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

Ezhil Sindhanai M Parvath¹; Rajesh Balakrishnan²; Selvamani Backianathan¹; Patricia Sebastian¹; Raju Titus Chacko²; Rima S³

¹Department of Radiation Oncology, Christian Medical College, Vellore - 632004. Tamil Nadu, India.
²Department of Medical Oncology, Christian Medical College, Vellore - 632004.
³Department of General Pathology, Christian Medical College, Vellore - 632004.

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.

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

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 to the 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-S5 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 the sacral 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 stable after each treatment course after relapse.

At his last follow up, in January 2023, reassessment imaging showed disease progression with significantly 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 those who did not (P = 0.05) [8].
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 chordoid 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 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 surgical margins, 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 Carbon ion 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 30 conformal radiation therapy to a total dose, 68Gy in 34 fractions. He was clinically well, ambulating and pain free for 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 with local 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 generally overexpress Platelet Derived Growth Factor Receptor-β (PDGFRB) and its phosphorylated form, whereas PDGFRα and KIT are less commonly expressed but phosphorylated and thus activated. Imatinib, a multiple tyrosine kinase inhibitor, mainly BCR-ABL, PDGFRα, KIT and PDGFRB has been used in treatment of chordomas likely by switching off of all Hub genes PDGFRB, KDR, and FGF2 in the pathogenesis of chordoma through the PI3K-AKT signalling pathway and 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.

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 pathway and 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.

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References


