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***Chapter 4***

# SPINAL CHORDOMAS

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## ABSTRACT

Spinal chordomas are a rare group of primary bony tumors of the axial skeleton. Though histologically they are classified as benign tumors, their indolent growth pattern allowing for sizable tumors at presentation and a high rate of recurrence place them into the category of functionally malignant spinal tumors.

Histologically, they have unique cellular architecture that are often pathognomonic for their diagnosis. Management and surgical treatments have advanced significantly over the last few years allowing for an increase in progression free survival.

Despite all that is known about spinal chordomas, there is much more that needs to be studied and learned. But it remains true that treating a patient with a spinal chordoma requires a multidisciplinary team approach, with neurosurgeons, neurologists, oncologists, radiation therapists and nurses working together. In this chapter, we discuss each of these topics in more detail.

## INTRODUCTION

Chordomas are rare benign tumors of the axial skeleton that are the most common primary malignant tumors of the spine in adults, typically occurring in middle-age adults [1]. They are most commonly seen along the clival skull base and sacrum, but may occur along the cervical, thoracic, or lumbar spine as well [2]. They present a unique challenge to neurosurgeons due to their growth within the spine and spinal canal, and their propensity to grow to immense sizes in the pelvis prior to clinical detection.

Chordomas are derived from undifferentiated notochord remnants that are found within the developing axial skeleton. [3]. Molecular studies have confirmed that these particular cells are the neoplastic cells that undergo transformation and uncontrolled division in chordoma tumors [4].

## PRESENTATION AND NATURAL HISTORY

Spinal chordomas are indolent tumors of the spine and skull base [5]. Due to their slow growth pattern, surrounding tissues are able to accommodate to the presence of this growing tumor [6]. This leads to the presentation of these tumors as extensive lesions with significant distortion of neighboring bone, tissue, and neural elements [6].

Thus, though these tumors are classically benign on histopathology, through their indolent growth pattern and high recurrent nature they functionally act as malignant oncologic lesions [6].

Sacral chordomas comprise 30% of spinal chordomas [1]. Spinal chordomas of the cervical, thoracic and lumbar spine are rare, with the lumbar spine being the more commonly encountered of the three [1]. Of known primary tumors of the sacral elements, chordomas account for over 50% of these tumors [7]. Chordomas are not classically seen in the pediatric population [1]. They are most commonly seen in males around 50-60 years of age [1].

The Surveillance, Epidemiology, and End Results (SEER) database detailed a median survival of 6.29 years with 5 year, 10 year, and 20 year survival decreasing abruptly to 68%, 40%, and 13%, respectively [1]. Factors that have been noted to affect survival include incomplete margins at the time of resection, large tumor burden initially, and degree of expansion of chordoma into nearby vital structures [8].

The clinical presentation of chordomas varies depending on the location. For example, patients with sacral chordomas most commonly present with localized low back pain with or without radicular symptoms [9]. Depending on the extent of tumor burden, patients may or may not present with bowel or bladder dysfunction.

Patients with cervical or thoracic chordomas may present with early myelopathy due to spinal cord compression [10]. Lumbar chordomas may present with focal back pain and/or radiculopathy from nerve root involvement of tumor [10]. Compared to cervical spine chordomas, sacral chordomas are less likely to present with neurological compromise [10].

## IMAGING

Chordomas may present in a variety of ways on imaging modalities. X-rays of the lumbosacral spine may demonstrate spotty areas of calcification, usually in tumors that are quite large.

The sacral spine may demonstrate remodeling on x-ray due to local growth. However x-rays typically do not capture the distal sacrum and so may miss tumors in this area [10]. Computerized tomography (CT) of the lumbosacral spine may also demonstrate areas of bony remodeling much more clearly than x-ray.

Further, chordomas presenting along the foramina may cause widening of the sacral foramina, visible on CT or x-ray. Chordomas along the posterior border of the vertebral bodies may demonstrate thinning and remodeling of the body locally. Magnetic resonance imaging of the lumbosacral spine will more clearly demonstrate an enhancing mass with associated soft tissue involvement around the spinal elements as well as nearby neural structure compression.

Additionally, chordomas typically invade the disc space in the spine, distinguishing them from other tumors [10]. PET CT may be used to detect any metastatic disease elsewhere upon presentation [10].

## DIFFERENTIAL DIAGNOSES

Spinal chordomas can mimic many other tumors of the spine. The differential diagnosis for these tumors include chondromas, chondrosarcomas, giant cell tumors the spine, multiple myeloma, and metastatic disease.

## MANAGEMENT

The histology of tumors is critical forproviding an accurate clinical diagnosis which will guide appropriate and focused treatments. For example, differentiating between a metastatic tumor, chordoma and chondrosarcoma is paramount in determining treatment and prognosis [10]. Therefore, it is often recommended to perform a fine needle CT-guided biopsy to obtain tissue diagnosis prior to any surgical or adjunctive therapy.

## PATHOLOGY

Chordomas classically are described as lobulated and rubbery tumors with a grayish-white color on gross pathology [11]. They are noted to have multiple fibrotic septae isolating various compartments of the tumor. They typically are not locally invasive or malignant. However, theirindolent growth processallows for remodeling of the neighboring bony structures of the spine as well as slow compression and distortion of nearby neural elements without the classical erosion seen in other bony tumors [11].

Histopathologically, chordoma cells have round nuclei with vacuolated cytoplasm. This abundant cytoplasm is what distinguishes this group of tumors from all others. The term given to chordoma cells due to their microscopic appearance is physaliferous, denoting presence of bubbles or vacuoles. Microscopically, chordoma cells react intensely for S-100 and other epithelial markers such as cytokeratins and epithelial membrane [12, 13].

There are various histopathologic varieties of chondromas. They may manifest as classical, chondroid or de-differentiated [14]. Chondroid chondromas classically show features of both chordoma and chondrosarcoma, a malignant cartilaginous tumor [14]. Brachyury, a notochordal developmental transcription factor, has recently emerged as a factor in the diagnosis of chordomas [15]. Identifying brachyury as a biomarker, along with cytokeratin staining, enhances the specifity and sensitivity of chondroma diagnosis to 100% and 98%, respectively [15]. These markers have proved helpful in distinguishing chondromas from other tumors of chondroid origin.

Significant research has been performed studying the various genetic properties of chordomas. It has been shown that certain receptors are overexpressed in these tumor cell lines, such as platelet-derived growth factors A/B and KIT receptors [16]. Studies

demonstrating reactivity of imatinib and sunitinib, a tyrosine-kinase inhibitor acting at the platelet-derived growth factor receptor level, have shown decreased tumor volume in patients with chordomas [17]. Other tumor markers include epidermal growth factor [EGF] receptor overexpression with EGF receptor inhibition studies done showing decreased tumor volume [18].

## CONSERVATIVE/ADJUNCTIVE TREATMENT STRATEGIES

Medical management in the treatment of spinal chordomas is typically done in anticipation of future surgical curative procedures. Pre-operative chemotherapy with alkylating agents and cisplatin have shown a better response rate in the de-differentiated subytpes [19]. The typical chemotherapeutic agents have been shown in multiple reviews to be a minimal clinical significance in the treatment of spinal chordomas [20].

Radiotherapy alone has been proven to be ineffective for the treatment of chordomas and has given them the classification of radioresistant tumors [10]. Doses of 40-60 Gy provide a 5-year local control of 10-40 % [10]. Proton beam therapy has gained momentum as an adjunctive treatment for chordomas with decreasing tissue injury and local control of tumor volume with 5-year local control rate of 50-60% [21].

Other radiation treatments currently under investigation include the use of carbon ion radiotherapy, along with helium and neon radiotherapy. Generally, the current recommendations are en bloc surgical resection along with post-operative proton beam radiotherapy, especially in patients with primary chordomas as opposed to recurrent tumors [22]. Recurrence may be managed with both re-operation or continued chemotherapy and radiation treatments, depending on the particular case [22].

## SURGICAL TECHNIQUE

Recent evidence in the literature confirms that en bloc resection of sacral chordomas with wide margins provides a significantly increased progression free survival. This strategy was first described in 1970 by Gunterberg et. al. in an attempt to cure these tumors [23].

Surgical technique depends on the location of the tumor. For example, surgical treatment for cervical chordomas is quite complex. Cervical chordomas are classified into three different types based on location in the cervical spine: C1-C3 are high cervical tumors, C5-C6 are mid cervical tumors, and C7-T1 are cervicothoracic tumors. En bloc resection is almost impossible for all types of cervical chordomas often due to the inability to sacrifice surrounding structures such as nerve roots and the vertebral artery, without causing significant neurological compromise [24].

Thus cervical chordomas are often treated with intralesional resection. The general approach for cervical chordomas is to perform release osteotomies and posterior tumor dissection with placement of instrumentation and posterolateral arthrodesis in the first stage. During the first stage, any sacrifice of nerve roots or the vertebral artery is performed. The second stage, typically 2-5 days after stage 1, involves anterior tumor dissection, en bloc excision of tumor, and anterior vertebral reconstruction [25].

High cervical chordomas generally require sacrifice of C1-4 nerve roots without risk of significant neurological deficits. However, vertebral artery sacrifice here can lead to severe neurological impairment. A cerebral angiogram with temporary balloon occlusion test is recommended pre-operatively. To achieve an en bloc resection for high cervical chordomas, a submandibular or transmandibular approach is needed. A high rate of posterior occipito-cervical fusion constructs is seen with this fusion and reconstruction procedure [25].

Mid cervical chordomas do not allow for sacrifice of the nerve roots or the vertebral artery. Pre-operative cerebral angiogram is once again recommended. An anterior approach using a modified Smith-Robinson approach with radical dissection of the soft tissues of the spine is performed with standard anterior and posterior column reconstruction [25].

Cervicothoracic chordoma resection does not allow nerve root sacrifice due to neurological impairment that may result. Vertebral arteries may be dissected free and preserved in this area. Anterior transcervical approach or median sternotomy may be performed for en bloc resection. Anterior and posterior reconstructions are then performed in standard fashion [25].

Thoracic chordomas may be approached in multiple stages as well. Typically stage 1 involves the posterior approach for long segment cervicothoracic instrumentation with vertebral release at the levels of interest.

Thoracic nerve roots may be sacrificed and the plane between the segmental arteries needs to be dissected to access anterior to the spinal canal. Tomita saws are then tunneled anterior to the spinal cord in preparation for the next stage. The ribs at the appropriate levels are subtotally resected as well. In stage 2, a lateral thoracotomy is performed to separate the soft tissue attachments to the vertebral bodies and tumor, and to reposition the Tomita saws. In stage 3, the vertebrectomy is completed via a left thoracotomy and appropriate reconstruction is performed [26].

Lumbar and sacrococcygeal chordomas are surgically managed in the standard 2 stage approach, with an initial posterior multilevel instrumentation and fusion with posterior element release, followed by an anterior en bloc resection with or without vertebral reconstruction, depending on extent of sacrectomy and preservation of sacroiliac joints [27]. Additionally, excision of the tumor must also include the removal of the biopsy tract and may involve the removal of a large region of skin. Multidisciplinary approaches with plastic surgery involvement should be considered for closure of large, complex skin defects.

An important factor to consider when performing sacrectomies is attempting to salvage the S2 nerve root. This is associated with a 50% chance of normal bowel and bladder function post-operatively, with sacral 3 root preservation increasing that percentage even higher. It has been shown that bilateral sacral 2 nerve root sparing along with unilateral sacral 3 root sparing is associated with normal bowel and bladder function [27]. If en bloc resection dictates resection of the sacral nerve roots, unilateral resection can result in acceptable clinical outcomes.

Unilateral preservation of S2-S5 results in satisfactory bowel control and minimal bladder and sexual dysfunction.

For ambulation, bilateral L5 and above must be spared for satisfactory gait, however bilateral S2 and above must be spared to walk normally (23-25).

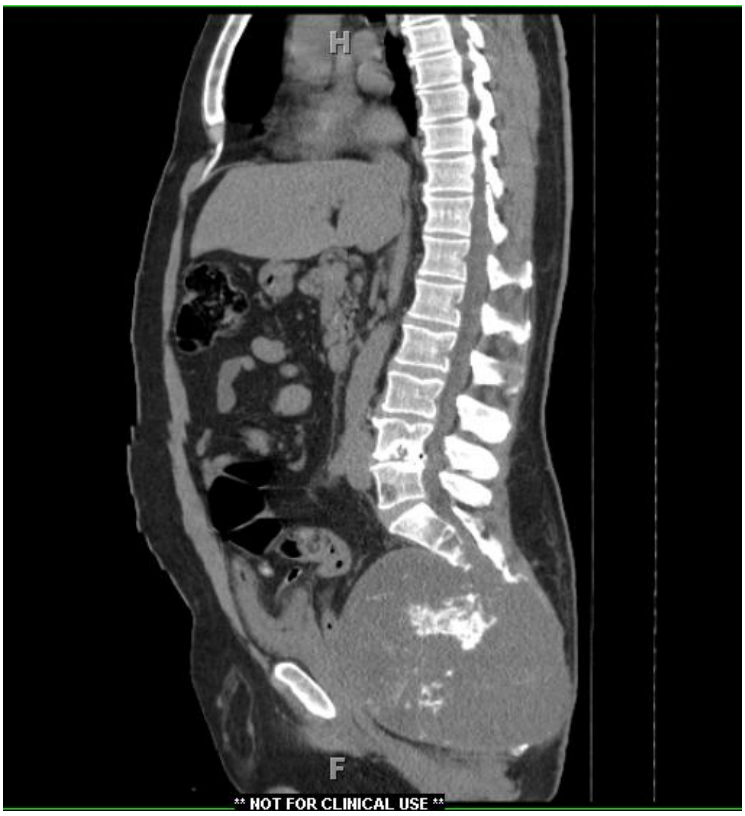


Figure 1. Pre-operative CT of sacrum showing large expansile tumor of the sacrum (The Johns Hopkins Hospital).

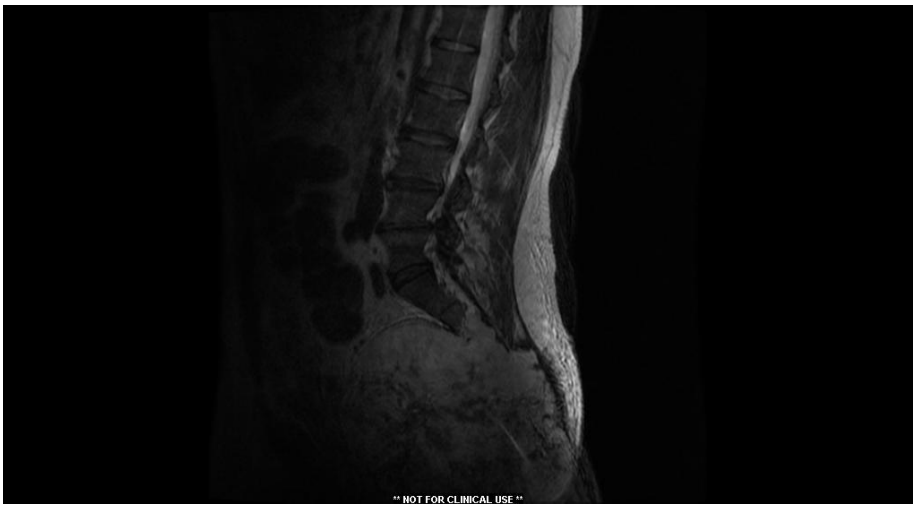


Figure 2. Pre-operative MRI of the sacrum showing a large expansile tumor of the sacrum with significant distortion of the surrounding tissues (The Johns Hopkins Hospital).

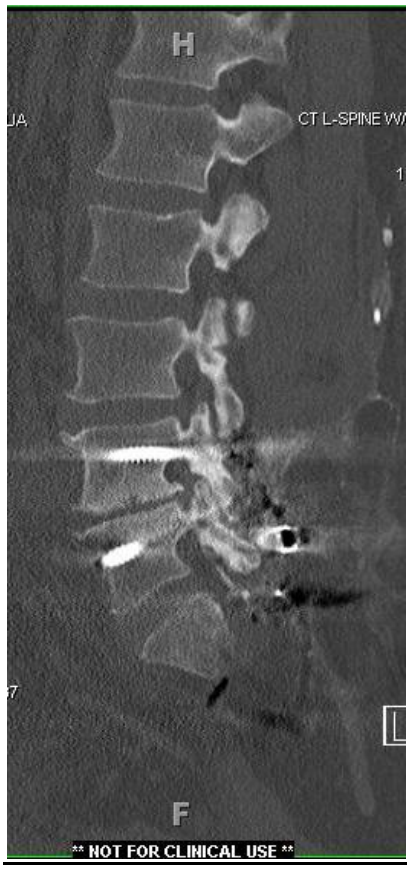


Figure 3. Post-operative CT scan of the lumbosacral spine showing a long segment lumbo-iliac posterior fixation and fusion and complete sacrectomy (The Johns Hopkins Hospital).

## OUTCOMES

En bloc resection of sacral chordoma affords the best prognosis for patients. [28] A two fold higher rate of local recurrence has been reported if the tumor capsule is violated during en bloc resection [29]. Subtotal resection recurrence rates have been reported to be around 8 months compared to the over 2 years recurrence rate with en bloc resection [28].

Metastatic disease for chordomas is quite rare but 5% of patients may present with lesions in the bone, lungs, and brain [28, 29]. Typically, however, local disease is considered the main problem affecting survival rather than metastatic disease [30].

## RECENT GENETIC AND MOLECULAR ADVANCES

The recent advent of using brachyury, a notochordal developmental transcription factor, along with cytokeratin staining has increased the diagnostic accuracy of chordomas dramatically. This gene is commonly seen in patients with the familial and sporadic chordomas [31].

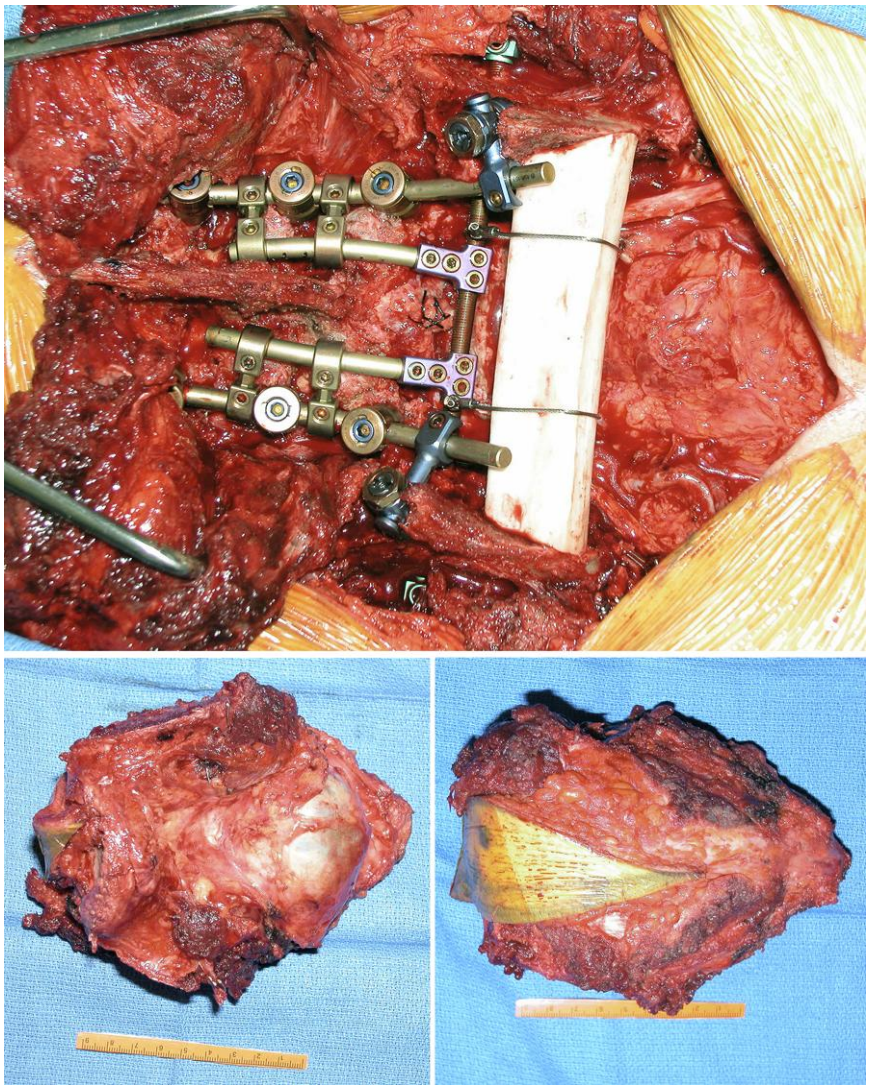

Figure 4. Gross specimen en bloc resection of sacrococcygeal chordomas along with post-operative posterior instrumentation (The Johns Hopkins Hospital).

Additionally, the discovery of tyrosine kinases and epidermal growth factor receptors, in addition to the platelet-derived growth factor receptors have led to ongoing clinical projects looking for possible inhibitory effects on chordoma tumor volume [32].

## SUMMARY

1) There are a wide variety of tumors along the sacral spine that may mimic chordomas requiring accurate diagnostic strategies prior to any surgical procedure.
2) En bloc resection of chordomas without violation of tumor capsule have demonstrated increased survival compared to en bloc resection with violation of tumor capsule.

3) Surgical treatment depends on location of tumor along spinal axis but generally involves multiple stages.
4) Adjunctive proton-beam radiotherapy is recommended after surgical resection.
5) Note that despite the more aggressive surgical approach toward patients with sacral chordomas, the ultimate goal is preservation of a patient's neurological function and quality of life, ahead of the desire for gross total resection.

## CONCLUSION

Spinal chordomas are rare benign tumors that may act aggressively through growth and expansion of surrounding neural and bony tissues. Patients may present with or without neurological disturbance depending on the level of the chordoma. Diagnosis involves magnetic resonance imaging of the spine demonstrating this tumor. Diagnosis often involves needle biopsy with pathology demonstrating the classic physaliferous cells of the chordoma. Surgical treatment includes multiple stages with an initial posterior segmental instrumentation followed by anterior en bloc resection of the pathologic sacrum and tumor with wide margins as appropriate. Chemotherapy and/or radiation may be used as pre-operative or post-operative adjunctive treatments. Finally, optimal care for the patient with sacral chordoma requires a true team approach, including members of neurosurgery, plastic surgery, nursing, oncology, and radiation therapy.

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