



## Case Report

# Indolent multicentric chordoma – A previously undescribed entity: A Case report and literature review

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## ABSTRACT

**Background:** Chordomas are rare neuraxial tumors arising from remnants of primitive notochord. They are generally slow-growing malignant neoplasms. Only four adult cases of multicentric chordomas have been reported, all with aggressive and rapid growth. Here, we present an unusual case of indolent multicentric chordomas involving cervical and thoracic spine, sacrum, and calvarium.

**Case Description:** A 60-year-old male was found to have multiple lesions throughout his neuroaxis incidentally on workup for colitis. A needle biopsy documented the diagnosis of chordoma. This has been followed for more than 4 years with no progression.

**Conclusion:** We present the first reported case of indolent multicentric chordomas. Due to the extreme rarity of indolent multicentric chordomas, close follow-up is needed and recommended.

**Keywords:** Chordoma, Indolent, Multicentric

## INTRODUCTION

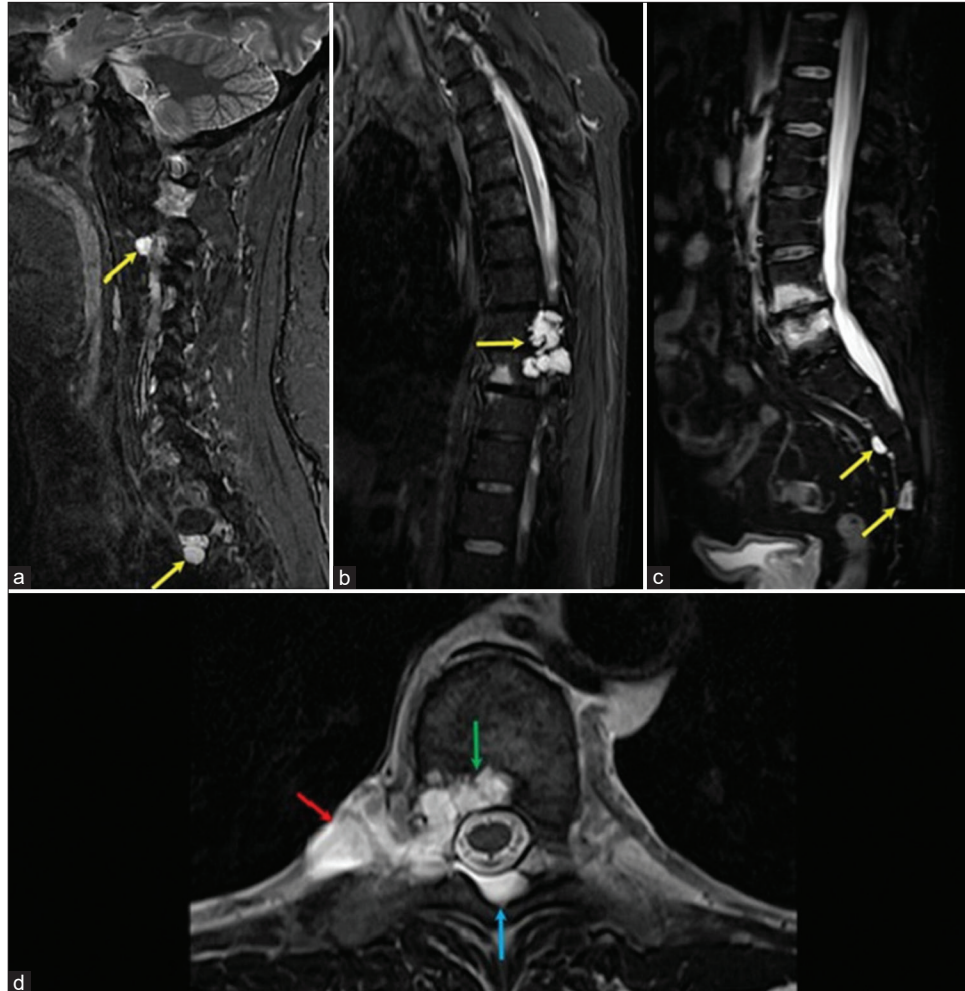
Chordomas are rare neuraxial tumors arising from remnants of primitive notochord. Chordomas generally are slow-growing malignant neoplasms, usually with aggressive clinical behavior with invasive bony erosion.<sup>[4,7]</sup> Only four adult cases involving multiple neuraxial regions, known as multicentric chordomas, have been reported.<sup>[1,5,8,10]</sup> Here, we present an unusual case of indolent multicentric chordomas involving cervical and thoracic spine, sacrum, and calvarium.

## CLINICAL PRESENTATION

A 60-year-old man with newly diagnosed colitis presented for a computed tomography (CT) scan of the abdomen for assessment. This incidentally demonstrated osteolytic lesions of the spine. CT and magnetic resonance imaging (MRI) scans of the entire neuroaxis were performed showing multiple lesions involving the cervical/thoracic spine, sacrum, and left parietal scalp/bone, Figure 1. MRI scans demonstrated multiple mildly enhancing spinal lesions with high T2 signal best seen on STIR (yellow arrows) at C2-3, C3-4, C5-6, T2-3, T3-4, T8-9, S2-3, and S4

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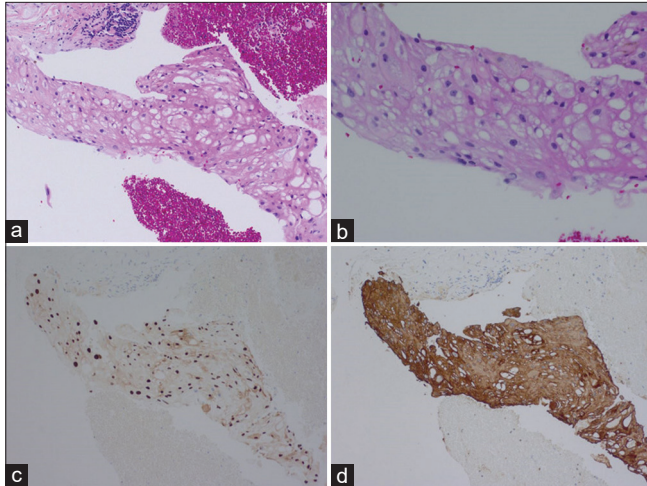
**Figure 1:** (a) STIR magnetic resonance imaging (MRI) parasagittal view of the cervical spine. (b) STIR MRI mid-sagittal view of thoracic spine. (c) MRI STIR mid-sagittal view of lumbar/sacral spine. (a-c) shows multiple mildly enhancing spinal lesions with very high T2 signal best seen on STIR (yellow arrows) at C2-3, C3-4, C5-6, T2-3, T3-4, T8-9, S2-3, and S4 levels. These lesions have variable bone and soft tissue involvement. (d) T2 axial image of the dominant lesion at T8-9 level, showing a lobulated T2-hyperintense lesion with well-defined margins involving bone (green arrow) with paraspinal (red arrow) and epidural (blue arrow) extension.

levels. The dominant lesion at T8-9 level shows a lobulated T2-hyperintense lesion with well-defined margins involving bone (green arrow) with paraspinal (red arrow) and epidural (blue arrow) extension. Initial neurosurgical consultation was obtained and immediate surgery was recommended. Because he was asymptomatic, the patient sought a second opinion, and serial observation was suggested.

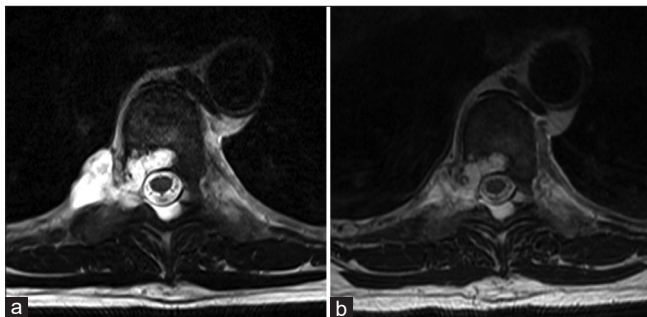
The patient sought a third opinion 2 years later after developing mild left calf and foot pain. A needle biopsy of the dominant lesion at the T8-9 level was performed in July 2020. Histological analysis of the paraspinal mass biopsy was consistent with chordoma. The specimen contained nests and lobules of cells with rounded nuclei and abundant eosinophilic vacuolated cytoplasm focally, with myxoid material seen

in the background, [Figure 2]. Immunohistochemical stains demonstrated that the tumor cells were positive for brachyury and AE1/3, supporting the diagnosis of chordoma. It was recommended that he be treated with proton beam radiosurgery for a 9-week period. A positron emission tomography scan was performed which showed the known lytic lesions; however, there was no fluorodeoxyglucose uptake.

He then presented at our facility for another opinion about optimal management of his condition in November, 2020. He underwent updated MRI scans of his entire neuroaxis to see if the lesions grew. The MRI scans showed no change in all locations. Figure 3 shows a comparison of T2 axial slices, through the dominant lesion at T8-9 level, showing no change of the area encroaching around the spinal cord.



**Figure 2:** (a and b) H&E sections from T8-9 vertebral body mass demonstrating enlarged multivacuolated and physaliphorous cells with round to ovoid nuclei. Immunohistochemical staining demonstrates strong nuclear positivity for brachyury (c) and strong cytoplasmic staining for AE 1/3 (d) These pathologic findings are classic for chordoma.



**Figure 3:** Axial T2 magnetic resonance imaging of the predominant lesion at T8-9. (a) Is from September 2018 outside films, (b) Is from November 2020. The area encroaching around the spinal cord has not changed.

Continued serial observation without further intervention was recommended. He has since had repeat imaging in November 2021 and May 2022 that, again, show no change in all of the lesions.

## DISCUSSION

The differential diagnosis for multiple vertebral body lytic and T2 hyperintense lesions includes metastasis, multiple myeloma, or plasmacytoma. Periosteal or exophytic lesions, which may be in atypical chordoma locations, can be mistaken for benign cysts. After the pathology slides from the biopsy were sent to our facility for review by our pathologist, the diagnosis was confirmed as multicentric chordoma.

Echordosis physaliphora was taken into consideration. Both chordoma and echordosis physaliphora are notochordal

remnants with the same characteristic pathological features. However, echordosis physaliphora is usually in a clival location and does not enhance with gadolinium infused MRIs.<sup>[9]</sup> There are no multicentric cases of echordosis physaliphora in the literature to date. Our patient's lesions are contrast enhancing and multicentric; therefore, the diagnosis of multicentric chordoma was made. Our patient is truly a multicentric case of chordoma rather than a metastatic case since the latter would indicate aggressive, spreading, and growing lesions. Our patient's multiple lesions have been stable for at least 2 years, and likely longer, as they were discovered incidentally.

Little is known about multicentric chordomas, as there have only been four previous cases in the literature.<sup>[1,5,8,10]</sup> The most common locations of chordomas are typically involving clival or sacrococcygeal regions, accounting for only 1–4% of primary bone tumors.<sup>[13]</sup> Up to 30% can develop distant metastasis including lungs, bone, liver, and soft tissues.<sup>[16]</sup> The first published case of multicentric chordoma was reported back in 1968 in a patient with skull base and sacral chordomas.<sup>[1]</sup> The histology was identical in both specimens, showing the characteristic chordoma physaliferous cells and intra- and extra-cellular mucus.

The literature on multicentric chordomas is scant<sup>[1,5,8,10]</sup> as most appear as single lesions with the ability to metastasize late. However, a retrospective review by Sebro *et al.* found that 16% of patients with chordomas were found to have other lesions in their axial skeleton consistent with chordoma.<sup>[15]</sup> The most common locations of chordomas are the sacrococcygeal area (50%), skull base (35%), and vertebral bodies (15%).<sup>[11]</sup> When chordomas appear in the vertebral bodies, they are more often located in the lumbar spine (61%), followed by cervical (28%), then thoracic (11%).<sup>[10,13]</sup>

Chordomas are remnants of notochord and are made up of epithelioid cells, with a dual epithelial-mesenchymal differentiation, immersed in a myxoid stroma. Chordomas are typically positive for EMA, cytokeratin, S100, and brachyury. Brachyury is a transcription factor involved in notochordal differentiation; its positivity is useful in the differential diagnosis from chondrosarcoma<sup>[16]</sup> and is thought to serve as an important diagnostic and prognostic biomarker.<sup>[12]</sup>

The gold standard of treatment for chordoma is surgery with wide margins; however, more than 50% can recur after treatment.<sup>[2-4]</sup> Treatment of chordomas is rapidly changing as new molecular developments emerge. In patients with inoperable chordomas or progressive disease, imatinib has been shown to arrest tumor growth.<sup>[7]</sup> Adding combinations with other targeted therapies, such as mTOR inhibitors,<sup>[17]</sup> adds to the possible armamentarium. Brachyury-specific T-cell activation has been explored with Phase 1 clinical trials through vector-based vaccines, showing promise.<sup>[6]</sup>

Chordomas are relatively radioresistant, requiring high-dose radiation therapy. Since chordomas are located around critical neuronal structures, highly conformal proton beam radiation is used. Resection, combined with chemoradiation increases the overall 5-year survival from 50% to 65%.<sup>[14]</sup>

## CONCLUSION

Despite the advancements in treatment for chordomas, little is known about multicentric chordomas, especially ones that are stable. Indolent lesions such as in our patient, with incidentally found multicentric chordomas, with the evidence of no progression for over 4 years have not been reported. We plan close follow-up, with his most recent stable imaging from May 2022, with serial imaging over the next 5 years. The entity of indolent multicentric chordoma is novel, and to the best of our knowledge, ours is the first reported case in the literature.

Verbal consent was obtained from the patient.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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## Conflicts of interest

There are no conflicts of interest.

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