



Original Article

# Chordoma: study of five cases

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## Keywords:

Chordoma;  
Notochord;  
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## ABSTRACT

**Background:** Chordoma is a rare slow growing but malignant midline bone tumor arising from the notochordal remnant and recapitulates the notochord at various stages of differentiation. They involve the axial skeleton. The aim of this study was to find the frequency of this tumor and to analyze the clinical, radiological and pathological findings.

**Materials and Methods:** Cases of chordoma diagnosed at B & B Hospital from January 1999 to November 2011 were studied for clinicopathologic features and immunohistochemical profile.

**Results:** There were 5 cases of chordoma during the study period. Females were affected more with male to female ratio of 1:1.5. Sixty percent of the tumors involved the sacrum, while 40% were intracranial and located at the base of the skull. Median age of diagnosis was 44.8 years. Four cases (80%) were conventional chordoma and 1 case (20%) was a chondroid variant. Two cases evaluated were immunoreactive for S-100 protein, pan-cytokeratin and EMA.

**Conclusion:** Though a low grade tumor with prolonged clinical course, chordomas can cause extensive local destruction with significant morbidity and mortality. Hence a prompt diagnosis with adequate excision is important to save the patient's life.

## INTRODUCTION

Chordoma is a rare malignant tumor that arises from the notochordal remnant.<sup>1,2</sup> It usually affect the sacrococcygeal region in adult, the sphenoccipital region in children.

It is a low to intermediate grade tumor and account for 1 to 4% of all primary malignant bone tumors.<sup>2,4</sup> In almost all cases, it occurs in the midline of the axial skeleton and affect men much more often than women with the male to female ratio of 2:1.<sup>2,6</sup> Most patients are in their fifth to seventh decades of life.<sup>4</sup> About 60% of the cases occur in the sacral region, 25% in the sphenoccipital / nasal and 15% in the cervico-thoraco-lumbar spine.<sup>3</sup> Chordomas grow slowly<sup>4,7</sup> but its treatment is difficult.<sup>2</sup> Prognosis has

improved with the modern surgical techniques of resection especially with tumors of the sacrum and the spine.<sup>3</sup> Its natural history is characterized by repeated episodes of local recurrences and an often fatal outcome.<sup>7</sup> Metastasis occurs to lungs, bone, soft tissue, lymph nodes and skin.<sup>3</sup> Patients surviving for a long time have significant morbidity due to neurological deficit.<sup>6</sup>

The aim of this study was to evaluate the cases diagnosed as chordoma in B&B hospital over the last decade and to correlate their clinical, radiological, pathological and immunohistochemical findings.

## MATERIALS AND METHODS

This was a retrospective study performed in the pathology department of B&B hospital. All necessary clinical and pathological details of the cases diagnosed with chordoma

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from January 1999 to November 2011 were retrieved from hospital record. Clinical and radiological features, histopathological findings, treatment and follow-up data were analyzed, and histopathological slides were reviewed. Blocks were collected and immunohistochemical evaluation for S-100 protein, cytokeratin and EMA performed in 2 cases. This was done using monoclonal antibodies (DAKO) with antigen-antibody streptavidin immunoperoxidase technique.

## RESULTS

There were 5 cases of chordoma during the study period of 12 years, which represented <1% of all bone tumors. Mean age of diagnosis was 44 years, with age ranging from 36-51 years.<sup>8</sup> Three (60%) of the patients were female and 2(40%) were male. Two (40%) were intracranial tumors located in the base of the skull, one involving the clivus and the other suprasellar region. The other 3 (60%) involved the sacrum.

Those with involvement of the base of the skull had symptoms due to raised intracranial pressure, including headache, vomiting and dizziness. The pain was typically aggravated on bending forward, lifting heavy weight and on exertion and was not relieved despite taking medicines. The patients with suprasellar tumor also had bilateral loss of vision with third nerve palsy and complete ptosis of right eye. She had diminished vision for past one month. However, power and sensation of all four limbs were intact. Patients with involvement of the sacral region had symptoms ranging from severe back pain with radiation to the lower limbs along with its weakness to constipation and difficulty in defecation. There was no history of trauma.

All the patients underwent surgical resection of the tumor, which was very difficult with the suprasellar tumor and the patient succumbed during the post-operative period.

MRI of all cases showed masses located in the affected regions(fig.1). The intracranial tumors were large sized, one showing destruction of the clivus and compression of adjacent structures with posterior displacement of the brainstem. There was also displacement of the posterior wall of the nasopharynx compressing the lumen. The other had mass in the sella extending to suprasellar cistern and

sphenoid sinus with involvement of right cavernous sinus. The sacral tumors showed lytic destructive lesions involving variable sacral regions and two of them with large presacral masses.

Grossly all the tumors were received in multiple pieces with lobulated and myxoid appearance. One of the intracranial tumors showed presence of hemorrhagic and necrotic areas and another one had abundant bluish cartilaginous structures.

Microscopically the tumors showed vaguely lobular architecture (fig.2) separated by fibrous septae (fig.3) and presence of large tumor cells with abundant vacuolated cytoplasm and paracentral to eccentrically situated nuclei (physaliphorous cells; fig.4). Some of the tumor cells were seen in cords and were small with eosinophilic cytoplasm and placed in a background of abundant myxoid matrix (fig.5). Mitotic figures were scanty. One of the intracranial tumors showed abundant cartilage of variable maturity. Hemorrhage and necroses were also seen in the other intracranial tumor.

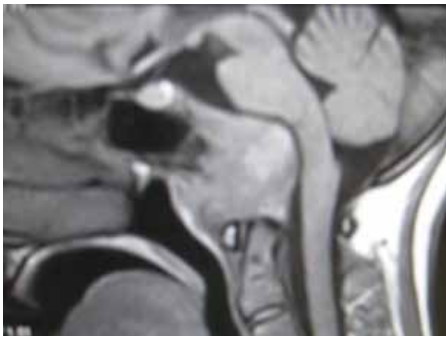
Both the tumors in which immunohistochemical evaluation was performed showed strong immunoreactivity with antibodies against S-100 protein and Pan-cytokeratin and Epithelial Membrane Antigen (fig.6, 7, 8).

## DISCUSSION

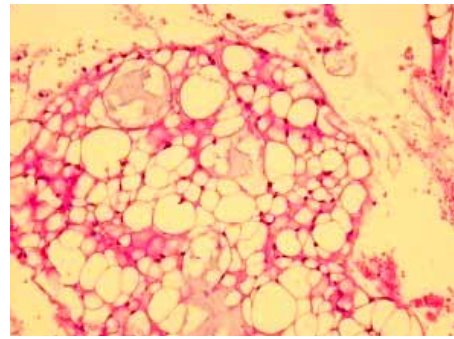
Chordoma is a rare malignant tumor that recapitulates the notochord.<sup>2,3,8</sup> It arises from the embryonic notochordal remnants along the length of the neuraxis at developmentally active sites.<sup>9</sup> Hence, it always occurs in the midline<sup>6</sup> of the axial skeleton.<sup>2</sup> All the cases in our study also involved the midline skeleton as with the cases described previously, thus further supporting its source of origin. In 1857, Virchow originally described chordomas when he named them ecchondrosis physaliphora, believing they were cartilaginous in origin. In 1895, Ribbert pierced a nucleus pulposus and found similar tumors. From this bit of evidence, he correctly surmised the notochordal origin of chordomas.<sup>9</sup> This is confirmed by the recent evidence that brachyury, a transcription factor involved in notochordal development, is detectable in the disease.<sup>1</sup>

**Table 1: A profile of patients with Chordoma**

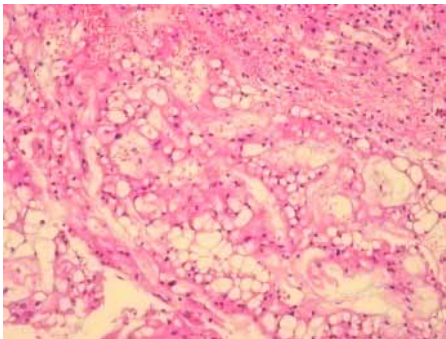
Case #	Age	Sex	Site of Tumor	Tumor Variant	Immunohistochemical profile		
					S-100	Pan-cytokeratin	EMA
1	4	F	Sacrum	Conventional Chordoma	NA	NA	NA
2	51	M	Sacrum	Conventional Chordoma	NA	NA	NA
3	36	F	Base of Skull (Clival)	Chondroid Chordoma	+ve	+ve	+ve
4	46	F	Base of Skull (Suprasellar)	Conventional Chordoma	+ve	+ve	+ve
5	47	M	Sacrum	Conventional Chordoma	NA	NA	NA



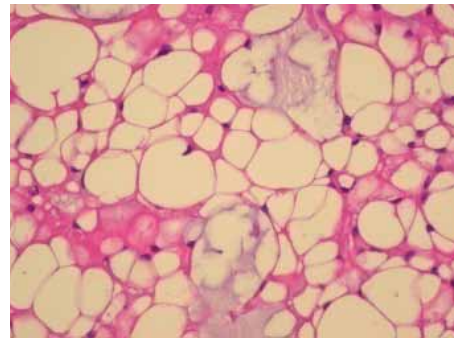
**Figure 1:** MRI image of clival tumor.



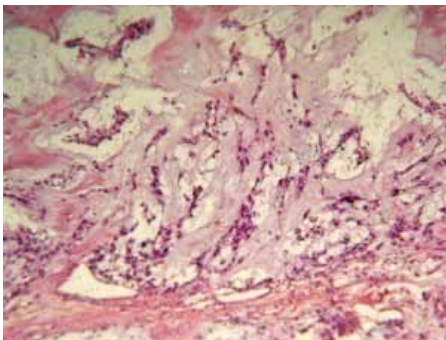
**Figure 2:** Tumor cells arranged in lobules (HE stain, X400).



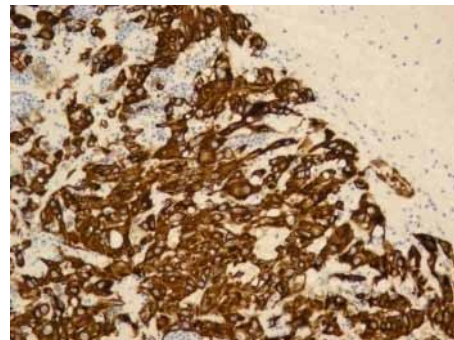
**Figure 3:** Tumor cells with adjacent fibrous septa (HE stain, X100).



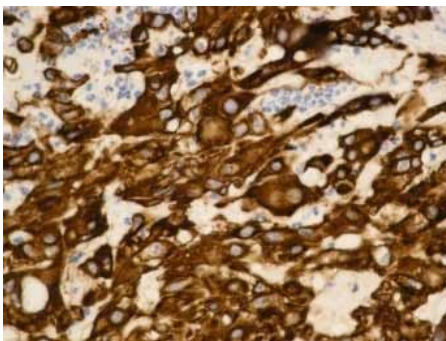
**Figure 4:** Physaliphorous cells with abundant vacuolated cytoplasm and paracentral to eccentrically situated nuclei (HE stain, X400).



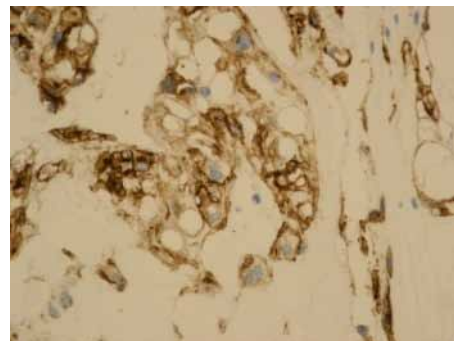
**Figure 5:** Small eosinophilic tumor cells within abundant background myxoid material (HE stain, X100).



**Figure 6:** Strong immunohistochemical reactivity for S-100 protein (Original magnification, X100).



**Figure 7:** Immunohistochemical reactivity for pan-cytokeratin (Original magnification, X100).



**Figure 8:** Immunohistochemical reactivity for EMA (Original magnification, X100).

Chordoma account for 1% to 4% of all bone tumors.<sup>2</sup> Rarity of the disease is also supported by our observation. There were only 5 cases representing <1% of all primary bone tumors found during the period of 12 years in a busy orthopedic center. However, the number could have significantly increased if the study involved a cancer care hospital.

Chordomas tend to occur at either ends of the spinal column.<sup>6</sup> About 50% arise in the sacrococcygeal area, 35% in the spheno-occipital area and the remainder along the cervico-thoraco-lumbar spine.<sup>7</sup> In Mayo clinic files more than half of all chordomas involved the sacrum, and 37% involved the clivus.<sup>5</sup> In a study done by Silvia Stacchiotti et al in Italy a total of 138 consecutive patients were identified, of which sacrum was involved in 78%, lumbar spine in 15% and cervical-dorsal spine in 7%.<sup>1</sup> Notochordal remnants that are extradural are most common at the sacrococcygeal region. Possibly this explains the sacrococcygeal region being the most common site of involvement.<sup>9</sup> Three of our cases involved the sacrum. The remaining two were in the intracranial location, one with involvement of the clivus and the other in the suprasellar region. Chordomas involving the sellar region are extremely rare. According to a recent review, only 22 patients have been described as possessing primarily intrasellar chordoma since 1960 and 43% of the patients were primarily diagnosed with a pituitary adenoma.<sup>10</sup> In our case series the preoperative diagnosis for one of the intracranial lesion was pituitary tumor. The rate of misdiagnosis might occur mainly because intrasellar chordomas mimic the clinical and imaging presentations of pituitary adenomas.<sup>10</sup> Although unusual, the suprasellar tumor has been included in the small number of cases in our study. It was aggressive in nature and was responsible for loss of vision and the mortality. Our study has followed the involvement of common axial spinal locations. Thoracic or lumbar vertebral tumor was not seen or any extra-axial tumor.

Its biological behavior is characterized by a generally slow aggressive local growth with a low to late tendency in metastasizing to distant sites including the lung, bone, soft tissues, lymph nodes, liver and skin.<sup>11</sup> Eventually, they may be responsible for mortality. All our patients also complained of having symptoms for more than a year to two years. Resection was difficult in all cases. However, four of them survived the postoperative period, whereas in one case with involvement of the skull, the tumor was large with extensive destruction of the adjacent structures along with third nerve palsy causing loss of vision. This patient did not survive. This shows that chordoma, though a low grade tumor with slow growth, may assume a large size enough to cause destruction of the local structures with significant morbidity and even mortality. Distant metastasis was not observed in any of the patients during the time of presentation. The disease recurrence and metastases, which may have occurred during the later periods, however, could

not be followed.

The clinical presentation is entirely dependent on the location of the chordoma. At the sacrum, common presenting symptoms are back and/or lower extremity pain. About one half of patients with chordomas have autonomic symptoms, particularly rectal dysfunction or urinary incontinence. About one half of patients with chordomas have a palpable sacral mass.<sup>9</sup>

With intracranial tumors, the most common presenting symptoms are diplopia and headache. Neurologic signs also occur in over one half of the patients, primarily as cranial nerve palsies. Palsies of cranial nerve VI and the sensory branch of V are the most common.<sup>9</sup> Both of our patients with intracranial tumors presented with severe headache, vomiting and dizziness. Third nerve palsy with loss of vision and inability to open eye was seen in one of them. Uncommon clinical presentations of intracranial tumors include CSF rhinorrhea, nasal obstruction, nasal bleeding, and subarachnoid hemorrhage.<sup>12</sup> None of these features were found in both of our patients with intracranial tumors.

When considering all locations, the male-to-female ratio is 2:1. However, skull base tumors, as a subgroup, tend to have a more equal sex distribution.<sup>9</sup> In this study female patients were more than male. This result probably is due to very small number of cases in the study.

Chordomas most commonly present after the age of thirty<sup>3</sup>, the sacrococcygeal tumors are more common in the fifth and sixth decades of life.<sup>7</sup> It is distinctly uncommon in patients younger than twenty years of age; the tumors in this age group tend to occur in the base of the skull and the cervical spine.<sup>5</sup> All the patients in our study were more than thirty years of age, thus involving the usual age group.

Four of the cases were conventional chordoma, while one of the intracranial tumors was a chondroid variant. The chondroid variant shows evidence of chondroid differentiation, in close proximity to zones of more conventional chordoma.<sup>4</sup> These occur exclusively in the spheno-occipital region<sup>4</sup> and reported to be associated with a better prognosis.<sup>3,6</sup> In 1973 Heffelfinger et al described chordomas of the base of the skull that showed prominent chondroid differentiation.<sup>6</sup>

This tumor is characterized by a dual epithelial mesenchymal differentiation, with immunostaining positive for EMA, cytokeratin, and S100.<sup>1</sup> The immunohistochemical evaluation performed in two of our cases followed similar pattern.

The vast majority of patients with chordoma have no other family member with this tumor. However, recent studies suggest that rare genetic or hereditary factors may increase the risk of relatives developing chordomas in some families,

which has been concluded by National cancer Institute, Genetic Epidemiology Branch as a mutated gene located on chromosome 7.<sup>8</sup> This aspect of the disease needs to be explored in our future study of chordomas.

## CONCLUSION

Chordoma is a rare neoplasm with a slow growth. However despite its indolent nature it has a potential for significant local destruction with resultant morbidity. Any cartilaginous tumor arising from the base of the skull with involvement of clivus should be suspected as chondroid variant of chordoma rather than a chondrosarcoma.

## ACKNOWLEDGEMENTS

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