International Journal of
Science Inventions Today
www.ijsit.com
ISSN 2319-5436
Review Article

CHORDOMA: RARE MALIGNANT BONE TUMOR RADIOLOGICAL FINDING CT SCAN, MRI AND BIOPSY

Dr. Abhinandan Gupta[1*], Kong Long[1], Prof. Huang Jing Bai[1], Dr. Deepikal Dhakal[1], XianWang Wang[2] and Dr. Sohan Kumar Sah [3]

[1]The First Affiliated Hospital of Yangtze University, jingzhou hubei P.R. China
Department of Medical Imaging and Nuclear Medicine, Clinical Medical College, Yangtze University, Jingzhou, Hubei, P.R. China
[2]Faculty of Medicine, Department of Laboratory Medicine, School of Basic Medicine, Yangtze University, Jingzhou, Hubei, P.R. China
[3]Department of nuclear medicine and medical imaging, clinical medical college of Yangtze university jingzhou central hospital, province- hubei, PR china

ABSTRACT

Chordoma is a rare malignant bone tumor that can arise anywhere along the central neural axis & many involve head & neck sites. It is most commonly seen in the skull base. The relative rarity of these tumors combined with the systemic anatomy of the head & neck pose diagnostic challenges to pathologist. This review article describes about related points in clinical, pathological, radiological finding & other features of chordoma & in this article we describe how these features can be used to help in formulating a differential diagnosis.

Keywords: chordoma; ct scan; mri; biopsy

INTRODUCTION

There are several type of brain tumor some are Astrocytoma, Medulloblastoma, Retinoblastoma, Chordoma, Craniopharyngioma, Oligodendroglioma, and Ependymoma[1]. In this review article explain about chordoma. Chordoma is a rare malignant bone tumor that is arises in the remnant of the embryonic notochord[2]. Chordoma are retains both epithelial and mesenchymal characters[3]. Chordoma is a exclusive body in that it is a malignant cancer derived from Remnants of the notochord, an embryonic structure that is Required for the induction of the neural plate in the embryonic disk. Among head and neck sites, the majority arise in the skull base with a small minority arising along the cervical spine. Chordomas have also been reported in extra-axial locations in the head and neck, as well as the nasopharynx, paranasal sinuses, lateral nasal wall, oropharynx, and the soft tissue of the neck (fig. 2) Some extra-axial chordomas of the nasopharynx are associated with a sinus tract extend from the clivus[4]. Chordomas tend to be slow growing tumors and symptoms of head and neck chordomas are related to mass effect with headache, neck pain, diplopia or cranial nerve palsy[4]. In the spine, they most commonly occur in the sacrococcygeal region, followed by the sphenooccipital region (fig. 3)[5]. They may, however, arise in the vertebral bodies as well, especially in the cervical spine[6]. They are uncommon tumors, representing less than 0.2% of all intracranial neoplasms[31]. Chordomas can present clinically in any age group, but their peak incidence is inpatients between 20 and 50 years of age, and less than 5% are identified in children[7] [30,31]. It is part of a group of malignant bone and soft tissue tumors called sarcomas. They can also come back, or back again, after treatment usually in the same place as the first tumor.

History:

In the beginning in 1857 Virchow give much details about chordomas when he named this disease is ecchondrosis physaliphora, believing they were cartilaginous in origin. Later than 1895 Ribbert pierced a nucleus pulposus and found similar tumors. From this bit of evidence, he in the approved manner surmises the notochordal origin of chordomas. Ecchordosis physaliphora is a term that refers to small, well-circumscribed, gelatinous masses adherent to the brainstem. Although composed of notochordal remnants, ecchordosis physaliphora seldom, if ever, progresses into chordoma[8]. Ecchordosis physaliphora is a reported finding in approximately 2% of autopsy examinations. Rare and benign intra-axial tumors of notochordal origin have been described as intraosseous benign notochordal cell tumors. These are distinguished from ecchordosis physaliphora by their intraosseous location and from chordoma by their well-demarcated radiographic appearance, bland histologic features, and lack of soft tissue extension. Although chordomas are usually slow-growing tumors, they are locally aggressive with a tendency to infiltrate into adjacent tissues and organs. Local recurrence results in tissue destruction and generally is the cause of death. Metastases are recognized but are uncommon

Epidemiology:

Chordomas are rare neoplasms. Chordomas generally occur in 3 locations, they are, the sacrum 50% of chordomas occur in the sacrum, intracranially at the clivus they only representing less than 0.2% of all

intracranial neoplasms. And along the spinal axis spinal axis chordomas are rare. When considering all locations, the male-to-female ratio is 2:1[1]. However, skull base tumors, as a subgroup, tend to have a more equal sex distribution. A number of reports indicate that chordomas are seen in all age groups, with the peak incidence varying by site. Intracranial chordomas present in a much younger age group than their spinal counterparts because the relevant anatomy of the clival region produces earlier clinical evidence. In one series of chordomas reviewed, the average age at diagnosis of all patients with chordomas was 56 years, with an average age range of 27-80 years. When considered by site, the average age for intracranial chordomas is 48 years; as a subgroup, chordomas of the sphenoccipital area have an average age is 38 years, the sacrococcygeal chordomas an average age is 56 years and vertebrae chordomas an average age is 46 years.

Chordomas account for approximately 1-4% of all malignant bone tumors and around 20% of primary tumors of the spinal column[9]. The incidence of chordoma is estimated to be approximately 1 / 1,000,000 people[1, 5]. About 300 new cases of each year are diagnosed in the United States and about 700 in all of Europe. Chordoma is diagnosed most often in people in their 50s and 60s, but it can occur at any age. Skull base chordomas occur more frequently in younger patients, while spinal chordomas are more common later in life. About twice as many men are diagnosed with chordoma as women. While chordoma can run in families, this is very rare. Chordoma is a low-grade malignant tumor arising from the remnants of the fetal notochord that usually occurs at either end of the neural axis, most often in the sacrococcygeal region (50%), followed in frequency by the sphenooccipital region (35% to 50%) and other spinal segmentregions (15%)[6] [32-35]. It almost always occurs in a sagittal or parasagittal location in relation to the spine; most commonly occurs in the fourth through seventh decades of life, with a 2:1 male is to female ratio; and is the most common primary malignant sacral tumor [36]. Grossly, chordomas are lobulated and surrounded by a pseudocapsule.

Etiology:

Chordomas are thought to arise from primitive notochordal remnants along the axial skeleton. During development, the notochord is surrounded by the developing vertebral column. In adults, remnants of the notochord are present as the nucleus pulposus of the intervertebral discs. Notochordal remnants that are extradural are most common at the sacrococcygeal region but can be found at any site along the length of the axial skeleton. The distribution of tumors matches the distribution of notochordal remnants[8]. A genetic basis has been described for some chordomas. However, most exhibit complex abnormal karyotypes including whole or partial losses of chromosomes 3, 4, 10, and 13, gains in chromosome 7, all have been implicated in the pathogenesis of chordomas[10]. Also, microsatellite instability resulting from DNA mismatch repair deficiencies has been demonstrated; however, no chordoma-specific translocations have been identified.

Presentation:

The clinical presentation is entirely dependent on the location of the chordoma. At the sacrum, common presenting symptoms are back and lower extremity pain or both can present. About ½ of patients with chordomas have autonomic symptoms, particularly rectal dysfunction or urinary incontinence. About ½ of patients with chordomas have a palpable sacral mass.

With intracranial tumors, the most common presenting symptoms are diplopia and headache[11]. 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.

Patients with tumors located along lower vertebrae may present with pain, bladder dysfunction, or lower extremity weakness. Patients with tumors located along cervical vertebrae present with hoarseness, dysphagia, and, seldom, pharyngeal bleeding. Other rare or unique symptoms have been reported but are the exception. The time span from the onset of symptoms to diagnosis is common more than 10 months or more. If they do spread, the most commonly affected places are the lungs, bone, skin and brain.

Anatomy:

The location of chordomas along the spinal canal is directly related to the location of notochord remnants, particularly at the ends of the spinal axis. Of chordomas, Sacrococcygeal is the most common location, accounting for approximately 50% of all chordomas and commonly involving the fourth and fifth sacral segments[12]. In this location, a male predilection has been reported and the tumor may be particularly large at presentation, the clival region is the second most common location, accounting for 35-50% of cases[6]. Typically the mass projects posteriorly at midline, indenting the pons; this characteristic appearance has been termed the so-called thumb sign. In contrast to sacrococcygeal tumours, there is no recognised gender difference. Vertebral chordomas of the vertebral bodies are rare, but nonetheless, after lymphoproliferative tumours, are the second most common primary malignancy of the spine in adults. They most commonly involve cervical (particularly C2), followed by lumbar, and then the thoracic spine. They often extend across the intervertebral disk space, involving more than one vertebral segment. They may extend into the epidural space compressing the spinal cord, or along the nerve roots enlarging the neural foramen[13].

Grossly, chordomas are variable in size. They are soft, gelatinous, smooth, or lobulated and are gray-white in color on their outer surface. On cut section, the tumor is homogeneous in color and consistency. Occasionally, calcifications or hemorrhages are present. Chordomas appear to be encapsulated when in soft tissue but not when they are located in bone. Chordoma is the most common primary malignant sacral tumor[14].

Pathophysiology:

Chordomas are characterized by slow growth, with local destruction of the bone and extension into the adjacent soft tissue. Very rarely, distant metastases are encountered. These tumors usually have a relatively indolent but prolonged course with multiple local recurrences. Eventually, they may be responsible for mortality.

Signs and Symptoms:

The most common signs of chordoma are pain and neurological changes.

Skull base chordomas most often cause headache, neck pain, or double vision (diplopia noted in 60% to 90% of cases) [37]. They may also affect facial sensation or movement, voice change, difficult in speech, problems in swallowing & feeling dizzy.

Chordomas of the spine and sacrum can cause changes in bowel and/or bladder function, pain, aching, tingling, numbness, or weakness of the arms and legs. Often, sacral chordomas do not cause symptoms until the tumor is quite large, and sometimes a lump is the first sign of a sacral chordoma.

Pathology Findings:

There are four subtypes of chordoma, which are classified based on how they look under a microscope[15]:

1. Conventional (or classic) chordoma is the most common form of chordoma. It is composed of a unique cell type that resembles notochordal cells and can have areas of chondroid appearance.
2. Poorly differentiated chordoma is a recently identified subtype. It can be more aggressive and faster growing than conventional chordoma, and is more common in pediatric and young adult patients, as well as in skull base and cervical patients. Pathologists can diagnose poorly differentiated chordoma by testing a tumor sample for deletion of a gene called INI-1. All poorly differentiated chordomas have loss of the INI-1 gene[9].
3. Dedifferentiated chordoma is more aggressive and generally grows faster than the other types of chordoma, and is more likely to metastasize than conventional chordoma[16]. It can also have loss of the INI-1 gene, but this is least common, worst prognosis. This type of chordoma is rare, occurring in only about 5 percent of patients, and is more common in pediatric patients[12, 16].
4. Chondroid chordoma is a term more commonly used in the past when it was difficult to distinguish conventional chordoma from chondrosarcoma. This is no longer a problem because brachyury is expressed in nearly all conventional chordomas, making them easier to distinguish from cartilaginous tumors like chondrosarcoma that do not express brachyury[17]. There is no evidence that chordomas with a chondroid appearance behave differently than conventional types that do not have this appearance. This is best prognosis [14].

Microscopically, conventional chordomas are composed of uniform cells with small oval or round eccentric nuclei and dense chromatin. The hallmark microscopic features of chordomas are the numerous, variably sized vacuoles located in the tumor cell cytoplasm, the physaliphorous cells (fig 1)[18]. Some tumor cells may have more solid or eosinophilic cytoplasm. A light microscopic view of a hematoxylin and eosin (H&E)–stained section of a chordoma showing the characteristic physaliphorous cells and mucinous matrix[18].

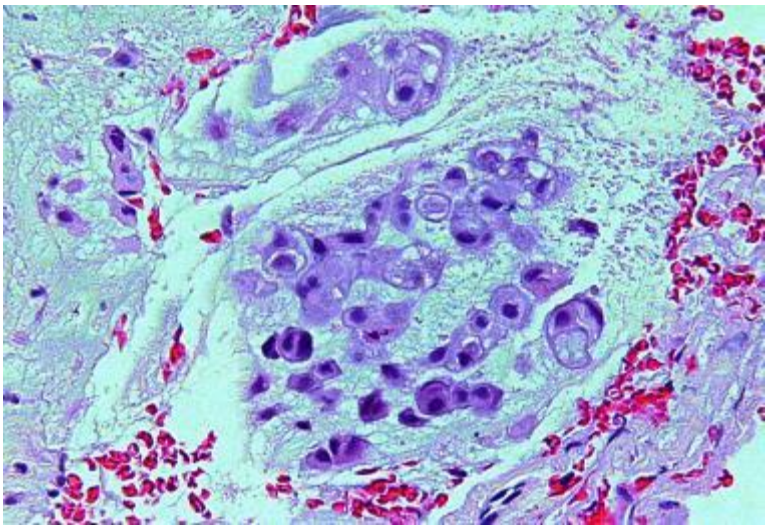


Figure 1: A higher magnification light microscopic view of a hematoxylin and eosin (H&E) stained section of a chordoma showing physaliphorous cells.

Laboratory Studies:

No laboratory studies are required for the evaluation of chordomas, except as needed for routine preoperative evaluation in patients scheduled to undergo surgical resection[8].

Diagnostic Procedures:

Chordoma tumors are typically detected through imaging tests, which show organs and other structures inside the body Plain radiographs may be useful to demonstrate the amount of bone involvement. Plain-film radiographs may show an ill-defined endosteal margin or a bulky mass in the soft tissue. The lesions also may be lytic[19]. In general, and especially in clival chordomas, erosion of the bone, particularly the tip of the clivus, and a sclerotic bone reaction are seen radiographically. The mass appears as a destructive well-demarcated lesion. The discovery of these features can better clarify the diagnosis of chordomas in the differential of bony lesions.

Imaging techniques of the clivus usually demonstrate features adequate for differentiating chordomas from other site-specific lesions. In the sacrum, radiographic features are more similar to other common bone tumors.

An MRI is the best way to see a chordoma and how it is affecting the tissue around it, such as muscles, nerves, and blood vessels. No matter where the tumor is located, an MRI of the entire spine should be performed to see if the tumor may have spread to or developed in other areas of the spine. Chordoma is best seen on an MRI with a setting called T2 weighted imaging[11].

Another imaging test called computed tomography, also called CT or CAT scan, is recommended in addition to MRI if it is not certain whether the tumor is chordoma. CT scans of the chest, abdomen, and pelvis are recommended to make sure there is no spread of tumor. CT evaluation is needed to assess the degree of bone involvement and to detect patterns of calcification within the lesion[14].

MRI provides excellent anatomical delineation of adjacent structures and is able to characterize the signal of the lesion usually allowing for a confident preoperative diagnosis. On T1-weighted MR images, the infiltrating tumor appears isointense to gray matter in 75% of patients and mildly hypointense in the remaining 25% (Fig. 2-A, B and C). In either case, the tumor presents a striking contrast to the diffusely hyperintense T1 signal of the adjacent normal marrow fat of the clivus[39,41]. On T2-weighted images, chordoma demonstrates moderate heterogeneity of signal with areas of hyperintensity intermixed with linear strands of hypointensity (Fig. 2-B)[11] [39-41]. After intravenous administration of contrast material, vary and heterogeneous contrast enhancement is seen within the tumor mass on both CT and MRI (see Fig.2-C[11, 20] [38]

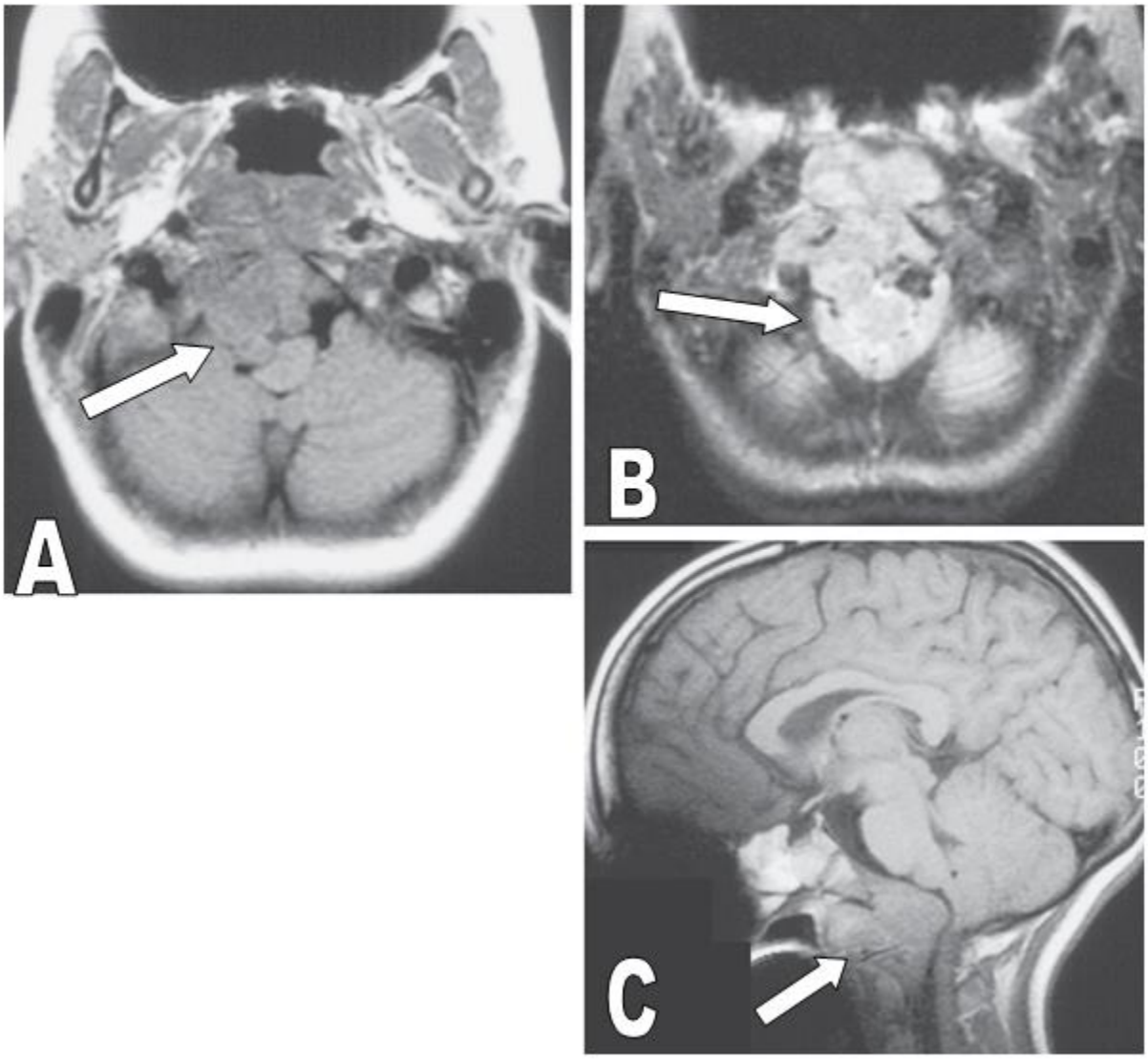
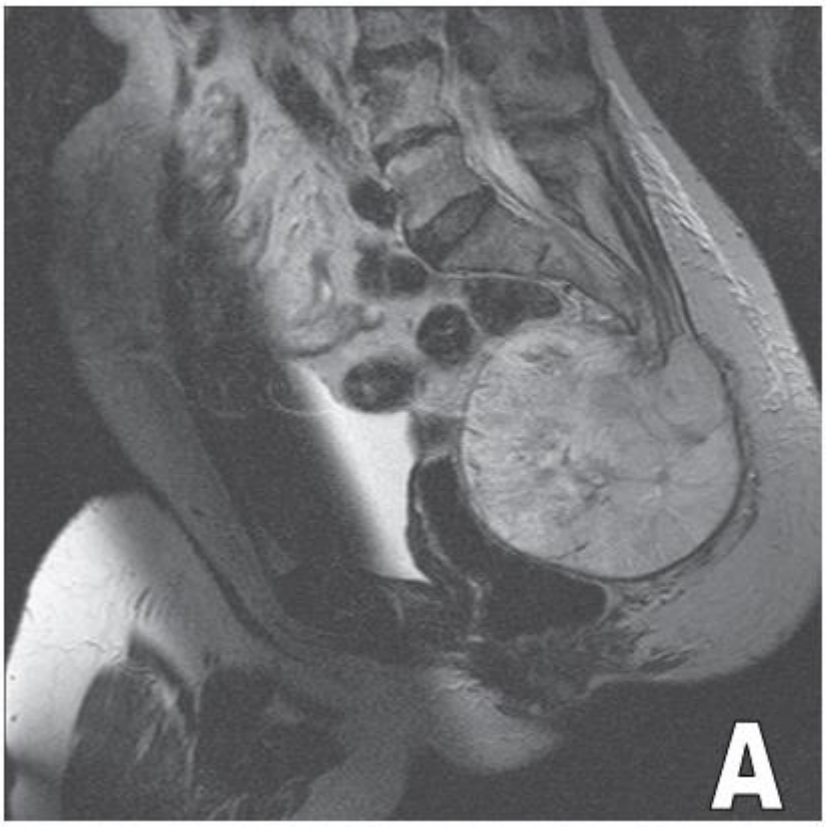


Figure 2-A, B and C: Chordoma of the lower clivus and foramen magnum. Axial T1-weighted (A) and T2-weighted (B) MR images through the level of the lower clivus demonstrate a sharply marginated lobulated mass in and to the right of the midline that is hypointense on T1 weighting and hyperintense on T2weighting and has destroyed the lower clivus, infiltrating anteriorly into the longuscolli muscles (*arrow* in B) and extending

posteriorly into the premedullary cistern (*arrow* in A), displacing the medulla posteriorly and indenting its right ventrolateral margin. In B**,** note that the tumor has encased the vertebral arteries bilaterally. C**,** Sagittal T1-weighted postgadolinium image demonstrates faint homogeneous contrast enhancement of this extensive tumor that presents anteriorly as a submucosal nasopharyngeal mass *(arrow)* and projects posteriorly to compress the medulla and upper cervical spinal cord against the posterior margin of the foramen magnum.

On radiography and CT, chordoma usually appears as a large lytic lesion in the midline, with an associated soft tissue mass. Intratumoral calcifications are common, especially in a sacrococcygeal chordoma. Sclerosis may be present[9]. On T2-weighted sequences, chordoma typically has very high signal intensity, with hypointense septations; the tumor is of low to intermediate signal intensity on T1-weighted sequences (Fig. 3 A and B). Contrast enhancement is variable. The tumor may extend into the epidural space and spread along the nerve root.



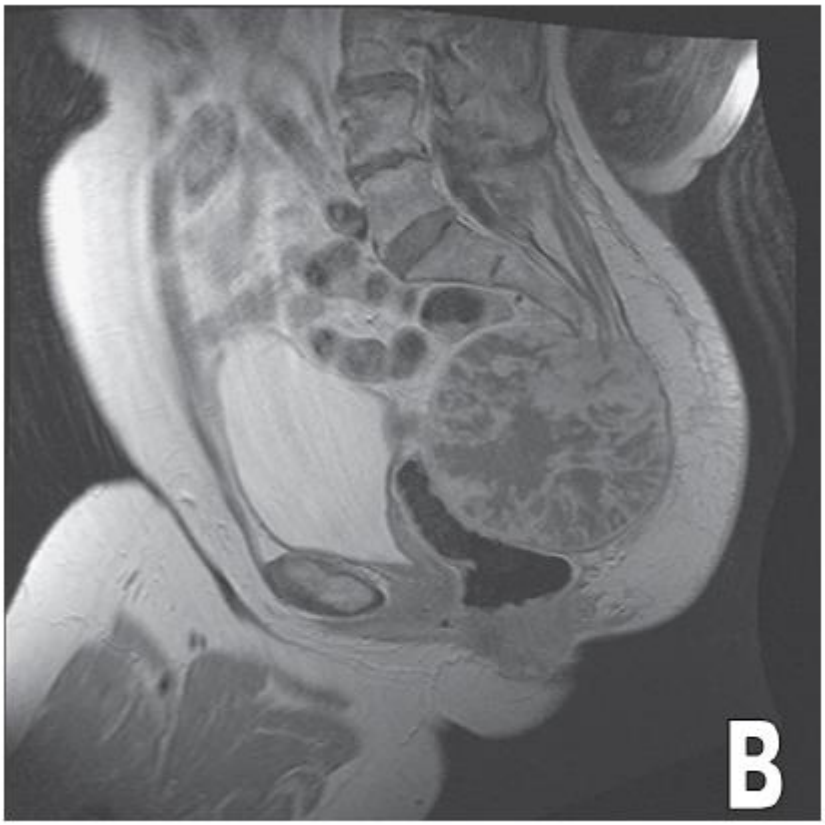


Figure 3 A and B: Sacrococcygeal chordoma. Sagittal T2-weighted (**A**) and postcontrast T1-weighted (**B**) sequences show a large, relatively heterogeneous tumor of the os coccygis.

Biopsies:

For sacral and mobile spine tumors, a trocar CT-guided biopsy is recommended and should be done from the back. Trocar CT-guided biopsy uses a CT scan to precisely direct the biopsy needle to the correct location. The biopsy needle is enclosed in a tube to keep tumor cells from spreading along the path of the needle this is often called seeding[8].

Skull base tumors can be difficult to reach safely for a biopsy, so your surgeon may opt for a biopsy during surgery. This means that a pathologist will be prepared to examine a sample of tumor tissue removed at the start of surgery and give an immediate diagnosis, and the surgical team will proceed with surgery based on that information.

Histologically, chordoma consists of clusters of large vacuolated physaliferous Greek for"bubble-bearing" cells interspersed with abundant extracellular mucinous material and separated into lobules by fibrous septa[30,31]. The clinical presentation of this slowly expanding neoplasmis insidious and depends on its precise location[21]. The majority of patients present with head or neck pain and cranial nerve deficits [31]. At histology, typical chordomas have cords of characteristic, highly vacuolated physaliphorous cells (fig.1) located in background of abundant mucin. Foci of cartilaginous tissue may be seen in chondroid chordomas. Sarcomatous elements may be encountered in dedifferentiated chordoma[42].

Treatment:

A multicenter phase II clinical trial has confirmed the clinical efficacy of imatinib mesylate in the treatment of chordoma[22]. Treatment with imatinib was successful in stabilizing tumor growth (84%) or shrinking tumor size (16%) in a cohort of patients with progressing, advanced chordoma. Imatinib is a tyrosine kinase inhibitor targeting several enzymes including platelet-derived growth factor receptor–β (PDGFRB), which can be expressed in chordomas.[22]

A combination of bevacizumab (an antivascular agent) and erlotinib (an epidermal growth factor receptor [EGRF] inhibitor) showed promising long-lasting control of chordoma growth[11]. Surgery remains the standard treatment for chordomas[23]. Adjuvant radiation therapy is used in cases in which incomplete resection is suspected However, there is a high local recurrence rate after surgery, for which palliative treatment using imaging-guided radio frequency ablation may be used[5, 24].

Preoperative Details:

As for any surgical patient, the normal preoperative history and physical are required. Other medical problems need to be stabilized or addressed (eg: cardiovascular, respiratory). Laboratory studies, including electrolytes, coagulation status, and blood count, are needed. Radiological studies (x-ray, CT scan, MRI) can be used for both evaluations of the tumor and other medical problems. Chest x-rays, ECGs, and blood cross match also may be important[10].

Contraindications:

Contraindications to surgery for excision of a chordoma primarily are related to general health of the patient and preexisting medical conditions. The patient should be evaluated for cardiac, pulmonary, hematological, or endocrine disorders as well as coagulation status[18]. These disorders need to be addressed and managed prior to surgery.

Differential diagnosis:

Chordoma is not always easy to diagnose and can be confused with other diseases, including:

Benign notochordal cell tumors (BNCT): These benign spine tumors can be seen on an MRI or CT scan and can sometimes look like chordoma. However, BNCT stay confined within the bone and do not spread into other tissues like chordomas can. If you have a suspected BNCT, you should have an MRI or CT scan from time to time to look for changes. Images should be reviewed by a radiologist with expertise in bone tumors[8, 25].

Chondrosarcoma: This type of bone cancer looks very similar to chordoma on CT and MRI. A specific type of MRI called diffusion MRI, or D-MRI, may help doctors tell the difference[9]. Sometimes it is only possible to know a tumor is not chondrosarcoma after having a biopsy. Skull base chondrosarcomas usually respond better to radiation than skull base chordomas, and have a better prognosis[3].

Giant cell tumor of the bone (GCTB): This tumor looks somewhat different on imaging tests than chordoma, and tends to be located in the upper part of the sacrum[5].

Schwannoma: These tumors damage the bone differently than chordomas do, look different on imaging tests, and do not spread to nearby muscles or joints[26].

Other tumors of the spine and skull base: These include other bone cancers such as Ewing sarcoma and osteosarcoma, as well as a type of nervous system tumor called a myxopapillary ependymoma. Lymphoma, a cancer of the body's immune system, and multiple myeloma, a blood cancer, can also cause tumors in these areas[25].

Metastasis (spread) of another cancer: Sometimes cancers in other places in the body can spread to the bones of the spine or skull base[7].

Plasmacytoma: Destructive vertebral body lesion (similar appearance to lytic metastases)[21].

Spinal lymphoma: Multifocal disease, heterogonous T2 signal[10].

Prognosis:

Metastatic disease occurs in up to 40% of patients, and the estimated 5- and 10-year overall survival rates are 87.8% and 48.9%, respectively [27]. Overall, chordomas tend to have a better prognosis than typical chordomas Chordomas are malignant and potentially life threatening tumors. Currently the median survival in the United States is about 7 years. The overall survival rates are 68% at 5 years and 40% at 10 years. The prognosis of chordomas generally depends on the extent and completeness of the tumor excision [28].

Follow-up:

Frequent follow-up is required because of the high rate of recurrence of these tumors. Tumor recurrence identified early is easier to treat. The average interval to recurrence is 3.8 years for radically resected tumors, 2.1 years for subtotal resection followed by radiation therapy, and 8 months for subtotal excision without adjuvant therapy. The interval of follow-up, including repeat MRI or CT scans, depends on the completeness of the resection. Because residual tumor drastically shortens the recurrence time, patients with known or suspected residual tumor need to be evaluated more frequently[29].

Complication:

Chordoma is a rare type of cancer that occurs in the bones of the skull base and spine. It is part of a group of malignant bone and soft tissue tumors called sarcomas. Chordomas account for about 3 percent of all bone tumors and about 20 percent of primary spinal tumors. They are the most common tumor of the sacrum and cervical spine[18]. A chordoma tumor usually grows slowly, often without symptoms at first, and then might cause symptoms for years.

Chordomas are complicated tumors to treat due to the involvement of critical structures such as the brainstem, spinal cord, and important nerves and arteries. They can also come back, or recur, after treatment usually in the same place as the first tumor.[29] This is called a local recurrence. In about 30 to 40 percent of patients, the tumor eventually spreads, or metastasizes, to other parts of the body.

CONCLUSION

Chordoma is a rare type of tumor, this disease can confirm by MRI and biopsy & chordoma can treated as well as but they can also appear back or return back again in same place as the first tumor was treated. Chordoma also called local recurrence. Most of the case saw they can spread or metastasize to other body part like lung, bone, skin and brain.

Acknowledgement:

This work was supported by grants from the National Natural Science Foundation of China (31700736), Hubei Province Health and Family Planning Scientific Research Project (WJ2016Y07), Hubei Province Scientific and Technological Research Project (Q20171306) and the College Students Innovative Entrepreneurial Training Program in Yangtze University (2018184)

Conflicts of Interest:

The authors declare no conflicts of interest

REFERENCES

1. Santegoeds, R.G.C., et al., State-of-the-Art Imaging in Human Chordoma of the Skull Base. Curr Radiol Rep, 2018. **6**(5): p. 16.
2. Pan, Y., et al., Analysis of prognostic factors for survival in patients with primary spinal chordoma using the SEER Registry from 1973 to 2014. J Orthop Surg Res, 2018. **13**(1): p. 76.
3. Almefty, K., et al., Chordoma and chondrosarcoma: similar, but quite different, skull base tumors. Cancer, 2007. **110**(11): p. 2457-67.
4. Wasserman, J.K., D. Gravel, and B. Purgina, Chordoma of the Head and Neck: A Review. Head Neck Pathol, 2018. **12**(2): p. 261-268.
5. Xu, Q., et al., Giant sacrococcygeal chordoma: A case report. Medicine (Baltimore), 2018. **97**(51): p. e13748.
6. McMaster, M.L., et al., Chordoma: incidence and survival patterns in the United States, 1973-1995. Cancer Causes Control, 2001. **12**(1): p. 1-11.
7. Redondo, A., et al., Malignant bone tumors (other than Ewing's): clinical practice guidelines for diagnosis, treatment and follow-up by Spanish Group for Research on Sarcomas (GEIS). Cancer Chemother Pharmacol, 2017. **80**(6): p. 1113-1131.
8. Yamaguchi, T., et al., Benign notochordal cell tumors: A comparative histological study of benign notochordal cell tumors, classic chordomas, and notochordal vestiges of fetal intervertebral discs. Am J Surg Pathol, 2004. **28**(6): p. 756-61.
9. Elefante, A., et al., Paravertebral high cervical chordoma. A case report. Neuroradiol J, 2013. **26**(2): p. 227-32.
10. Nguyen, R.P., et al., Extraosseous chordoma of the nasopharynx. AJNR Am J Neuroradiol, 2009. **30**(4): p. 803-7.

11. Lebellec, L., et al., Advanced chordoma treated by first-line molecular targeted therapies: Outcomes and prognostic factors. A retrospective study of the French Sarcoma Group (GSF/GETO) and the Association des Neuro-Oncologues d'Expression Francaise (ANOCEF). Eur J Cancer, 2017. **79**: p. 119-128.
12. Mobley, B.C., et al., Loss of SMARCB1/INI1 expression in poorly differentiated chordomas. Acta Neuropathol, 2010. **120**(6): p. 745-53.
13. Sciubba, D.M., et al., Chordoma of the spinal column. Neurosurg Clin N Am, 2008. **19**(1): p. 5-15.
14. Forsyth, P.A., et al., Intracranial chordomas: a clinicopathological and prognostic study of 51 cases. J Neurosurg, 1993. **78**(5): p. 741-7.
15. Chugh, R., et al., Chordoma: the nonsarcoma primary bone tumor. Oncologist, 2007. **12**(11): p. 1344-50.
16. Tomlinson, F.H., et al., Sarcomatous transformation in cranial chordoma. Neurosurgery, 1992. **31**(1): p. 13-8.
17. Jian, J., et al., The embryonic transcription factor Brachyury confers chordoma chemoresistance via upregulating CA9. American journal of translational research, 2018. **10**(3): p. 936-947.
18. Cui, F., et al., Humeral metastasis of sacrococcygeal chordoma detected by fluorine-18 fluorodeoxyglucose positron emission tomography-computed tomography: A case report. Radiology case reports, 2018. **13**(2): p. 449-452.
19. Kataria, S.P., et al., Chordoma of skull base presenting as nasopharyngeal mass. J Neurosci Rural Pract, 2013. **4**(Suppl 1): p. S95-7.
20. Abe, S., et al., Parachordoma with multiple metastases. J Comput Assist Tomogr, 2003. **27**(4): p. 634-8.
21. Gladstone, H.B., J.W. Bailet, and J.P. Rowland, Chordoma of the oropharynx: an unusual presentation and review of the literature. Otolaryngol Head Neck Surg, 1998. **118**(1): p. 104-7.
22. Stacchiotti, S., et al., Phase II study of imatinib in advanced chordoma. J Clin Oncol, 2012. **30**(9): p. 914-20.
23. Hug, E.B., et al., Proton radiation therapy for chordomas and chondrosarcomas of the skull base. J Neurosurg, 1999. **91**(3): p. 432-9.
24. Sahgal, A., et al., Image-guided, intensity-modulated radiation therapy (IG-IMRT) for skull base chordoma and chondrosarcoma: preliminary outcomes. Neuro Oncol, 2015. **17**(6): p. 889-94.
25. Deshpande, V., et al., Intraosseous benign notochord cell tumors (BNCT): further evidence supporting a relationship to chordoma. Am J Surg Pathol, 2007. **31**(10): p. 1573-7.
26. Tao, Z.Z., et al., Paranasal sinuses chordoma in pediatric patient: a case report and literature review. Int J Pediatr Otorhinolaryngol, 2005. **69**(10): p. 1415-8.
27. Jones, P.S., et al., Outcomes and patterns of care in adult skull base chordomas from the Surveillance, Epidemiology, and End Results (SEER) database. J Clin Neurosci, 2014. **21**(9): p. 1490-6.
28. Wu, Z., et al., Prognostic factors for long-term outcome of patients with surgical resection of skull base chordomas-106 cases review in one institution. Neurosurg Rev, 2010. **33**(4): p. 451-6.
29. Dabska, M., Parachordoma: a new clinicopathologic entity. Cancer, 1977. **40**(4): p. 1586-92.

30. Coons SW, Ashby LS: Pathology of intracranial neoplasms. Neuroimaging Clin North Am 9:615-649, 1999.
31. Harsh GR IV: Chordomas and chondrosarcomas of the skull base. In Kaye AH, Laws ER Jr (eds): Brain Tumors: An EncyclopedicApproach, 2nd ed. London, Churchill Livingstone, 2001, pp 857-868.
32. Dahan H, Arrive L, Wendum D, et al: Retrorectal developmental cysts in adults: Clinical and radiologic-histopathologic review, differential diagnosis, and treatment. Radiographics 21:575-584, 2001.
33. Papanicolaou N, Yoder IC, Lee MJ: Primary retroperitoneal neoplasms: How close can we come in making the correct diagnosis? Urol Radiol 14:221-228, 1992.
34. Sung MS, Lee GK, Kang HS, et al: Sacrococcygeal chordoma: MR imaging in 30 patients. Skeletal Radiol 34:87-94, 2005.
35. Sze G, Uichanco LS 3rd, Brant-Zawadzki MN, et al: Chordomas: MR imaging. Radiology 166:187-191, 1988.
36. Diel J, Ortiz O, Losada RA, et al: The sacrum: Pathologic spectrum, multimodality imaging, and subspecialty approach. Radiographics 21:83-104, 2001.
37. Forsyth PA, Cascino TL, Shaw EG, et al: Intracranial chordomas: A clinicopathological and prognostic study of 51 cases. J Neurosurg 78:741-747, 1993.
38. Doucet V, Peretti-Viton P, Figarella-Branger D, et al: MRI of intracranial chordomas: Extent of tumour and contrast enhancement: Criteria for differential diagnosis. Neuroradiology 39:571-576, 1997.
39. Lum C, Kucharczyk W, Montanera WJ, Becker LE: The sella turcica and parasellar region. In Atlas SW (ed): Magnetic Resonance Imaging of the Brain and Spine, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, 2002, pp 1283-1362.
40. Meyers SP, Hirsch WL Jr, Curtin HD, et al: Chondrosarcomas of the skull base: MR imaging features. Radiology 184:103-108, 1992.
41. Nelson JS, Bruner JM, Wiestler OD, et al: Ganglioglioma and gangliocytoma. In Kleihues P, Cavenee WK (eds): Pathology and Genetics of Tumours of the Nervous System. Lyon, International Agency for Research on Cancer, 2000, pp 96-102.
42. Murphey MD, Andrews CL, Flemming DJ, et al: From the archives of the AFIP. Primary tumors of the spine: Radiologic pathologic correlation. Radiographics 16:1131-1158, 1996.