table

Tab.1 Comparison of typical spinal CMF cases reported in the past decade with the present case

Feature	Typical Spinal CMF (2016-2025 Average)	Present Case (2026 Report)	Clinical/Scientific Significance
Location	Lower thoracic or lumbar spine	C1 (Atlas) Epidural	Extreme anatomical rarity; high surgical risk
S-100 Expression	20-30% weakly positive	Negative (-)	Key to excluding chordoma and neurogenic tumors
SMA / Desmin	Almost entirely negative	SMA (+) / Desmin (focal +)	First report of clear myogenic differentiation
Ki-67 Index	< 2% (Benign threshold)	5% (Borderline active)	Suggests higher risk of local invasion/recurrence
P53 Status	Wild-type / No mutation	Nonsense mutation (Null-pattern)	Suggests potential genomic instability
Treatment	Conventional curettage/resection	Ultrasonic en bloc resection + stability preservation	Demonstrates highest precision in spinal surgery

Figures

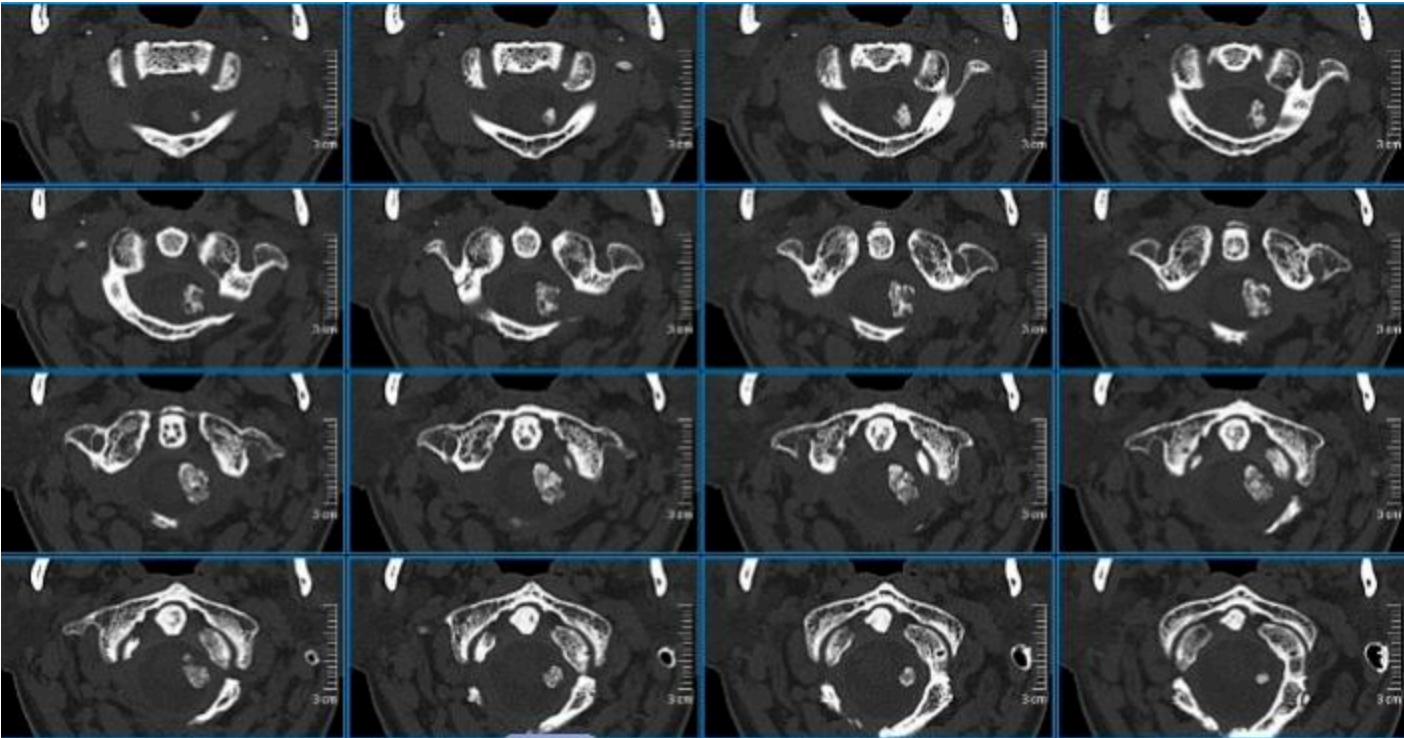


Figure 1

Description: Representative axial CT slices at the C1-C2 level demonstrate an expansive, osteolytic lesion predominantly involving the posterior arch and the right lateral mass of the atlas (C1). Matrix Characteristics: The lesion exhibits a "stippled" or "patchy" internal calcification pattern within a low-

density matrix, which is highly suggestive of a cartilaginous origin. Bone Alterations: Significant cortical thinning and focal cortical breakthrough are observed, with the tumor extending into the spinal canal and narrowing the available space for the spinal cord. No significant periosteal reaction is noted, consistent with the slow-growing nature of CMF.

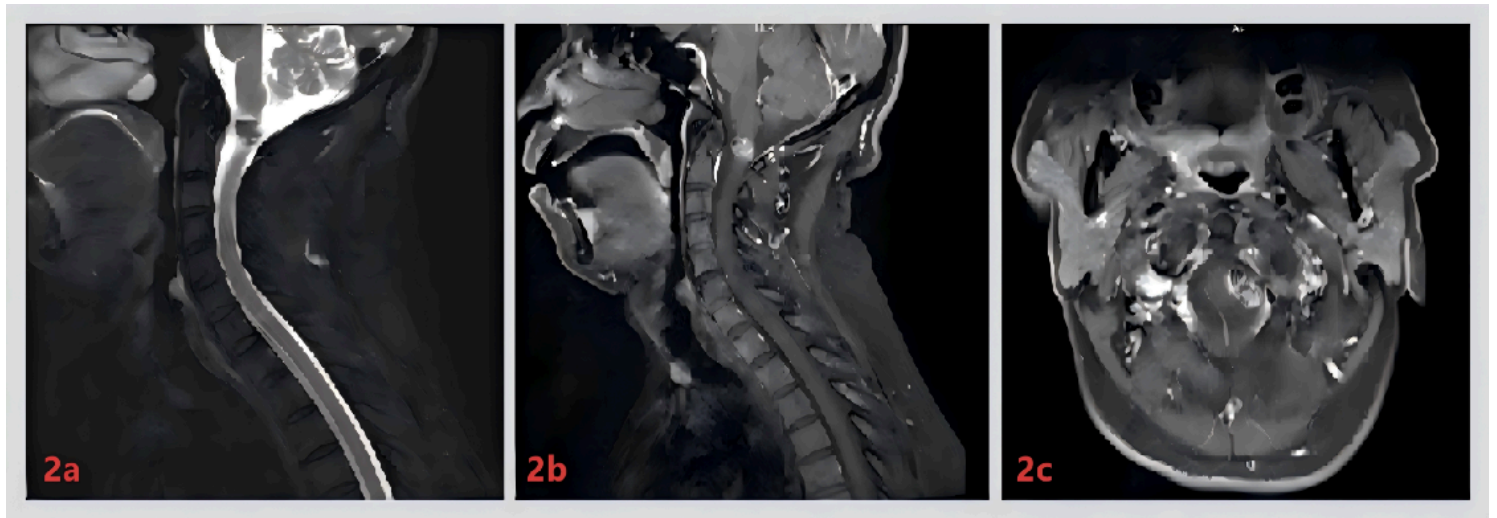


Figure 2

(2a) Sagittal T2-weighted imaging (T2WI) shows a lobulated, well-circumscribed extradural mass at the C1 vertebral level. The lesion displays distinct hyperintensity and exerts significant posterior compression on the high cervical spinal cord. (2b) Sagittal post-contrast T1-weighted imaging (T1WI) demonstrates the mass as heterogeneously isointense to subtly hypointense compared to the spinal cord, with limited internal enhancement. (2c) Axial post-contrast T1WI at the level of the mass confirms its posterior and right-sided extradural location, with severe compression and deviation of the spinal cord. The lesion has a lobulated contour and an enhancement pattern typical of a myxoid-containing tumor, with focal, patchy, and peripheral enhancement. Note the preservation of the vertebral arteries in this view.



Figure 3

(3a) Three-dimensional computed tomography angiography (3D-CTA) reconstruction provided spatial visualization of the cervical and intracranial vasculature, elucidating the precise anatomical relationship between the bilateral vertebral arteries (particularly the V3 segments) and the C1 extradural tumor; this facilitated the planning of a safe surgical corridor for en bloc resection. (3b) The venous phase of digital subtraction angiography (DSA) demonstrated patency of the dural venous sinuses and internal jugular veins, with no evidence of venous congestion or tumor-induced outflow obstruction. (3c) Selective arterial phase DSA visualized the intracranial circulation and revealed an absence of significant pathological tumor blush. These findings confirm the hypovascular nature of the lesion and the lack of major arterial feeders from the carotid or vertebral systems, consistent with the characteristic profile of a benign chondroid neoplasm.

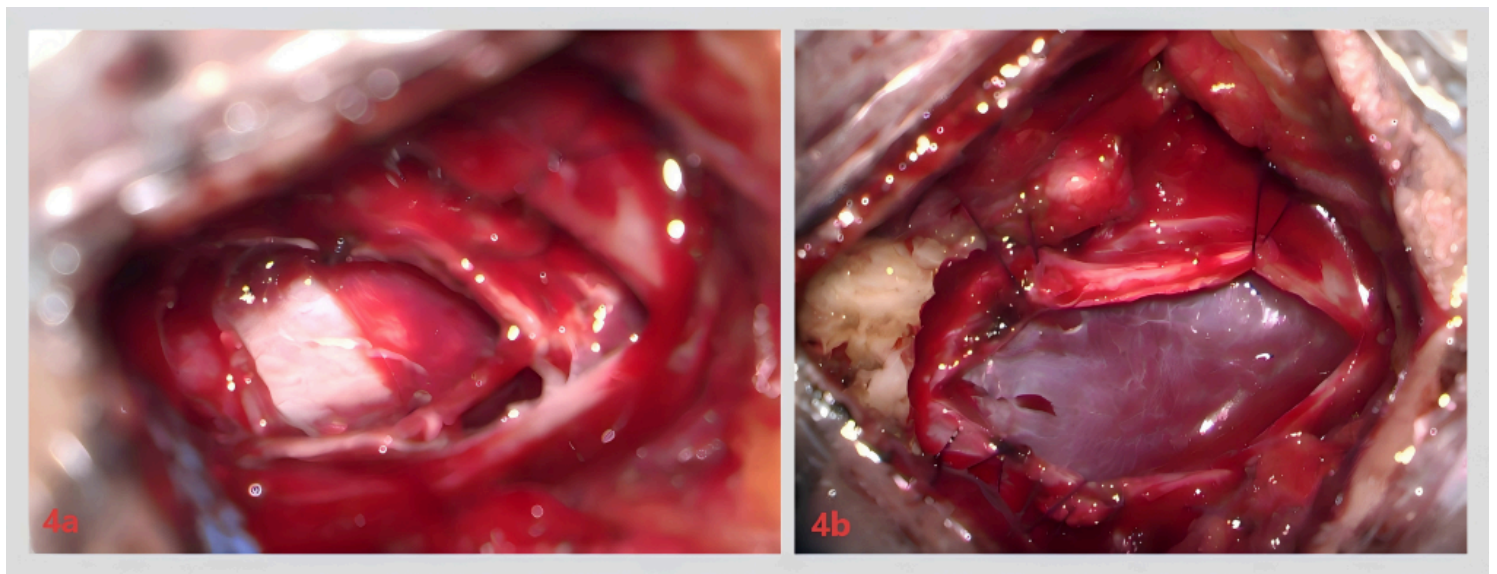


Figure 4

(4a) Tumor exposure: The dura mater is opened via a midline incision and retracted with stay sutures to maximize the surgical corridor. An intradural mass (grayish-white solid lesion) is well-visualized, causing significant compression on the spinal cord. (4b) Post-resection and decompression: The surgical field after gross total resection of the tumor. The mass effect is eliminated, and the spinal cord is adequately decompressed and anatomically restored, with an intact arachnoid surface and a clean tumor bed without active bleeding.

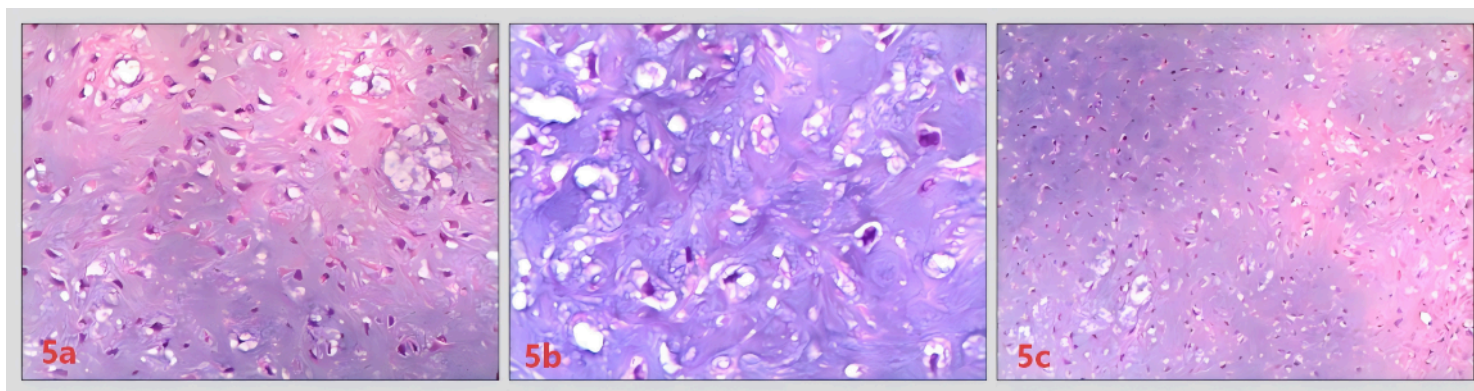


Figure 5

Postoperative pathology: Consistent with chondromyxoid fibroma. (5a) HE $\times 40$; (5b) HE $\times 100$; (5c) HE $\times 200$.

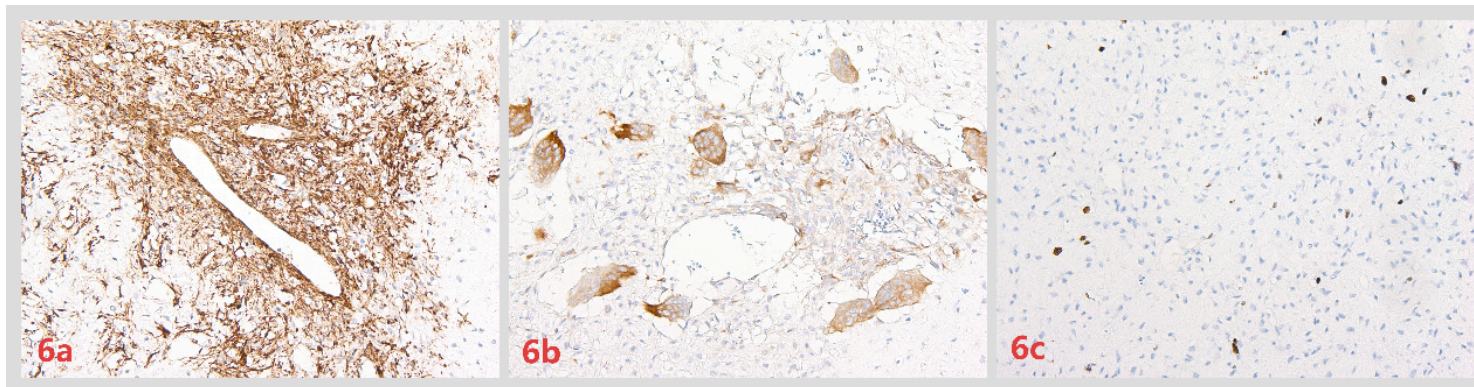


Figure 6

Immunohistochemical staining results: (6a) SMA (+); (6b) Desmin (focal +); (6c) Ki-67 (index: 5%).

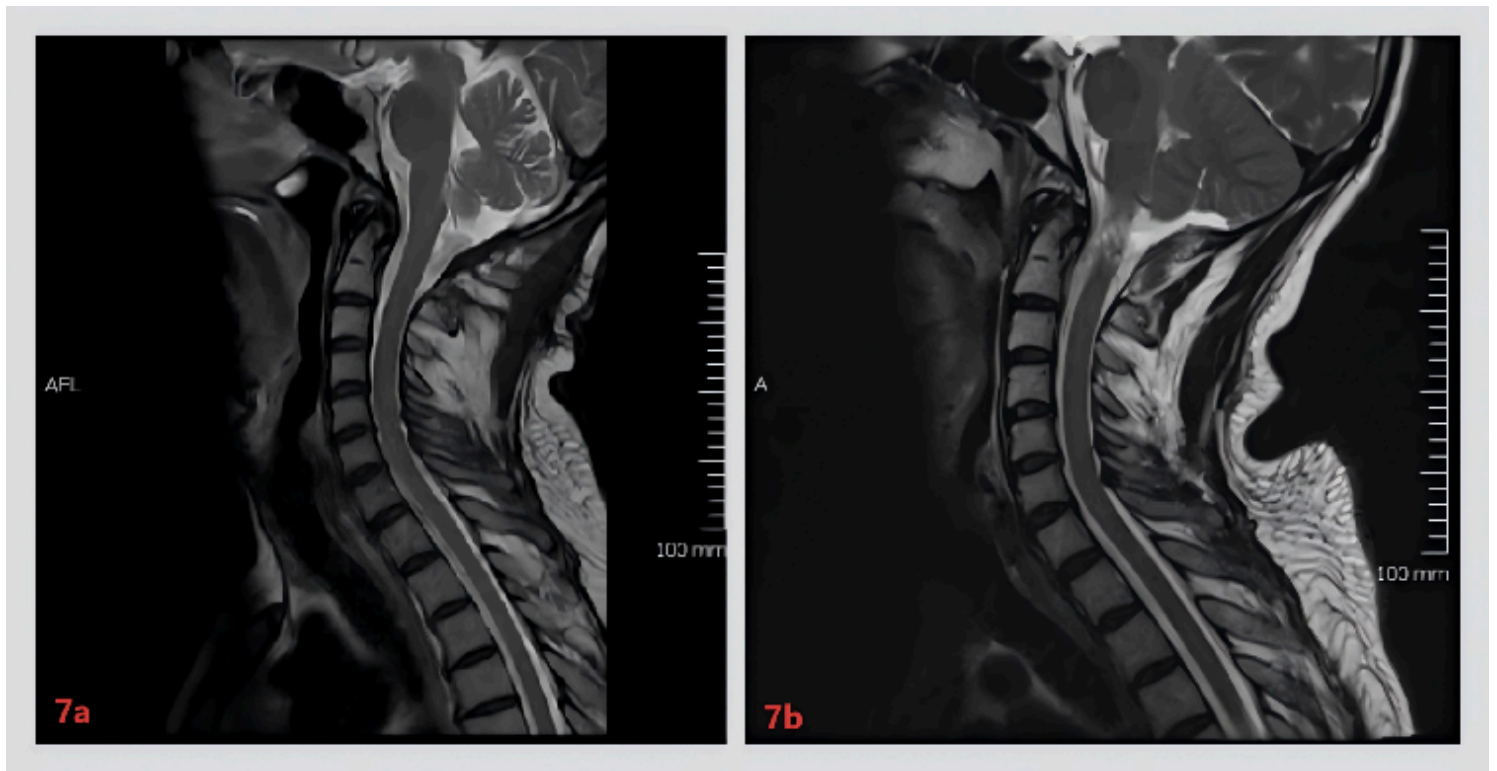


Figure 7

Postoperative follow-up sagittal MR images demonstrating postoperative changes and complete resolution of the abnormal signal. (7a) Follow-up at 1 month postoperatively; (7b) Follow-up at 4 months postoperatively.