

Fibrocartilaginous mesenchymoma of the distal femur with focal MDM2 and CDK4 expression but no MDM2 amplification: a case report

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Case Report

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Abstract

Background

Fibrocartilaginous mesenchymoma (FM) is a rare primary bone tumor recognized as a distinct entity in the 2020 WHO Classification.

Case presentation

We report a 14-year-old boy with left knee pain after minor trauma. Imaging revealed an aggressive osteolytic lesion in the distal femur. Histology showed a biphasic pattern of spindle cells and hyaline cartilage, with immunohistochemistry revealing SMA, SATB2, and S100 expression, as well as focal weak MDM2 and CDK4 expression. Molecular testing revealed no GNAS or IDH1 mutations and no MDM2 amplification, supporting the diagnosis of FM. The patient underwent complete surgical removal of the lesion. At one-year follow-up, there was no recurrence.

Conclusions

This case illustrates the potential diagnostic challenge posed by FM with focal MDM2 and CDK4 expression and suggests that combining morphological and molecular analyses can help support accurate diagnosis and management.

Introduction

FM is a rare primary bone tumor, recently recognized as a distinct entity in the 2020 WHO Classification of Tumors of Soft Tissue and Bone(1). This borderline tumor predominantly affects the metaphyses of long bones in adolescents(2, 3) and features a biphasic histological pattern of spindle cell mesenchymal tissue and hyaline cartilage(4). Due to its rarity, the full clinicopathological spectrum and prognostic factors of FM remain incompletely characterized. Diagnosing FM is often complicated by its morphological similarities to fibrocartilaginous dysplasia (FCD), usually linked to GNAS mutations(5), and low-grade central osteosarcoma (LGCO), marked by MDM2 amplification(6). In this report, we present a case of FM occurring in the distal femur of a 14-year-old male. The tumor exhibited classic fibrocartilaginous histology and was negative for GNAS mutations, helping distinguish it from FCD. While immunohistochemistry revealed focal expression of MDM2 and CDK4, the absence of MDM2 amplification, confirmed via fluorescence in situ hybridization (FISH), was helpful in supporting the final diagnosis.

Case Presentation

A previously healthy 14-year-old male was referred to our institution with an eight-day history of localized left knee pain following minor trauma. The patient had no significant past medical history and no relevant family history of bone tumors or hereditary disorders. No prior interventions were performed before referral to our institution; the patient had not received any medical, surgical, or alternative treatments related to the knee lesion.

Physical examination was unremarkable, with no evidence of local tenderness, swelling, or palpable mass. Initial radiographic imaging revealed an osteolytic and destructive lesion located in the left distal femoral metaphysis (Fig. 1A). CT reconstruction further demonstrated the aggressive features of the lesion, including cortical disruption and an associated soft tissue mass, which raised suspicion for a malignant neoplasm (Fig. 1B). Radiographically, the osteolytic lesion was observed to abut and partially erode the lateral aspect of the distal femoral physis (growth plate), while the medial physis appeared relatively unaffected. This involvement contributed to the observed left genu valgum

deformity. Based on the above imaging findings, an ultrasound-guided soft tissue biopsy was subsequently performed. The biopsy findings were highly suggestive of FM. The patient underwent complete surgical removal of the lesion, including curettage of the distal femoral tumor, with reconstruction and medial distal femoral epiphysiodesis to address the associated deformity. Histopathological evaluation confirmed negative margins (R0 resection).

The curettage specimen was submitted in multiple fragments from two samples, measuring 4.0 × 3.0 × 1.8 cm and 8.0 × 4.0 × 4.0 cm, respectively. Grossly, part of the specimen showed a cartilaginous cap measuring up to 0.4 cm in thickness, with admixed bone fragments. Microscopically, the lesion was composed predominantly of proliferative fibrous tissue arranged in diffuse, fascicular, or woven patterns, admixed with abundant hyaline cartilage in an irregular distribution (Fig. 2A). In focal areas, the cartilaginous component showed a growth plate-like appearance, with enchondral ossification and focal trabecular bone formation (Fig. 2B). Mild to moderate cytologic atypia was noted in a subset of tumor cells, and mitotic activity was low, without atypical mitotic figures (Fig. 2C). Immunohistochemically, the fibrous component was positive for SMA (Fig. 2D) and SATB2 (Fig. 2E), whereas S100 highlighted the cartilaginous component. Ki-67 showed a low proliferation index of approximately 5% (Fig. 2F). MDM2 showed focal weak positivity (Fig. 2G), with similar focal positivity for CDK4, and p53 exhibited a wild-type staining pattern (Fig. 2H). Overall, the morphologic and immunophenotypic findings were supportive of fibrocartilaginous mesenchymoma, and molecular studies were subsequently performed to help distinguish FM from FCD and LGCO. Sanger sequencing revealed no pathogenic mutations in GNAS or IDH1 (Fig. 2I), and fluorescence in situ hybridization (FISH) demonstrated no MDM2 amplification (Fig. 2J). These results supported the diagnosis of FM and helped distinguish it from FCD and LGCO.

Given the rarity of the disease, there is still a lack of robust evidence demonstrating the efficacy of adjuvant therapy. Surgical resection remains the treatment of choice. Therefore, no adjuvant therapy was administered postoperatively. At the one-year follow-up, the patient reported no significant discomfort, and no significant abnormalities were identified on imaging.

Discussion

FM represents a rare primary bone neoplasm, with fewer than 45 cases reported worldwide (Table 1) since its initial characterization by Dahlin et al. in 1984 (4, 7). While previously considered a variant of FCD(8, 9), FM is now recognized as a distinct clinicopathological entity. This reclassification is primarily based on genetic distinctions: FCD is frequently associated with GNAS mutations, whereas such mutations are typically absent in FM(4). Consequently, the 2020 WHO Classification of Soft Tissue and Bone Tumors officially designates FM as a distinct mesenchymal tumor of bone(1).

FM predominantly affects children and adolescents(2), with a median age of 13 years. It typically arises in the metaphyses of long bones, such as the femur, tibia, and humerus(3). Clinical presentation is often insidious, with lesions discovered incidentally or following minor trauma(10), as seen in our 14-year-old patient. Radiographically, FM presents as an expansile, osteolytic lesion that may disrupt the cortex or extend into soft tissue.

The primary concern in the current case was the process of differential diagnosis. Among the major histologic mimics, FCD and LGCO are particularly important because both may overlap with FM morphologically. FCD shares several features with FM, including fibrous stroma, irregular trabecular bone, and cartilaginous islands, but is genetically defined by activating GNAS mutations(11, 12). In our case, no GNAS mutation was detected, which argued against FCD. This molecular finding was especially valuable because the presence of growth plate-like cartilage and enchondral ossification may otherwise raise the possibility of a fibro-osseous or cartilaginous lesion within this spectrum.

The differentiation from LGCO was particularly important in this case because the tumor showed focal weak nuclear expression of MDM2 and CDK4. In spindle cell bone lesions, this immunophenotype may raise suspicion for LGCO, a malignant bone-forming tumor commonly associated with MDM2 and/or CDK4 amplification(13). However, focal immunoreactivity does not necessarily correlate with underlying gene amplification. In the present case, FISH demonstrated no MDM2 amplification, suggesting that LGCO is unlikely despite the potentially misleading immunohistochemical findings. This point is diagnostically important, as overinterpretation of focal MDM2 or CDK4 staining could potentially lead to misdiagnosis as LGCO and inappropriate clinical management.

Consequently, this case highlights that diagnosing FM should not rely solely on morphological and immunohistochemical assessments when significant differential diagnoses exist. Accurate classification requires correlating the biphasic morphology with molecular findings, including GNAS testing to rule out FCD and MDM2 amplification analysis to exclude LGCO. The strength of this report lies in the comprehensive integration of histopathology, immunohistochemistry, and molecular analyses, which facilitated precise differentiation of FM from its mimics. However, as a single-case report with a relatively short follow-up, the findings are limited, and further studies with additional cases and longer surveillance are needed to better understand recurrence risk and long-term outcomes.

Clinically, FM is considered a borderline tumor with locally aggressive behavior, and complete surgical removal with clear margins remains the preferred approach to reduce the risk of recurrence. In this case, the patient underwent complete surgical removal of the lesion. Evidence supporting adjuvant radiotherapy or chemotherapy remains limited. Overall, this case emphasizes the value of careful clinicopathological and molecular evaluation in rare bone tumors and may provide useful information for diagnosis and clinical management.

Conclusions

This case illustrates that FM may pose diagnostic difficulties when MDM2 and CDK4 show focal immunohistochemical expression. Correlating morphology with molecular findings, particularly GNAS mutation testing and MDM2 amplification analysis, may help differentiate FM from morphologically similar bone lesions and reduce the risk of misdiagnosis as LGCO.

Abbreviations

FM Fibrocartilaginous Mesenchymoma

FISH fluorescence In Situ Hybridization

FCD fibrocartilaginous Dysplasia

LGCO Low-grade Central Osteosarcoma

Declarations

Competing interests

The authors declare no conflicts of interest.

Authors' contributions

Conceptualization, B.L. and Y.P.; methodology, S.Z.; writing – original draft, Y.P.; writing – review & editing, Y.P., Z.W., X.L. and B.L.; funding acquisition, B.L. All authors have read and agreed to the published version of the manuscript.

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Availability of data and materials

The raw sequencing data (FASTQ files) generated in this study have been deposited in the National Center for Biotechnology Information (NCBI) Sequence Read Archive (SRA) under BioProject accession number PRJNA1541115, available at <https://www.ncbi.nlm.nih.gov/sra/PRJNA1541115>. The original sequencing chromatogram files (.ab1) have been deposited in the Figshare repository and are publicly accessible at <https://doi.org/10.6084/m9.figshare.34222203>.

Ethical Approval and Accordance: This study reports a single clinical case and did not involve a prospective interventional study. The requirement for formal ethics committee approval was waived by the Shandong Provincial Hospital Human Biomedical Research Ethics Committee in accordance with the institution's policy for single-patient case reports. All procedures involving human tissue specimens and clinical data were conducted in accordance with relevant institutional and national ethical guidelines and regulations, as well as the ethical principles of the Declaration of Helsinki and its subsequent amendments.

Consent to participate: Written informed consent to participate was obtained from the patient's parent.

Consent to publish: Written informed consent to publish the anonymized clinical data and figures was obtained from the patient's parent.

Clinical trial number

Not applicable.

References

1. Choi JH, Ro JY. The 2020 WHO Classification of Tumors of Bone: An Updated Review. *Adv Anat Pathol*. 2021;28(3):119–38. 10.1097/pap.000000000000293.
2. Dahlin DC, Bertoni F, Beabout JW, Campanacci M. Fibrocartilaginous mesenchymoma with low-grade malignancy. *Skeletal Radiol*. 1984;12(4):263–9. 10.1007/BF00349507.
3. Gedikoglu G, Aksoy MC, Ruacan S. Fibrocartilaginous mesenchymoma of the distal femur: case report and literature review. *Pathol Int*. 2001;51(8):638–42. 10.1046/j.1440-1827.2001.01247.x.
4. Gambarotti M, Righi A, Vanel D, Cocchi S, Benini S, Elli FM, et al. Fibrocartilaginous mesenchymoma of bone: a single-institution experience with molecular investigations and a review of the literature. *Histopathology*. 2017;71(1):134–42. 10.1111/his.13201.
5. Drolshagen LF, Reynolds WA, Marcus NW. Fibrocartilaginous dysplasia of bone. *Radiology*. 1985;156(1):32. 10.1148/radiology.156.1.4001418.
6. Khal AA, Aiba H, Righi A, Gambarotti M, Atherley O'Meally AO, Manfrini M, et al. Diagnostic challenges in low-grade central osteosarcoma. *Bone Joint J*. 2024;199–106. 10.1302/0301-620x.106b1.Bjj-2023-0531.R1. 106-b.
7. Hui M, Uppin SG, Narayanan R, Rao KN, Kumar BA. Fibrocartilaginous mesenchymoma of pelvis-a potential diagnostic pitfall. *Skeletal Radiol*. 2023;52(4):791–5. 10.1007/s00256-022-04167-6.

8. Bhaduri A, Deshpande RB. Fibrocartilagenous mesenchymoma versus fibrocartilagenous dysplasia-: are these a single entity? *Am J Surg Pathol*. 1995;19(12):1447–8. 10.1097/00000478-199512000-00015.
9. Lin J, Shulman SC, Steelman CK, Oskoue SV, Reith JD, Simoneaux SF, et al. Fibrocartilaginous mesenchymoma, a unique osseous lesion: case report with review of the literature. *Skeletal Radiol*. 2011;40(11):1495–9. 10.1007/s00256-011-1189-0.
10. Martínez-Lage JF, Alarcón F, Hernández-Barceló JE, Almagro M-J, Alfaro R, Galera-Miñarro A. Fibrocartilaginous mesenchymoma of the spine in a child: a case report. *Child's Nerv Syst*. 2010;26(3):385–9. 10.1007/s00381-009-1042-0.
11. Kovacs SK, Manassaporn A, Nielsen GP, Hung YP. Molecular and immunohistochemical testing of bone tumours: review and update. *Histopathology*. 2023;82(6):794–811. 10.1111/his.14845.
12. Alshalan A, Asiri Y, AlGarni A, Tayara B. Fibrocartilaginous dysplasia: What do we know so far? *Radiol Case Rep*. 2023;18(5):1763–6. 10.1016/j.radcr.2023.01.074.
13. Dujardin F, Binh MB, Bouvier C, Gomez-Bouchet A, Larousserie F, Muret A, et al. MDM2 and CDK4 immunohistochemistry is a valuable tool in the differential diagnosis of low-grade osteosarcomas and other primary fibro-osseous lesions of the bone. *Mod Pathol*. 2011;24(5):624–37. 10.1038/modpathol.2010.229.

Tables

Table 1
Summary of Published Research on Fibrocartilaginous Mesenchymal Tumors to Date

Author	n	Year of Publication	Age	Sex	Site of onset	gene mutation	Follow-Up Time(months)	Follow-Up results
Rashed Al-Khudairi(7)	1	2025	28	F	the left first rib	No	24	No
Sean V. Cahill(4)	1	2024	19	F	T11	No	36	No
Huang J(8)	4	2023	10	F	Sacrum, involving the L5 facet joint	NR	18	No
			7	F	the distal right ulna	No	5	Five months after surgery, indications of local tumor recurrence were observed. No additional intervention was undertaken at that moment, and the patient was later lost to follow-up.
			11	M	the proximal metaphysis of the left tibia	No	11	No
			11	M	The distal metaphysis of the left radius	No	7	No
Monalisa Hui(5)	1	2022	36	M	The pelvis, involving the left ilium, acetabulum, pubic symphysis, and superior/inferior pubic rami	NR	6	No
R F Dong(6)	1	2021	13	M	L3	No	108	No
Sun-Ju Oh	1	2021	17	M	the right fifth rib	NR	12	No
Julio Javier Masquijo(3)	1	2014	4	M	the proximal metaphysis of the right humerus	NR	24	No
n: number of patients; NR: not reported in the study								

Author	n	Year of Publication	Age	Sex	Site of onset	gene mutation	Follow-Up Time(months)	Follow-Up results
Yusuke Takahashi(8)	1	2013	17	F	the right pubis	NR	12	No
Vishal Kumar(4)	1	2012	19months	F	the proximal right tibia	NR	14	No
Jenny Lin(9)	1	2011	11	M	the proximal left humerus	No	24	No
Juan F. Martinez-Lage(6)	1	2009	9	M	T12	NR	24	No
n: number of patients; NR: not reported in the study								

Figures

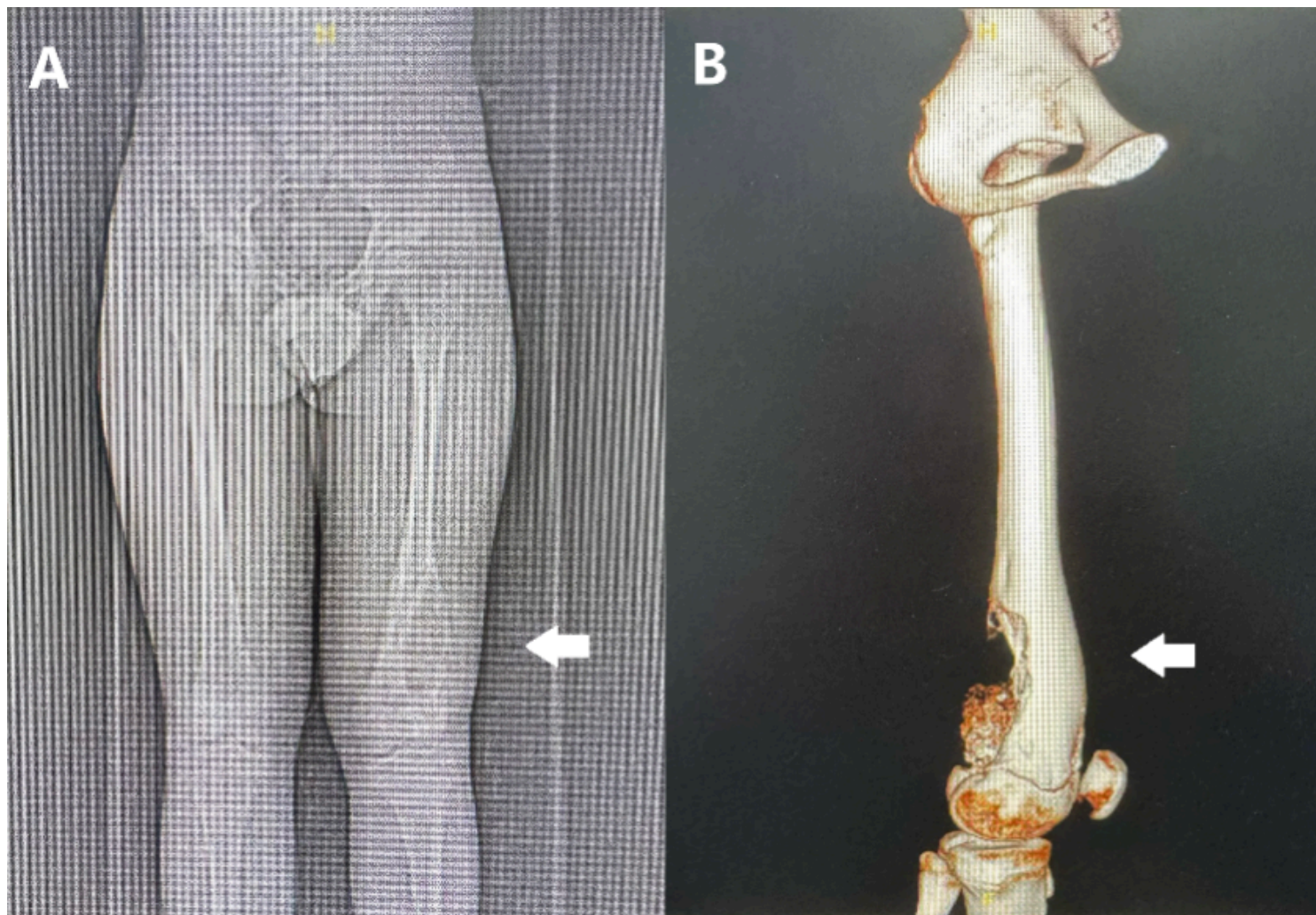


Figure 1

(A) Initial radiographic imaging revealed an osteolytic and destructive lesion located in the left distal femoral metaphysis (white arrow); (B) The CT reconstruction further highlighted the aggressive appearance of the lesion,

characterized by cortical disruption and an associated soft tissue mass, raising suspicion for a malignant neoplasm (white arrow).

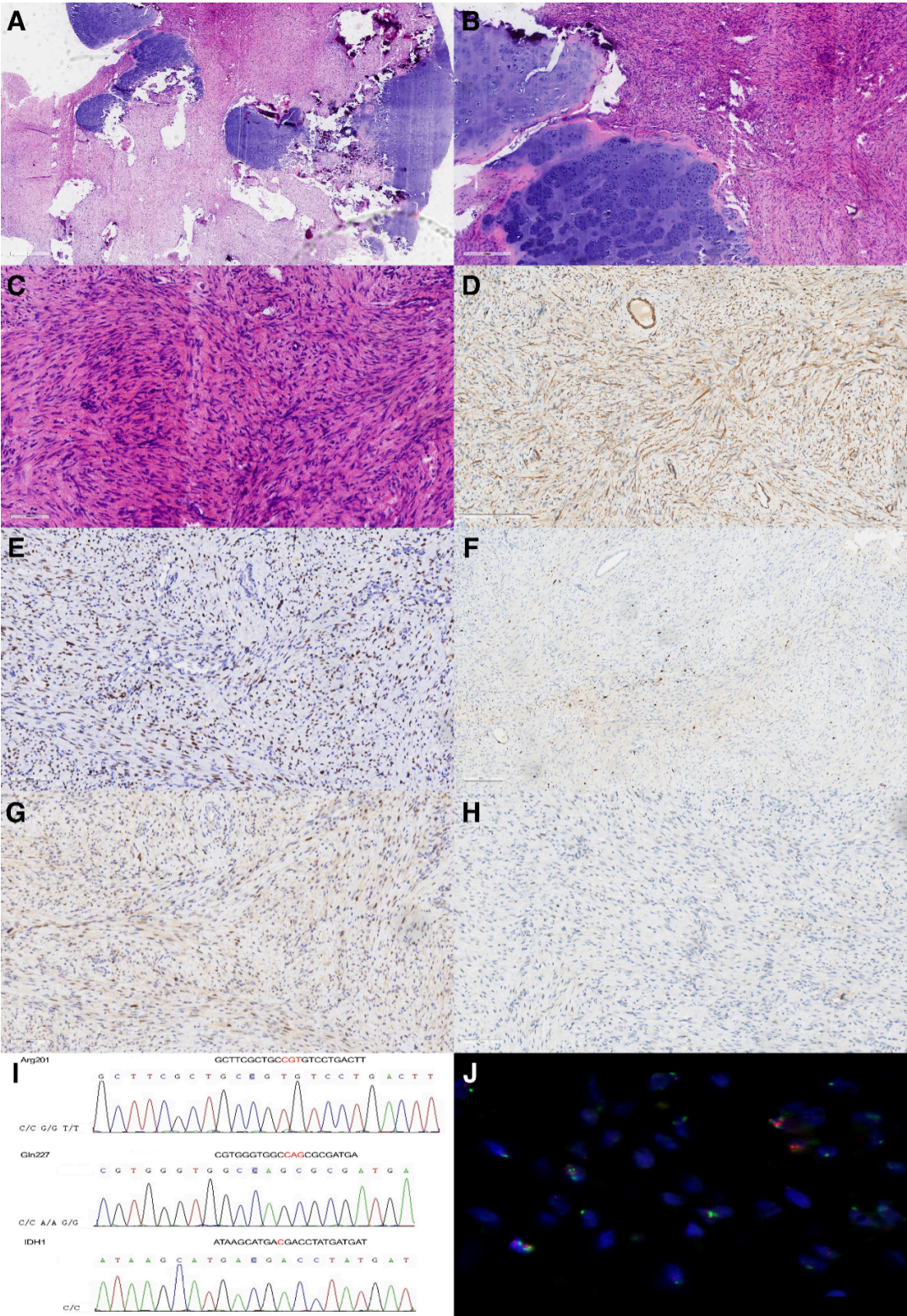


Figure 2

Histopathological, immunohistochemical, and molecular findings. (A) H&E-stained section showing intermingled fibrous and cartilaginous tissue. (B) Foci of chondroid ossification. (C) Sheets of diffusely arranged spindle cells. Immunohistochemistry showed positivity for (D) SMA and (E) SATB2 in the fibrous component. (F) Ki-67 labeling index

was approximately 5%. (G) Focal heterogeneous MDM2 expression. (H) p53 showed a wild-type staining pattern. (I) Targeted Sanger sequencing electropherograms of GNAS and IDH1. (J) FISH analysis demonstrated the absence of MDM2 gene amplification.