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RECURRENT AND REFRACTORY SACRAL CHORDOMA: A CASE REPORT AND MEDICAL ONCOLOGY MANAGEMENT

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ABSTRACT

Background: Chordoma is a rare malignant bone tumor arising from embryonic remnants of the notochord. It most commonly affects the sacrum and skull base. It is characterized by a high risk of local recurrence and, less frequently, distant metastasis. Complete surgical resection, when feasible, combined with high-dose radiotherapy, are the cornerstone of treatment. Systemic treatment options remain limited in locally advanced or recurrent disease that is not amenable to local therapy.[1,11] **Case Report:** We report the case of a 63-year-old hypertensive man followed since 2020 for sacral chordoma. Surgical resection was performed on March 19, 2020, followed by adjuvant radiotherapy to a total dose of 60 Gy, completed on September 25, 2020. Histopathological examination was consistent with conventional chordoma, with clear bone margins but lateral margins that were difficult to assess because of capsular rupture. In 2023, the disease recurred and neither surgery nor re-irradiation was considered feasible. Systemic treatment with imatinib 400 mg/day was initiated and subsequently increased to 800 mg/day because of further progression. Despite this strategy, radiological progression occurred in 2025. Imatinib was temporarily discontinued because of intolerance. Doxorubicin chemotherapy was subsequently administered, but the patient was lost to follow-up. In January 2026, further local progression led to the initiation of pazopanib at 800 mg/day. At the time of writing, the patient remains on pazopanib with an ECOG/WHO performance status of 1–2, and clinical and radiological reassessment is ongoing. **Discussion:** Management of unresectable recurrent chordoma requires a multidisciplinary approach. Imatinib is among the best-studied targeted therapies because of the frequent expression of PDGFR in chordoma.[2,5,6] This case illustrates the therapeutic challenges of recurrent chordoma and the importance of management in an expert center, with discussion of targeted options, clinical trials, and molecular characterization whenever available.[2,10,11] In a phase II study of 56 patients with advanced PDGFB/PDGFRB-positive chordoma, imatinib 800 mg/day produced an objective RECIST response in only 2% of patients, whereas prolonged disease stabilization was observed in a substantial proportion. Other tyrosine kinase inhibitors, including antiangiogenic agents targeting VEGFR such as pazopanib, may be considered after imatinib failure, although the level of evidence remains low.[5,8,9,10] **Conclusion:** Unresectable, non-re-irradiable recurrent sacral chordoma represents a complex therapeutic situation. The absence of systemic treatments validated by randomized trials requires individualized treatment strategies. Imatinib may provide disease control in selected patients, whereas pazopanib may be considered as a salvage option after progression, although supporting evidence remains limited. Improved molecular characterization and enrollment in clinical trials remain important.[2,10,11,12]

KEYWORDS: sacral chordoma, local recurrence, imatinib, pazopanib, PDGFR, targeted therapy.

INTRODUCTION

Chordoma is a rare malignant tumor of notochordal origin and accounts for a small proportion of primary bone tumors. It is an uncommon axial skeletal malignancy that predominantly arises in the sacrum and skull base.[1,11]

Histologically, conventional chordoma is characterized

by a lobulated and cordonal proliferation of epithelioid cells embedded in a myxoid matrix, with variable numbers of physaliphorous cells.[4]

Immunohistochemistry supports the diagnosis by demonstrating expression of cytokeratins, epithelial membrane antigen (EMA), and S100 protein. Brachyury, a marker of notochordal differentiation encoded by TBXT, is the most specific immunohistochemical marker for chordoma.[3,4,12]

Although chordoma generally has a slow course, it is locally aggressive, with a substantial risk of local recurrence and morbidity related to extension into adjacent bone, neural structures, and soft tissues.[1,11]

Initial management is primarily based on complete surgical resection with adequate margins whenever anatomically feasible. High-dose radiotherapy may be added, particularly when surgical margins are inadequate or the risk of local recurrence is high. Current international consensus emphasizes treatment in experienced multidisciplinary centers.[1,11]

Management of recurrent disease should be discussed within a multidisciplinary team in a center experienced in rare tumors and sarcomas.[2,11]

The situation becomes particularly challenging in patients with unresectable recurrence who cannot undergo further irradiation. The efficacy of systemic treatments is limited, and no standard cytotoxic chemotherapy has been established for this indication. Current evidence is based mainly on small phase II trials, retrospective series, and case reports.[2,8,10]

Among targeted therapies, imatinib has been the most extensively studied because PDGFR is frequently expressed in chordoma. Other tyrosine kinase inhibitors targeting angiogenic pathways, such as pazopanib, have also been investigated, but the available evidence remains limited.[8,10,13]

We report the case of a patient with recurrent, unresectable, and non-re-irradiable sacral chordoma who sequentially received imatinib, doxorubicin chemotherapy, and pazopanib after several episodes of disease progression.

Clinical Case

The patient was a 63-year-old hypertensive man without health insurance coverage who had been followed since 2020 for sacral chordoma.

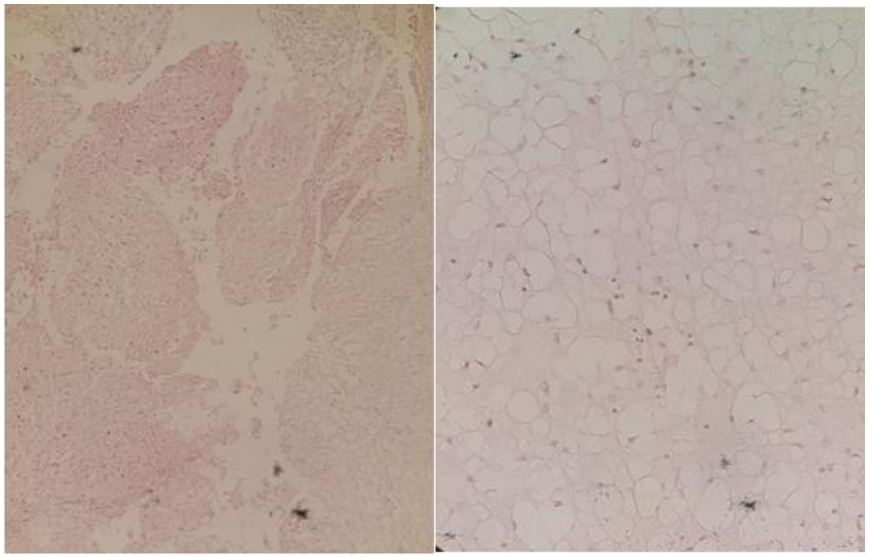
The patient underwent surgical excision of the sacral tumor on March 19, 2020.

Histopathological examination of the surgical specimen was consistent with conventional chordoma.

Histological examination showed a lobulated and cordonal tumor proliferation embedded in a myxoid background. It consisted of large epithelioid cells with abundant eosinophilic cytoplasm and oval nuclei showing moderate to marked atypia. Occasional physaliphorous cells with vacuolated cytoplasm were observed. Mitoses were rare.

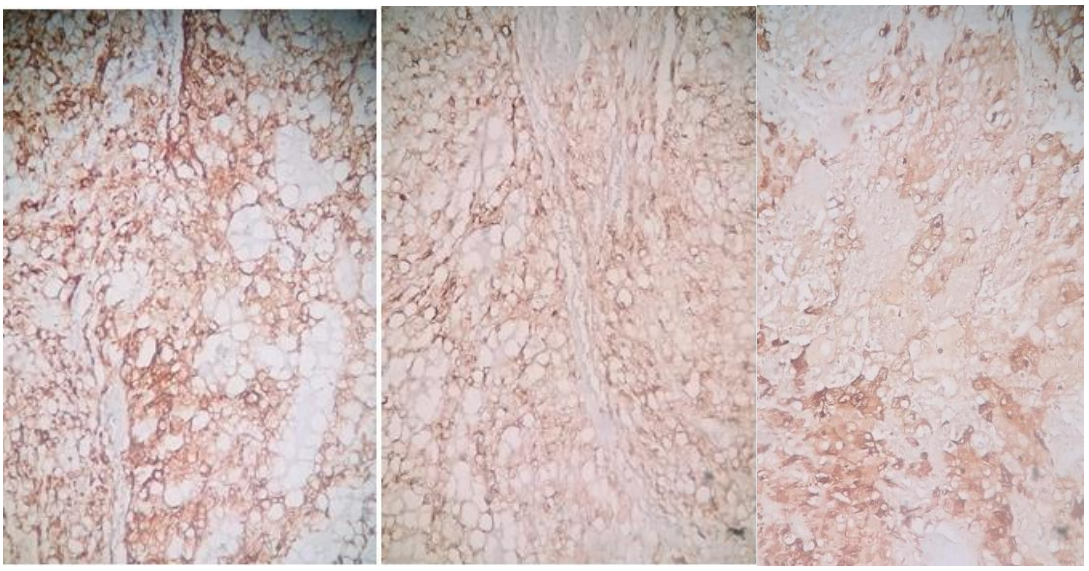
The tumor was surrounded by a fibrous capsule separating it from the adjacent adipose and muscle tissue. However, the lateral resection margins were difficult to assess in areas of capsular rupture. The bone margins were reported as clear.

Because of the risk of local recurrence, adjuvant radiotherapy was delivered to a total dose of 60 Gy, completed on September 25, 2020. The patient was subsequently placed under surveillance.



Histopathological and immunohistochemical features of conventional sacral chordoma. (A) Lobulated and cordonal tumor proliferation embedded in a myxoid extracellular matrix (H&E, ×100). (B) Characteristic physaliphorous cells with abundant vacuolated cytoplasm (H&E, ×200).

Histopathological section showing characteristic lobules of vacuolated physaliphorous cells embedded in a myxoid extracellular matrix (hematoxylin-eosin, ×100 and ×200).



Immunohistochemistry profile of the tumor.
Neoplastic cells showing positive immunoreactivity for AE1/AE3, EMA, and S100 protein, respectively (×200).

These morphological and immunohistochemical features are compatible with conventional chordoma. Expression of cytokeratins, EMA, and S100 is classically described in chordoma, while the presence of physaliphorous cells within a myxoid matrix represents a characteristic morphological feature.[3,4]

Pelvic MRI in February 2023, compared with the examination performed on June 13, 2022, showed a right-sided sacral mass with imaging features compatible with conventional chordoma and suggestive of local recurrence.

Thoraco-abdomino-pelvic CT performed on September 27, 2023, demonstrated a right-sided lytic soft-tissue tumor centered on S2–S3, with involvement of the right S3 nerve root and no distant metastatic disease.

Repeat surgery was considered but the patient was deemed unsuitable for resection. Given the previous 60-Gy irradiation, re-irradiation was not pursued. This decision is consistent with international recommendations, which reserve re-irradiation for situations in which adequate tumor coverage can be achieved without exceeding organ-at-risk constraints.[2]

Because salvage surgery and further irradiation were not feasible, the patient was referred to medical oncology for consideration of systemic treatment.

Imatinib was initiated at 400 mg/day. The patient subsequently developed radiological progression after five cycles. Pelvic MRI on March 29, 2024, showed enlargement of the lesion involving the posterior arch of S3 on the right, consistent with tumor progression.

Thoraco-abdomino-pelvic CT confirmed enlargement of the lytic lesion centered on S2–S3.

Given the absence of local treatment options and the potential rationale for intensified PDGFR inhibition, imatinib was continued at 800 mg/day.

Despite dose escalation, the disease progressed. Pelvic MRI on June 23, 2025, showed a 21% increase in lesion size, with extension from the posterior arch of S3 toward S1, still predominantly right-sided. Thoraco-abdomino-pelvic CT on July 7, 2025, showed a 23% increase in the size of the lytic lesion centered on S2–S3.

Imatinib was interrupted for one month because of intolerance.

Chemotherapy was initiated after progression on imatinib 800 mg/day and because no locoregional treatment was feasible. However, the patient was subsequently lost to follow-up.

Further progression was documented on CT in January 2026, with an approximately 30% increase in the lytic tumor centered on S2–S3.

Given the recurrent, locally advanced, unresectable, and previously irradiated nature of the disease, together with progression on imatinib and doxorubicin, a new targeted treatment strategy was selected.
Pazopanib was initiated at 800 mg/day.

At the time of writing, the patient remains on pazopanib with an ECOG/WHO performance status of 1–2. Clinical and radiological reassessment is ongoing to evaluate treatment response and clinical benefit.

At present, neither efficacy nor treatment failure can be concluded because the assessment is still ongoing.

DISCUSSION

1- A rare tumor with predominantly locoregional progression

Chordoma is a rare malignant tumor with a generally slow but locally aggressive course. The sacrum is one of its main sites of origin. The risk of local recurrence is particularly high when the initial resection does not achieve wide and clearly assessable margins.[1,11]

In our patient, the initial pathological examination confirmed conventional chordoma, with lobulated and cordonal architecture, physaliphorous cells, and a myxoid matrix. Tumor expression of AE1/AE3, EMA, and S100 further supported the diagnosis, as these markers are frequently expressed in chordoma.[4]

Three years after initial treatment, the disease recurred. The sacral location, extension into bone, and nerve-root involvement made management particularly challenging.

2- Role of surgery and radiotherapy:

Complete surgery with adequate margins is the reference local treatment whenever feasible. High-dose radiotherapy contributes to locoregional control, particularly when complete surgery is impossible or margins are inadequate.[1,11] Salvage surgery is preferred when recurrence can be completely resected with acceptable morbidity. However, feasibility depends on tumor extent, involved anatomical structures, and previous treatments.[2]

Our patient had previously received adjuvant radiotherapy to 60 Gy after the initial surgery. At recurrence, neither further surgery nor re-irradiation was feasible.

This represents one of the most difficult clinical scenarios in chordoma and requires consideration of systemic strategies.[2]

3- **Role of Imatinib**

PDGFR is frequently expressed in chordoma, providing the biological rationale for imatinib, a tyrosine kinase inhibitor that targets several kinases including PDGFR.[5,6]

The prospective phase II study by Stacchiotti et al. evaluated imatinib at 800 mg/day in patients with advanced chordoma expressing PDGFB and/or PDGFRB. Among 50 patients evaluable according to RECIST, only one partial response was observed, corresponding to an objective response rate of 2%. In contrast, 35 of 50 patients (70%) had stable disease. These findings indicate that the main benefit of imatinib is disease stabilization rather than tumor shrinkage.[5]

A retrospective series of 48 patients treated with imatinib 800 mg/day reported stable disease as the best response in 74% of patients, with a median progression-free survival of 9.9 months.[6]

In our case, initial use of imatinib was therefore consistent with the available evidence. However, the patient experienced progression despite escalation from 400 to 800 mg/day.

It should also be emphasized that dose escalation should not be interpreted as a proven strategy to restore sensitivity after progression. The 800-mg/day dose mainly corresponds to the dose used in the principal clinical studies.[5,6]

4- What should be done after progression on imatinib?

Therapeutic options after progression on imatinib remain poorly defined.

A phase II study evaluated the combination of imatinib and everolimus in patients with progressing advanced chordoma. Although the rationale was to simultaneously inhibit complementary molecular pathways, this combination has not become a standard treatment.[7]

Other tyrosine kinase inhibitors have been investigated, including sorafenib, sunitinib, pazopanib, and some EGFR inhibitors. A systematic review highlights the substantial heterogeneity of the available data and the absence of a formally established standard treatment after progression.[8,13]

A recent multicenter European retrospective series confirms this difficulty. Among molecularly targeted treatments used in clinical practice, objective response rates remained low, while disease stabilization represented the main benefit observed. Median progression-free survival was 6.5 months in first line and 10 months in second line in this retrospective series.[10]

5- Role of pazopanib

Pazopanib is a multitargeted tyrosine kinase inhibitor with antiangiogenic activity, including inhibition of VEGFR, PDGFR, and c-KIT.

Its use in chordoma is mainly supported by a biological rationale involving angiogenesis and by limited clinical data.[8,10]

A systematic review of targeted therapies in chordoma identified several patients treated with pazopanib, but the sample sizes were very small.[8]

Clinical observations nevertheless suggest potential activity. In a reported case of sacral chordoma, pazopanib was started at 400 mg/day and increased to 800 mg/day, resulting in marked tumor reduction and a progression-free survival of 14 months.[9]

In our patient, pazopanib was initiated at 800 mg/day after progression on imatinib and after one line of doxorubicin.

The patient is currently receiving treatment with an ECOG/WHO performance status of 1–2. Preservation of performance status supports continuation of systemic therapy and justifies close assessment of treatment response.

However, because treatment is ongoing, the efficacy of pazopanib cannot yet be determined. Subsequent follow-up will establish whether the disease remains stable, responds, or progresses during treatment.

6- Role of chemotherapy

Cytotoxic chemotherapy has generally limited activity in chordoma. Historically, several agents have been used, including anthracyclines, alkylating agents, and combination chemotherapy, mainly in advanced or metastatic settings.[2]

Data in adults are particularly limited and do not allow a standard sequence to be defined after failure of targeted therapies. International recommendations therefore emphasize clinical trial enrollment whenever possible.[2,10]

In our patient, doxorubicin should be regarded as a salvage option in the setting of refractory disease rather than as a chordoma-specific, validated treatment.

7- Role of molecular profiling

Contemporary chordoma management increasingly incorporates molecular profiling into the selection of systemic treatments, particularly after failure of multiple lines.[10,12,13]

Brachyury, encoded by the TBXT gene, is a major diagnostic marker and a potential therapeutic target.[3,12]

Beyond PDGFR expression, several molecular alterations have been described, particularly involving the PI3K/AKT/mTOR and EGFR pathways and other signaling pathways involved in tumor growth. These alterations represent potential avenues for the development of targeted therapies.[12,13]

In a patient such as ours, characterized by multiple treatment lines and persistent progression, molecular tumor profiling could be relevant if technically and financially accessible. It may identify a potentially actionable alteration and, importantly, facilitate access to a clinical trial.[10,12,13]

Contemporary approaches also consider PD-L1 expression, mutational status, and other biomarkers that may help guide investigational immunotherapy or targeted therapy.

CONCLUSION

Recurrent sacral chordoma represents a particularly complex therapeutic situation when salvage surgery and re-irradiation are no longer possible.

Our case illustrates the therapeutic course of a sacral chordoma initially treated with surgery and radiotherapy, followed by local recurrence and progression despite imatinib dose escalation. Doxorubicin was subsequently used as salvage therapy, followed by pazopanib after further progression.

Imatinib remains one of the best-documented targeted therapies in advanced chordoma, with activity driven mainly by disease stabilization rather than objective responses.[5,6]

Pazopanib may represent a salvage option after progression, but the level of evidence remains low and it cannot currently be considered a defined standard of care.[8,9,10]

This case emphasizes the importance of multidisciplinary discussion in an expert center, regular reassessment of locoregional treatment feasibility, molecular characterization when possible, and, preferably, enrollment in clinical trials evaluating novel targeted or immunotherapeutic strategies.[2,10,11,12]

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