MEDDOCS Open Access Publisher

Annals of Oncology Case Reports

Open Access | Case Report

Metastatic Sacral Chordoma - A Case Report Unveiling the Achievements and Progress in Recent Management Strategies

Ezhil Sindhanai M Parvath[1]*; Rajesh Balakrishnan[1]*; Selvamani Backianathan[1]; Patricia Sebastian[1]; Raju Titus Chacko[2]; Rima S[3]

[1]Department of Radiation Oncology, Christian Medical College, Vellore - 632004. Tamil Nadu, India.

[2]Department of Medical Oncology, Christian Medical College, Vellore - 632004.

[3]Department of General Pathology, Christian Medical College, Vellore - 632004.

***Corresponding Author(s): Ezhil Sindhanai M Parvath[1] & Rajesh Balakrishnan[2]**

[1]Department of Radiation Oncology, Christian Medical College, Vellore - 632004. Tamil Nadu, India.

[2]Department of Radiation Oncology, Christian Medical College, Vellore - 632004. Tamil Nadu, India.

Tel: +91-9944436360 & +91-9442169744;

Email: ezhilsindhanai@gmail.com; rajeshb@cmcvellore.ac.in

Received: Mar 15, 2024

Accepted: April 04, 2024

Published Online: April 11, 2024

Journal: Annals of Oncology Case Reports

Publisher: MedDocs Publishers LLC

Online edition: http://meddocsonline.org/

Keywords: Sacral chordoma; Metastasis; Targeted therapy; Lenvatinib.

Abstract

Chordomas are rare tumors that grow slowly, tend to recur locally and seldom metastasize. They originate from residual primitive notochordal tissues along the axial skeleton and are typically found in the sacrococcygeal region (50%), clivus (35%), and vertebral bodies (15%). The median reported survival is 6.29 years with a 10-year survival rate of 39.9%. In this report, we describe the case details of a patient with sacral chordoma who developed metastases to the lungs, liver, and bones, which is a rare occurrence. He was treated with multiple lines of therapy, resulting in a longer survival.

A 40-year-old gentleman was evaluated for low back pain and was diagnosed to have sacral chordoma. He underwent R2 resection followed by radiation therapy. After four years, he developed metastases in the T11-12 vertebral body. He had surgery and histopathology confirmed metastatic chordoma and he was offered adjuvant radiation therapy and was started on Imatinib, but he defaulted the treatment. Nine months later, he was found to have metastases in the liver, lungs, and bones. Biopsy from the liver lesion was confirmed as metastatic chordoma, He was treated with Pazopanib, which was later changed to Lenvatinib on progression, and he continued to receive the treatment until the present time, showing a partial treatment response for 18 months before disease progression.

Molecular targeted therapies have been shown to provide effective local control and prolong survival in patients with chordoma. Since this disease tends to progress slowly, long-term follow-up is critical, and patients should be evaluated for local recurrence or metastasis based on their symptoms. Asymptomatic patients should also undergo surveillance CT scans during follow-up to detect potentially treatable recurrences.

Cite this article: Ezhil Sindhanai MP & Rajesh B, Backianathan S, Sebastian P, Titus Chacko R, et al. Metastatic Sacral Chordoma - A case report unveiling the Achievements and Progress in Recent Management Strategies. Ann Oncol Case Rep. 2024; 4(1): 1017.

Introduction

Chordomas are rare, primarily malignant tumors that grow slowly and very rarely metastasize. They arise from persistence of primitive notochordal remnants along the axial skeleton. They commonly occur in the sacrococcygeal region (50%), clivus (35%) and vertebral bodies (15%). The median survival reported is 6.29 years and a 10-year survival of 39.9% [1].

We present the details of a patient with sacral chordoma with lung, liver, and bone metastases to add tothe growing number of reports of metastasis from sacral chordoma, and a long survival following metastasis after multiple lines of treatment especially targeted therapy.

Case

A 41-year-old gentleman was evaluated for lower back pain radiating to bilateral S1 dermatomes for 1-1/2 years in July 2016 with progressively worsening of urinary and bowel incontinence and sexual dysfunction. There was no motor deficit. Clinically, he had decrease in touch and pain sensation by 50% in bilateral S2 dermatomes and absent in the S3-5 dermatomes. Bilateral knee jerks were present while the ankle jerks were absent.

On evaluation, he had a 10x7x8 cm presacral mass extending from S2 to the coccyx with erosion of thesacral ala and extension of the mass into the sacral foramina. CT guided biopsy confirmed it as chordoma. His treatment details and clinical status thereafter are depicted in Figure 1, 2. His clinical condition improved after the initial treatment until the next progression and he remained clinically stableafter each treatment course after relapse.

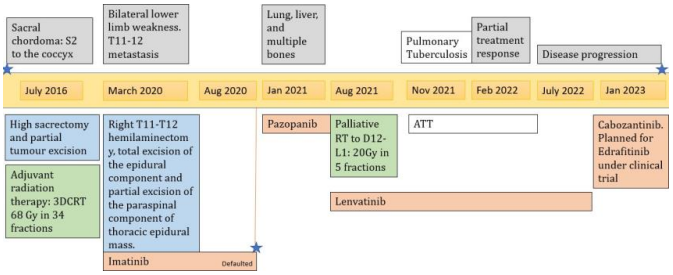

Figure 1: Timeline of disease status, management and treatment response.

At his last follow up, in January 2023, reassessment imaging showed disease progression withsignificantly increased soft tissue density adjacent to right ischium and gluteus maximus muscle. He was offered options of Edrafitinib or Cabozantinib. He was started on Cabozantinib.

Discussion

Chordomas are locally aggressive and extremely rare tumors that typically arise from the sacrococcygeal region. A significant proportion of patients, ranging from 5 to 30%, may present with locoregional relapse and distant metastasis, with reports of spread to various sites including the lymphnodes, liver, lungs, peritoneum, skin, heart, brain, and spine [2-9]. However, patient survival with metastatic disease can vary widely and depends on both the site of primary and metastasis. Metastatic disease is always associated with a poor prognosis. The median survival from the time of initial diagnosis was 130.4 months for patients who developed metastatic disease and 159.3 months for thosewho did not (P = 0.05) [8].

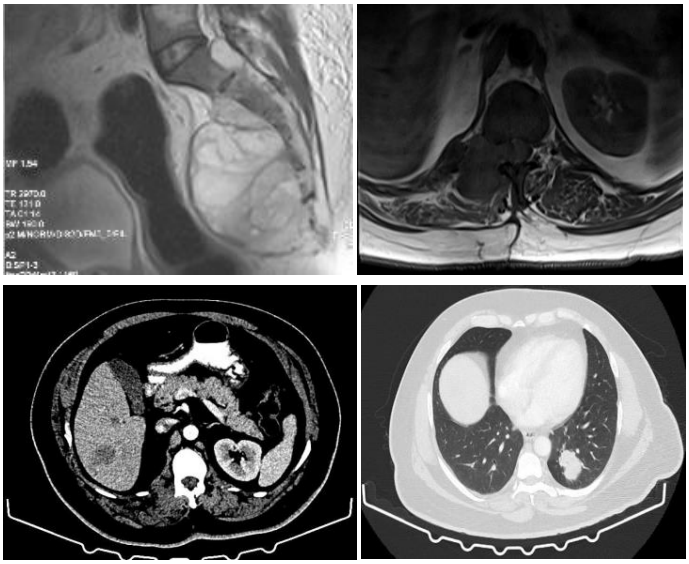

Figure 2: **(a)** MRI showing a 10x7x8 cm presacral mass extending from S2 to the coccyx with erosion of the sacral ala and extension of the mass into the sacral foramina.
(b) MR image showing a soft tissue lesion extending into spinal foramina at T10 vertebral body level with erosion.
(c) Axial section of CT scan showing liver lesion.
(d) Axial section of CT scan showing lesion in lower lobe of left lung.

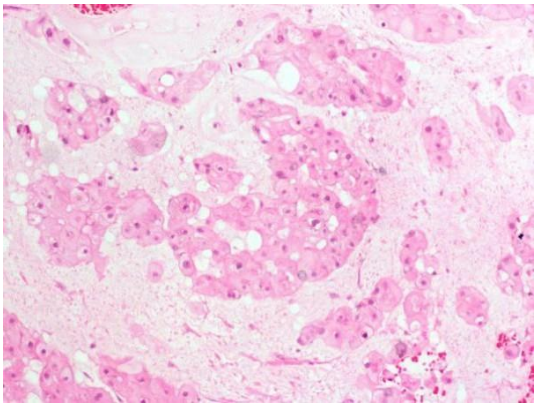

Figure 3: Nests and cords of tumour cells set in a myxoid matrix - (X200) - H&E stain.

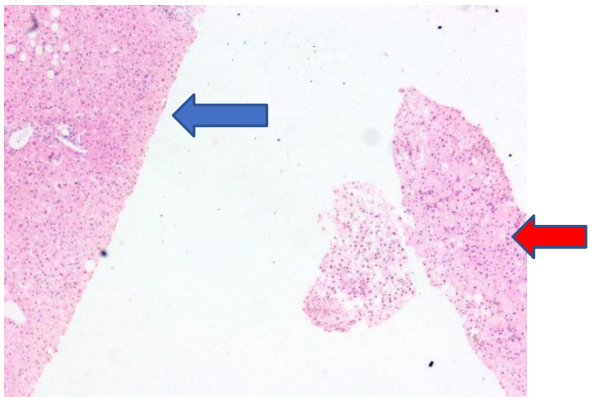

Figure 4: Nests and cords of tumour cells set in a myxoid matrix - (X200) - H&E stain.

Histopathology

Rarely chordomas have been reported to undergo dedifferentiation when it recurs and significantly worsens prognosis [10]. The biopsy for our patient did not show any dedifferentiated component, but asmall focus of chondroid differentiation was observed. Positive markers for S-100, pan cytokeratin, and brachyury are consistent with a diagnosis of chordoma [4].

Surgery

Chordomas tend to be locally destructive requiring en bloc resection and reconstruction in most cases. Our patient underwent high sacrectomy and partial tumour excision leaving behind some tumor which was infiltrating the right sacroiliac joint and the S1 vertebral body. A right gluteal myocutaneous advancement flap cover was used to close the defect. On surgical histopathology, tumour reached uptothe nearest inked soft tissue and bone resection margin.

Radiation therapy

The use of radiation therapy as a primary or adjuvant treatment for chordomas is a topic of debate. However, it is recommended for patients with surgically inaccessible lesions, positive or close surgicalmargins, or incomplete removal of the tumor. High dose radiotherapy with surgery has proven to favorably affect the disease free interval [11]. 5-year local control with conventional radiation therapy at 40-60Gy was only 10-40%. With advances in radiation techniques like SBRT, Proton and Carbonion therapy, more strategic targeting of neoplasms with higher doses of radiation is feasible, with 2 year local control 90% [12-14].

Our patient received adjuvant radiation therapy following initial resection in 2016 with 3D conformal radiation therapy to a total dose, 68Gy in 34 fractions. He was clinically well, ambulating and pain freefor 3 years and 2 months.

Follow up

Chordomas have varied biological behaviours, being aggressive or indolent [15,16]. Follow-up recommendations for chordoma patients are scarce, but due to their high risk of recurrence and metastasis, yearly imaging is suggested. The patient in this case study experienced his first metastasis to T11-12 vertebral body at 38 months after initial treatment requiring surgery and palliative radiation therapy [16]. However, after a year, imaging showed metastases to the liver, lungs, and bones along withlocal disease recurrence.

Systemic therapy

Chordomas are generally not responsive to conventional chemotherapy. Several molecular targeted therapies have been used in patients with recurrent or metastatic disease. Chordomas generallyoverexpress Platelet Derived Growth Factor Receptor-β (PDGFRB) and its phosphorylated form, whereas PDGFRA and KIT are less commonly expressed but phosphorylated and thus activated. Imatinib, a multiple tyrosine kinase inhibitor, mainly BCR-ABL, PDGFRA, KIT and PDGFRB has been used in treatment of chordomas likely by switching off of all three receptors [3]. Other drugs include epidermalgrowth factor receptor inhibitors (cetuximab, gefitinib, erlotinib) and mTOR pathways inhibitors (sirolimus, Everolimus, Rapamycin) [6]. Monotherapy with TKIs is recommended as the first-line management, and for drug resistant chordoma, a combination therapy (two TKIs or TKI plus mTOR inhibitor) may be tried [17]. Brachyury vaccine has shown promising therapeutic strategy but requires more clinical trials to evaluate its safety and efficacy [18].

Our patient was started on Imatinib after the first disease progression/ metastasis. With the next progression, he was started on Pazopanib and later Lenvatinib. But he continued to have stable diseaseor partial response and later progressed.

Conclusion

Adequate safe resection is the preferred treatment for chordomas. Adjuvant therapy is controversial, but it does contribute to long-term disease control and survival. The involvement of Hub genes PDGFRB, KDR, and FGF2 in the pathogenesis of chordoma through the PI3K-AKT signalling pathwayand the Rap1 signalling pathways enables molecular targeted therapy for better disease control and longer survival [17] As this disease has an indolent course, regular long-term follow-up is essential and a work-up for possible local recurrence or metastatic workup based on the symptomatology should be done. In asymptomatic patients at follow-up, surveillance CT scans can detect potentially treatable recurrences.

Strengths and weakness

Metastatic chordomas generally have a poor prognosis and survival. Our patient had a longer survival with several lines of management even though had a progressive disease and has been on regular follow-up. However, the quality-of-life assessment would have helped in complete assessment.

Acknowledgements: The author offers many thanks to all staff of the Department of Radiation Oncology, Department of Medical Oncology, and Department of Pathology for supporting all works.

References

1. McMaster ML, Goldstein AM, Bromley CM, et al. Chordoma: Incidence and survival patterns in the United States, 1973-1995. Cancer Causes Control 12, 1-11 (2001).
2. McPherson CM, Suki D, McCutcheon IE, Gokaslan ZL, Rhines LD, et al. Metastatic disease from spinal chordoma: A 10-year experience. J Neurosurg Spine. 2006; 5(4): 277-80.
3. Rohatgi S, Ramaiya NH, Jagannathan JP, Howard SA, Shinagare AB, et al. Metastatic Chordoma: Report of the Two Cases and Review of the Literature. Eurasian J Med. 2015 ; 47(2): 151-4.
4. Gleghorn K, Goodwin B, Sanchez R. Cutaneous Metastasis from Sacral Chordoma. Am J Dermatopathol. 2017; 39(4): e54-7.
5. Komanapalli C. Chest Wall Invasion from Metastatic Chordoma. 2023. https://www.ctsnet.org/article/chest-wall-invasion-metastatic-chordoma
6. Stefàno PL, Barletta G, Andrei V, Cerillo AG, Nesi G, et al. Cardiac Metastasis of Sacral Chordoma. Ann Thorac Surg. 2021; 111(5): e319-21.
7. Bai R, Zhao ZQ, Wang YX, Zhao W, Wu LS, et al. Sacral and thoracic chordoma with pulmonary metastases: A case report and review of the literature. Mol Clin Oncol. 2021; 14(1): 17.
8. Young VA, Curtis KM, Temple HT, Eismont FJ, DeLaney TF, et al. Characteristics and Patterns of Metastatic Disease from Chordoma. Sarcoma. 2015; 2015: 517657.
9. Radaelli S, Stacchiotti S, Ruggieri P, Donati D, Casali PG, et al. Sacral Chordoma: Long-term Outcome of a Large Series of Patients Surgically Treated at Two Reference Centers. Spine. 2016; 41(12): 1049-57.

10. Morimitsu Y, Aoki T, Yokoyama K, Hashimoto H. Sarcomatoid chordoma: Chordoma with a massive malignant spindle-cell component. Skeletal Radiol. 2000; 29(12): 721-5.

11. Chen K wu, Yang H lin, Kandimalla Y, Liu J yong, Wang G lin. Review of current treatment of sacral chordoma. Orthop Surg. 2009; 1(3): 238-44.

12. Walcott BP, Nahed BV, Mohyeldin A, Coumans JV, Kahle KT, et al. Chordoma: Current concepts, management, and future directions. Lancet Oncol. 2012; 13(2): e69-76.

13. Konieczkowski DJ, DeLaney TF, Yamada Y (Josh). Radiation Strategies for Spine Chordoma: Proton Beam, Carbon Ions, and Stereotactic Body Radiation Therapy. Neurosurg Clin N Am. 2020; 31(2): 263-88.

14. Walser M, Bojaxhiu B, Kawashiro S, Tran S, Beer J, et al. Clinical Outcome of Sacral Chordoma Patients Treated with Pencil Beam Scanning Proton Therapy. Clin Oncol. 2021; 33(12): e578-85.

15. Erkmen CP, Barth RJ, Raman V. Case report: Successful treatment of recurrent chordoma and bilateral pulmonary metastases following an 11-year disease-free period. Int J Surg Case Rep. 2014; 5(7): 424-7.

16. Azarpira N, Solooki S, Sepidbakht S, Mardani R. Humeral metastasis from a sacrococcygeal chordoma: A case report. J Med Case Reports. 2011; 5(1): 339.

17. Xu G, Liu C, Liang T, Zhang Z, Jiang J, et al. Gene expression profile and bioinformatics analysis revealed key molecular characteristics of chordoma-before and after TNF- a treatment. Medicine (Baltimore). 2020; 99(3): e18790.

18. Meng T, Jin J, Jiang C, Huang R, Yin H, et al. Molecular Targeted Therapy in the Treatment of Chordoma: A Systematic Review. Front Oncol. 2019; 9: 30.