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CHORDOMA

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SUMMARY

Chordomas are aggressive, locally invasive and rare tumors with a poor prognosis. They arise from the remnants of the embryonic notochord. They occur in the whole vertebral column, and are most commonly seen in the sacrum, the base of the skull and the mobile spine. They are usually diagnosed at a late stage with advanced growth. These tumors are minimally responsive to radiotherapy and chemotherapy, and so the main treatment is surgical resection. Survival and local control of the tumor depend on the achievement of wide resection of the tumor with appropriate surgical margins. Due to the essential anatomical localization of the tumors, the generally high stage of the tumor at the time of diagnosis, and the need for resection of important structures during surgery, a high rate of postoperative morbidity may be present.

Key words: Chordoma, sacrum tumor, benign notochordial cell tumor, spine tumor.

Level of evidence: Review article, Level V.

ÖZET

Kordomalar agresif, lokal invaziv, düşük prognozlu nadir görülen bir tümörlerdir. Embriyonik notokord artıklarından gelişirler. Tüm vertebral kolonu tutabilmekle birlikte en sık sırasıyla sakrum, kafa tabanı ve mobil omurgaları tutarlar. Genelde teşhis edildiklerinde ileri derecede büyümüş olarak bulunurlar. Bu tümörler radyoterapiye ve kemoterapiye düşük derecede yanıt verdiği için tedavinin en önemli bölümünü cerrahi rezeksiyon oluşturur. Hasta sağ kalımı ve tümörün lokal kontrolü yüksek oranda tümörün uygun cerrahi sınırlarla geniş eksizyonunun yapılabilmesine bağlıdır. Tümörün bulunduğu önemli anatomik lokalizasyonlar ve teşhis edildiğinde ilerlemiş olması ve cerrahi tedavi sırasında önemli yapıların rezeke edilmesi sebebiyle geniş eksizyon sonrasında önemli oranda morbidite gelişebilir.

Anahtar kelimeler: Kordoma, sakrum tümörü, benign notokord hücre tümörü, omurga tümörü.

Kanıt düzeyi: Derleme, Düzey V.

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INTRODUCTION:

Chordomas are primary malignant bone tumors that are rarely seen and grow slowly. They are the fourth most common malign bone tumor with an incidence of about 0.1/100,000 [22,23]. They are seen twice as frequently in males than in females and are generally observed in late decades. When they are observed in young patients, the tumor often occurs in the base of the skull, and tumors found in this region generally represent only 5% of chordomas[28]. The average age at diagnosis is 58.5 years, and the incidence increases with age[22,28].

Chordomas develop from intraosseous embryonic notochord remnants and therefore they occur in the midline, through the axial skeleton from the skull base to the coccyx. In terms of frequency, they occur most in the sacrum (50–60%), the base of the skull (25–30%), the cervical region (10%), and the thoracolumbar vertebrae (5%)[21,28]. They are usually diagnosed in the late period, as they are low-grade tumors that show a slow progression in the pelvis, deep in the sacrum. At this stage, they mostly cause wide bone destruction and invade important neurological structures[29].

Chordomas have low sensitivity to conventional radiotherapy and chemotherapy[11,13,28,37,41]. Therefore, the main treatment consists of surgical excision. The best prognosis is obtained with sacrectomy applied with wide resection borders[2,11,13,33,37]. During wide excision, complications such as ambulatory dysfunction, sexual dysfunction, and anal and bladder incontinence can be observed postoperatively in the lower extremities, due to the need for wide nerve root and ligament excision[11,13,28,37,41]. The recurrence rate is high and 5–40% metastasis is observed in patients[1-4,16,18,32,37,40]. In the literature, the 5- and 10-year survival rates after sacrectomy were reported as 45–77% and 28–50%, respectively[13,33,31,35].

CLINICAL FINDINGS:

The growth of chordomas is slow and therefore they are usually found at an advanced stage when they are diagnosed. Although the clinical findings vary according to the localization of the lesions, the most common complaint independent of localization is pain. The pain has an insidious characteristic that slowly increases[4,7]. The tumors often extend to the spinal canal and can cause compression of the medulla, cauda equina, or nerve roots. As a result, signs such as weakness, decreased sensation, bowel and bladder incontinence, and sexual dysfunction can develop.

Chordomas in the base of the skull generally grow in the clivus and give signs of cranial nerve paralysis. Large chordomas placed in the sacrum can cause endocrinopathies. Other rare signs are epistaxis and intracranial bleeding[24,25]. While cervically-localized chordomas can give signs such as airway obstruction, retropharyngeal mass, dysphagia, dysphonia, or Horner syndrome[4], sacral-localized chordomas can cause signs of rectal dysfunction such as obstipation, constipation, tenesmus, and hemorrhoids, due to presacral tension[14]. In studies, the average occurrence and duration of symptoms has been reported as varying between 4 and 40 months[7,13].

Although chordomas do not initially metastasize, distant metastasis can be observed due to late diagnosis. When they are diagnosed, about 5% of chordomas can metastasize to the lung, bone, skin, or brain. In advanced stages of the disease, metastasis can be found at a rate of 65% [6,12]. However, it has been stated that metastasis does not affect survival as much as the local progression of the tumor[8]. The most important factor in terms of mortality is local recurrence, and therefore it is vital to provide a suitable resection distance for the borders during surgical resection[4,13,41].

IMAGING METHODS:

In direct X-rays, chordomas are classically observed as midline-localized osteolytic lesions with internal calcification. However, they often cannot be noticed in direct antero-posterior X-rays. By computerized tomography (CT), chordomas can be observed as osteosclerotic regions or mixed osteolytic and osteosclerotic bone destruction foci (Figures-1,2). In CT, amorphous intratumoral calcification foci are

observed in 30–90% of cases[26,30]. In more than 50% of cases, a tissue-attached fibrous pseudocapsule of a myxoid type can be observed[30].

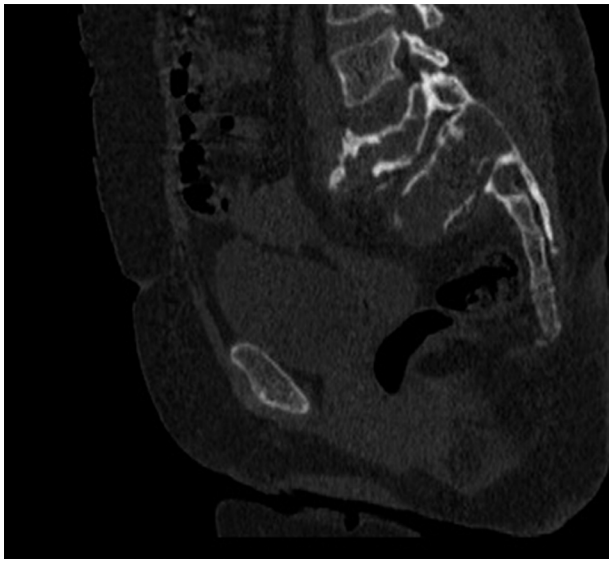

Figure-1. Sagittal computerized tomography section showing chordoma (Metin Sabancı Baltalimanı Bone diseases, Training and Research Hospital, Fotofilm Center Archive).

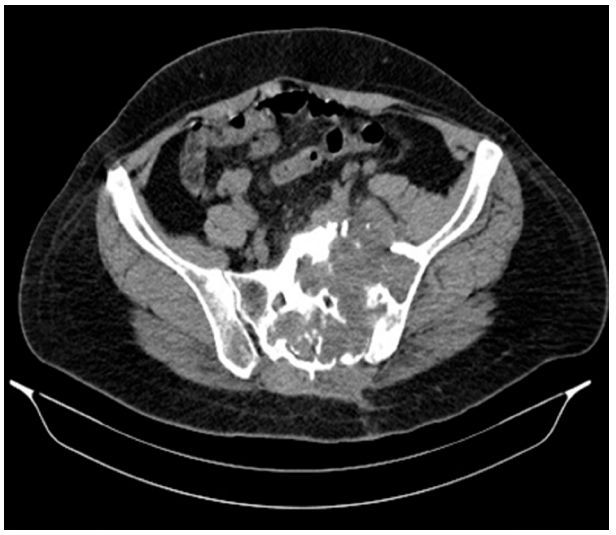

Figure-2. Sagittal computerized tomography showing chordoma (Metin Sabancı Baltalimanı Bone diseases, Training and Research Hospital, Fotofilm Center Archive).

In magnetic resonance imaging (MRI), when chordomas are compared with muscle tissue in T1-weighted images, they are observed between isointense and hypointense and with hemorrhagic and cystic changes due to calcification. They are observed as being heterogeneous and hyperintense in T2-weighted images. In both CT and MRI, a high rate of contrast involvement is seen with gadolinium[26] (Figure-3).

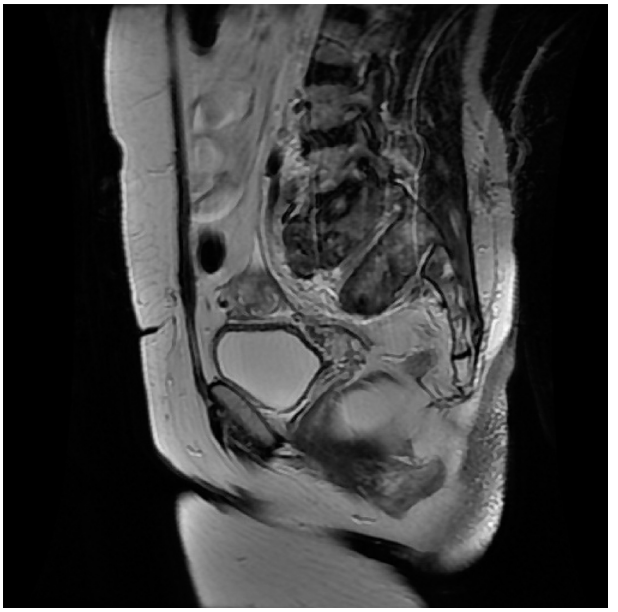

Figure-3. Sagittal MRI section showing chordoma (Metin Sabancı Baltalimanı Bone diseases, Training and Research Hospital, Fotofilm Center Archive).

DIFFERENTIAL DIAGNOSIS:

Although chordomas are the most common primary malign tumors of the sacrum and mobile spines, most sacral and spinal neoplasms consist of metastatic lesions and multiple myeloma[26]. Although chordomas can be confused with plasmacytomas due to lytic images, a positive scintigraphic involvement is present with chordomas. Osteomyelitis and lymphoma can be also radiographically confused with chordoma, but these conditions reveal totally different clinical landscapes[17]. Other lesions that can be confused, benign notochordial remnants, do not cause bone destruction or cortical irregularity. These lesions are generally asymptomatic[42].

In radiographic images, chordoma are differentiated from chondrosarcoma and metastatic lesions by the lack of accompanying soft tissue masses[17]. Other primary sacral tumors include benign lesions, such as giant cell tumors, aneurysmal bone cysts, osteoid osteoma, osteoblastoma, hemangioma, and nerve sheath tumors, and malignant lesions such as Ewing sarcoma, primitive neuroectodermal tumors, osteosarcoma, Paget's sarcoma, multiple myeloma, and plasmacytoma[19,26]. Additionally, in primary vertebral lesions, teratoma and dermoid should also be considered[20].

In histopathological examinations, immuno-histochemical examinations can be helpful for differential diagnosis of chordomas showing similarities with choroid meningioma, chondroma, chondrosarcoma, melanoma and metastatic adenosarcoma. Many chordomas show S100 immunoreactivity. Thus, chordomas can be differentiated from metastatic adenosarcomas and meningiomas[27]. They can also be differentiated from chondromas, chondrosarcomas and melanomas by displayed epithelial membrane antigen immune reactivity[27].

TREATMENT:

The basis of chordoma treatment is composed of surgery. Wide en bloc excision is essential for treatment due to the low-grade nature of these lesions. It is also essential to obtain wide clear surgical borders. In the surgical treatment of sacral chordomas, wide en bloc surgical excision was first defined by Stener and Gunterberg in 1970 [36]. Then, this technique was the basis of surgical treatment. In sacral chordoma resection, amputation is performed in a distal part of the sacrum or the whole sacrum is resected. Also, some adjacent parts of the pelvic bone can be removed to obtain a clear surgical border. During these processes necessary for wide resection, it can be necessary to sacrifice one or more nerve roots. As a result, motor and sensory deficit, sphincter dysfunction and sexual dysfunction can occur. Resections can be classified according to the localization of the removed upper segment or sacrificed upper nerve root. Thus, sacral amputations can be classified as lower (amputations in which at least one S4 root is sacrificed or are further distal), moderate (amputations in which at least one S3 root is sacrificed), or upper (amputations in which at least one S2 nerve root is sacrificed). Total sacrectomy involves the sacrifice of both S1 roots[39].

Generally, while ipsilateral resection of the sacral nerve roots causes ipsilateral motor and sensory deficit, the intestinal and bladder functions are preserved. In lower sacral amputations, sphincter functions are generally preserved, but perineal sensory loss and sexual dysfunction can be often observed[39]. In moderate sacral amputations, functional losses of varying degrees can be observed. In most patients, saddle type anesthesia is frequent and sphincter control decreases, but motor function is generally full[5]. In most cases in which at least one of the S3 roots is preserved, normal intestinal and bladder functions are present. In cases in which at least one of the S2 roots is preserved, limited urinary and fecal continence are present, while sphincter functions are disrupted in most cases[39]. In upper sacral amputations and total sacrectomy, postoperative motor deficits can occur, especially in ankle plantar flexion, due to resection of the S1 root. In these patients, sphincter control is totallylost and saddle type anesthesia and sexual dysfunction are present[5,36].

Surgical treatment of chordomas is difficult due to the complex regional anatomy, the advanced stage at diagnosis, and projection and invasion of adjacent tissues. Therefore, a surgical team including oncological surgeons, neurosurgery specialists, orthopedic surgeons and cosmetic surgeons should be involved in surgery. The application of advanced instrumentation techniques (such as iliac screws, transiliac bars etc.) can be necessary to prevent spinopelvic instability, especially for patients who received upper sacral amputation and total sacrectomy after tumor excision (Figure-4)[21]. Also, the application of a rotational gluteal flap or a transpelvic vertical rectus abdominis myocutaneous flap can be necessary for healthy wound healing, filling dead spaces, and closure of possible skin defects[15].

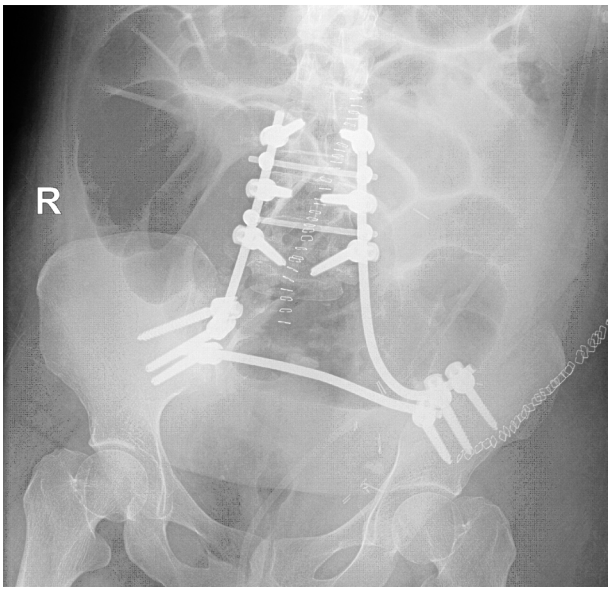

Figure-4. Reconstruction using transpedicular and iliac screws after total sacrectomy (Metin Sabancı Baltalimanı Bone diseases, Training and Research Hospital, Fotofilm Center Archive).

The aim of surgery of chordomas found in the spinal body is en bloc resection providing clear surgical borders. In intralesionary excisions, a high rate of recurrence is observed, which negatively affects survival[4,7]. For patients for whom the capsule was damaged during en bloc resection, Kaiser et al. showed almost twice as much local recurrence[23]. Therefore, the affected spinal body should be removed as a single block. To achieve this, a posterior and anterior combination of transpleural thoracotomy, thoraco-abdominal and retroperitoneal abdominal approaches is necessary[8]. First, en bloc removal of the posterior elements is carried out, and then the anterior part is resected. Lastly, spinal reconstruction is carried out.

Wide en bloc resection is not always possible due to the tumor size, the tumor extension, or the excessive morbidity that the tumor will cause. In this situation, although it is obligatory to work intralesionarily, extracapsular excision of the tumor, at least, should be provided without damaging the pseudocapsule. Then, these patients should receive adjuvant radiotherapy in order to provide local control of the residual tumor[10].

As for sacral chordomas, treatment of upper cervically-localized chordomas is difficult due to the complex anatomy and presence of sensitive structures. They can spread to the retropharyngeal space or the epidural region. Multidisciplinary teams, including cosmetic surgeons and otorhinolaryngologists, should perform surgery. A transglossal or transmandibular approach from the anterior can be preferred in treatment. Therefore, extracapsular excision can be performed by reaching the tumor pseudocapsule. Instrumentation should be carried out for stability. As a result of damage to adjacent sensitive structures, complications such as dysphagia, dysphonia and Horner syndrome can develop.

In cases where complete resection is not possible or the surgical border is positive, radiotherapy can be used as an adjuvant treatment even though its efficacy has not been proved. Due to the proximity to sensitive neurological structures, treatment of chordomas with standard radiotherapy is difficult. These tumors are relatively resistant to radiation. Therefore, higher doses of 60–70 Gy that the tumor cannot tolerate should be applied. Also, implants used for reconstruction can prevent accurate targeting by forming artifacts[10].

Chordomas are highly resistant to chemotherapy. Chemotherapy can only be effective for rarely seen high-grade dedifferentiated chordomas. Casali et al. used imatinib, a PDGFR-beta (platelet derived growth factor receptor) inhibitor, in 18 patients, and reported positive results for many patients[9]. After treatment, a decrease in the contrast involvement was observed over the course of one year. In another study including 31 patients, imatinib increased PDGFR-beta activation and expression[38]. In the light of these studies, imatinib treatment seems promising. Anti-angiogenic agents and epidermal growth factor receptor inhibitors have been also tried[10].

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