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Sacrococcygeal chordoma: review of the topic

Cordoma sacrococcígeo: revisión del tema

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ABSTRACT

Chordoma is a malignant primary tumor that resembles notochordal differentiation. Its maximum incidence is between the fifth and sixth decades of life, and men are affected more frequently than women in a ratio of 2:1; half of cases are located in the sacrococcygeal region. They are uncommon slow-growing lesions that originate in the midline. Its treatment is surgical through wide or radical resection. Total sacrectomies involve lumbopelvic dissociation, therefore it is important to stabilize the area and achieve adequate coverage of reconstruction. Treatment of the lesions involve great operational complexity and generate neurological sequelae mainly related to sphincter control, depending on the level resection. The incidence of morbidity and mortality in sacrococcygeal resections is high. Patients diagnosed with chordoma should be treated in highly specialized units.

RESUMEN

El cordoma es un tumor maligno primario que resume diferenciación notocordal. Su máxima incidencia es entre la quinta y sexta décadas de la vida, y los hombres son afectados más frecuentemente que las mujeres en relación 2:1; la mitad de los casos se localizan en la región sacrocoxígea. Son lesiones infrecuentes de lento crecimiento que se originan en la línea media. Su tratamiento es quirúrgico mediante resección amplia o radical. Las sacrectomías totales implican disociación lumbopélvica, por ende es importante estabilizar la zona y lograr una cobertura adecuada de la reconstrucción. Son lesiones cuyo tratamiento implica gran complejidad operativa y genera secuelas neurológicas principalmente relacionadas con el control de esfínteres, las que dependerán del nivel de resección. La incidencia de morbilidad y mortalidad en resecciones sacrococcígeas, es alta. Los pacientes con diagnóstico de cordoma deben ser tratados en unidades altamente especializadas.

INTRODUCTION

Chordomas are relatively rare malignant tumors of the spine, which arise from ectopic rests of notocordal tissue.[1,2] In 2020 World Health Organization (WHO) described 3 types of chordoma. Conventional chordoma, dedifferentiated chordoma and poorly differentiated chordoma.[3-5] Chordoma represents only 1-4% of all primary malignant bone neoplasms,[6-11] is the most common primary malignant tumor within the spine,[6] is the most common tumor of any type involving the sacrum,[6,12-15] and approximately 50% of all chordomas are sacrococcygeal in origin.[6,13,16,17] Chordoma treatment is eminently surgical through wide or radical

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resection (partial sacrectomy, total sacrectomy or extended sacrectomy), and is usually associated with important sequelae mainly related to sphincter control. Patients treated with previous intralesional surgery have a higher risk of local recurrence.[17] Sacrectomies are rare procedures characterized by great surgical complexity and a high incidence of complications, even in highly specialized units.

The main objective of this document is to present a general overview of a rare neoplasm whose surgical treatment is extremely complex and generates important sequelae, in addition to the fact that the incidence of therapeutic complications in sacrectomy is high, and with important risks at different levels.

Embryology

Chordomas are presumed to derive from undifferentiated, extradural, vestigial remnants of the notochord, an embryonic structure that coordinates cell fate and development. The notochord itself is a longitudinal, axial structure located centrally within humans and all other members of the phylum *Chordata* during embryological development.[15] The spine develops from mesodermal structure known as somites. The development of somites proceeds from a cranial to caudal direction which occurs on either side of the notochord and neural tube. Somites are made up of 3 layers: sclerotome (vertebral bodies and annulus fibrosus), myotome and dermatome.[18,19]

Epidemiology

Chordomas may present at any age, but mostly arise in patients between 40 and 60 years of age[20] and males are more commonly affected than females.[15] Less than 5% of cases occur before the age of 20.[20]

Chordomas are typically sporadic but a number of suspected familial forms have been documented, with a variety of familial genetic mutations identified in these cases, including recurrent germ-line mutations in the T gene (6p27), which encodes brachyury.[15] Chordomas have also been reported to arise in association with other pathological syndromes, such as tuberous sclerosis complex,[3,15] Ollier disease and Maffucci syndrome.[15]

Clinical features

Clinical signs are usually non-specific[8,12,21] and depend on the lesion's anatomic location[9,20] and size.[9,14] Chordomas are indolent-slow-growing masses, therefore they are often clinically silent until late stages of the disease.[9] Sacral chordoma results in chronic back pain or urinary/bowel dysfunction due to nerve root compression.[20] Most of the sacrococcygeal chordomas are initially presented with a considerable extra axial tumoral growth,[22] and often palpated as a mass on rectal examination.[13,14] Anterior expansion into the presacral space with unilateral impingement of S2 or S3 is usually associated with mild –to– moderate bladder, bowel, and sexual dysfunction, while bilateral affection usually result in complete dysfunction.[14] The rectum is not involved anteriorly through the presacral fascia.[13,23]

The most common presenting symptom is local pain[10] and tenderness resulting from periosteal stretching from cortical expansion, mass effect, and compression of neighboring structures. Increasing compression of nerve roots can impair reflex arcs and provokes multiradicular sensory deficits to the uni or bilateral buttocks, posterior thigh, leg, external genitalia, and perineum depending on the level of tumor extension.[13,14] The average duration of symptoms prior to diagnosis is 2 years.[13,24]

Imaging

Many sacral tumors remain clinically silent and are incidentally discovered during workup of minor trauma.[14]

Chordoma is typically a lytic, destructive lesion arising in the midline. It grows slowly expanding the bone, and is frequently associated with a large mass.[3] The sacrum may be excluded from initial radiographic studies as these lesions can be located below the sacral 2 (S2) vertebrae or are obscured by bowel gas or stool.[14]

Computed tomography imaging usually demonstrates a midline, expansible, destructive lobulated mass that invades adjacent tissues, with lytic bone destruction and soft tissue extension. Calcifications within the lesion are present in 30-70% of patients,[9] and typically represent entrapped fragments of native bone, not matrix mineralization[20] *(Figure 1)*.

On MRI, the mass is lobular, septated, and heterogeneous, showing intermediate to low –signal on T1– weighted images (but frequently containing high–signal foci as result of intratumoral microhemorrhage), and hyperintensity on T2–weighted images[3,9,15,16] *(Figure 2)*.

Chordoma shows low activity on technetium isotope bone scans, but there may be uptake at the margin and there is moderate avidity for FDG on PET studies.[3]

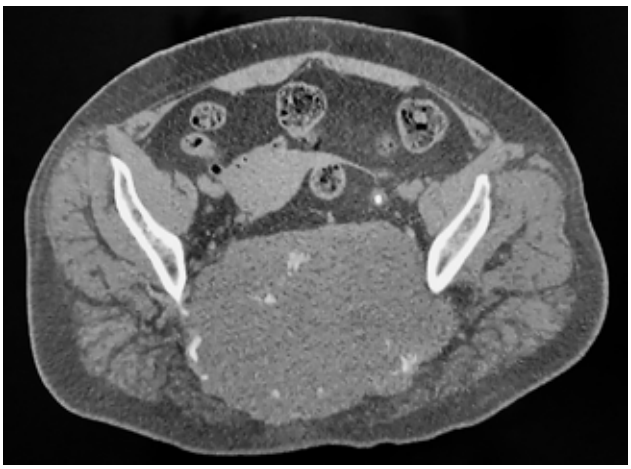

Figure 1: Computed tomography is an excellent diagnostic aid to show the extent of a lesion and its relationship with surrounding structures.

Macroscopic appearance

Macroscopically, sacrococcygeal chordomas are usually well–demarcated by a pseudocapsule. Virtually all tumors involve bone, with extension into adjacent soft tissue and skeletal muscle. The cut surface of the tumor is characteristically soft, gelatinous, mucoid, and hemorrhagic.[16]

Conventional chordoma

Conventional chordoma is a malignant tumor with a phenotype that resembles notochord and that commonly arises in the axial skeleton.[3]

Conventional chordoma is composed of large epithelioid cells with clear to light eosinophilic cytoplasm, separated into lobules by fibrous septa. The tumor cells may have bubbly cytoplasm (physaliphorous cells). They are arranged as cords and nests embedded within an abundant extracellular myxoid matrix, or as more–densely arranged epithelioid packets[3] *(Figure 3)*. Nuclear atypia is only mild to moderate and mitoses are infrequent.[15] Necrosis is often present and may be extensive.[20]

Chondroid chordoma, a subtype of conventional chordoma,[3] contains areas in which the matrix has the appearance of hyaline cartilage. This may be focally identified or diffusely present throughout the lesion.[20]

The most specific marker of chordoma is brachyury, a nuclear protein associated with notochord differentiation. While expression of brachyury is highly specific for chordoma, poorly differentiated tumors and dedifferentiated areas may demonstrate loss of brachyury immunoreactivity.[9]

Metastasis are not frequent and most of the pathologists consider conventional chordomas as on a low malignant degree.[22]

Conventional chordoma is the most common type of chordoma.[11,15]

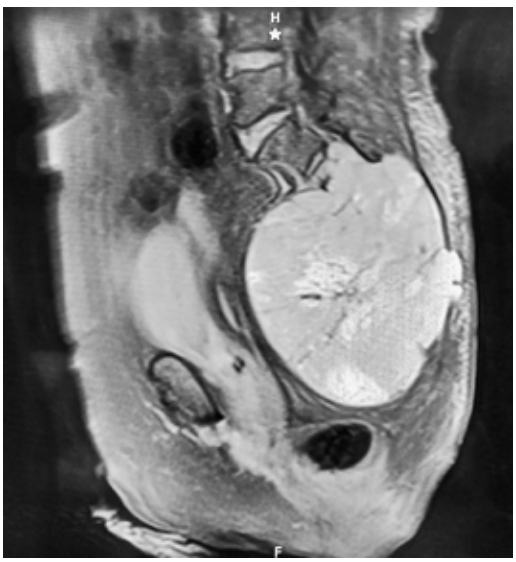

Figure 2: Magnetic resonance imaging shows us the extension of a neoplasia both intra and extracompartmentally.

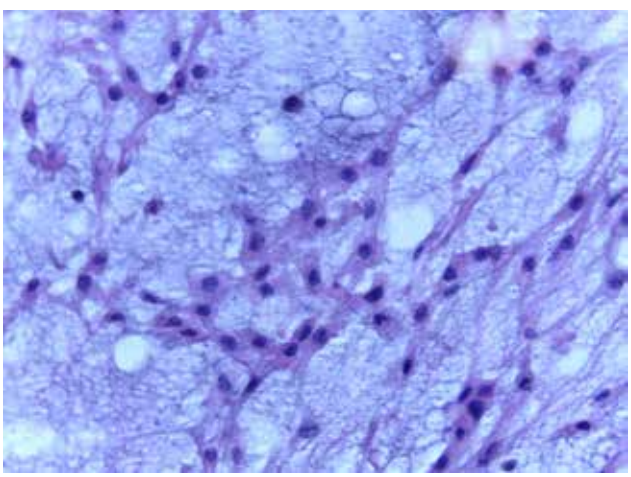

Figure 3: Microscopic appearance of conventional chordoma (Hematoxylin & Eosin 40X). Nest of physaliphorous tumor cells with atypical eccentric nucleus, and abundant eosinophilic vacuolated cytoplasm.

Dedifferentiated chordoma

Dedifferentiated chordoma is a chordoma with biphasic appearance characterized by conventional chordoma and high–grade sarcoma;[4,20] sarcoma is usually high–grade undifferentiated pleomorphic sarcoma, and dedifferentiation results from ongoing cumulative mutations in the conventional chordoma cells.[25] Osteosarcomatous and rhabdomyosarcomatous differentiation can be seen, and the dedifferentiated component of the tumor can show focal cytokeratin expression but does not express brachyury.[4]

Dedifferentiated chordoma accounts for 2-8% of all chordomas[26] and can occur *de novo* or as malignant transformation of previously treated chordoma.[4,26] The etiology of dedifferentiated chordoma is unknown and has similar locations and clinical manifestations to those of conventional chordoma.[4]

Dedifferentiated chordoma carries a poor prognosis with rapid local progression, distant metastasis, and treatment resistance.[26]

Poorly differentiated chordoma

The WHO's definition establishes that is a poorly differentiated neoplasm of unknown etiology, with notochordal differentiation, usually arising in the axial skeleton, and characterized by loss of SMARCB1 expression.[5] SMARCB1 is a chromatin remodeling member of the SWI/SNF complex. It is known to be lost in a number of sarcomas including malignant rhabdoid tumor, epithelioid sarcoma, epithelioid malignant peripheral nerve sheat tumor, and myoepithelial carcinoma.[27]

Poorly differentiated chordoma has distinctive features differentiating it from other subtypes of chordoma. It occurs more commonly in young adults and children,[20,28] with a slight female predominance.[20]

The most common location of poorly differentiated chordoma is the skull base, followed by the cervical spine and rarely the sacrococcygeal region.[5,20]

By immunohistochemical staging, the tumor cells are diffusely positive for cytokeratin and brachyury, and negative for SMARCB1. The nuclear loss of SMARCB1 expression, which is critical to establish the diagnosis, is due to a homozygous SMARCB1 deletion that can be identified by FISH study in most cases.[28] The tumor cells are negative or variably positive for S-100 protein.[27,28]

Differential diagnosis

The differential diagnosis of sacral tumors is extensive, and although metastasis are the most common lesions, a broad spectrum of primary bone tumors can arise from sacral components.[12]

Differential diagnosis of conventional chordoma includes chondrosarcoma, chordoid meningioma, myoepithelial tumor of bone and metastatic carcinoma.[3] Differential diagnosis of dedifferentiated chordoma is mainly with dedifferentiated chondrosarcoma,[4] and differential diagnosis of poorly differentiated chordoma is with malignant rhabdoid tumor, atypical teratoid/rhabdoid tumor, epithelioid sarcoma, rhabdoid meningioma, metastatic carcinoma, chondrosarcoma, and other types of chordoma, particularly dedifferentiated chordoma.[28]

Treatment

Chordomas pose a considerable treatment challenge due to their midline location, predilection for affecting critical neurovascular anatomy, indolent growth patterns, tendency to seed/recur, and resistance to traditional chemoradiotherapeutic modalities;[15] in fact, surgery with negative margins is the treatment that offers the best option for longer progression-free survival.[8,17,29] Chordoma represents the most common neoplasm that gets benefit from sacrectomy.[30] The gold standard treatment for chordomas is *en bloc* resection with wide margins and proton-based radiotherapy.[9]

The first *en bloc* sacrectomy was described in 1952.[31] *En bloc* resection involves the surgical removal of the entirety of a tumor without violating its capsule, and requires resection of the lesion encased by a continuous margin of healthy tissue,[32] which can be achieved by wide or radical resection *(Figures 4 to 6)*.

The term total sacrectomy refers to resection and attachment of the dural sac below S1, with the resection extending to L4, L5 and to the iliac region if necessary.[33] Total sacrectomy, extended sacrectomy and hemisacrectomy are rare and demanding surgical procedures that cause instability and discontinuity between the spine and pelvis and generate major soft tissue defects.[34] Sacral tumors that lend themselves to *en bloc* resection can either be approached via a combined or posterior–only approach.[32] Selection of the appropriate surgical approach is vital to resect sacral tumors completely.[8]

Surgical procedures for sacral tumors are classified into four types on the basis of extension of tumors and the level of sacral resection: **Type I.** Low sacral

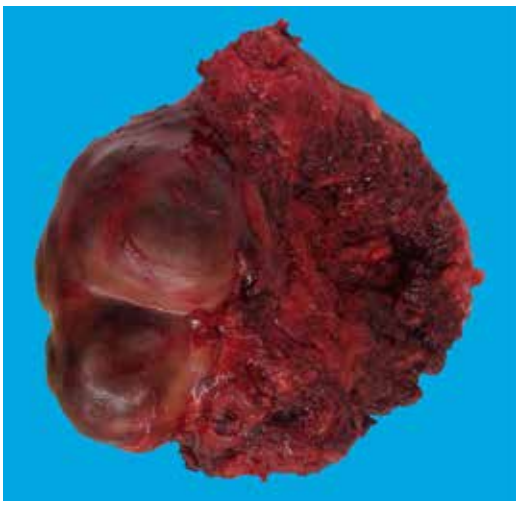

Figure 4: Surgical piece resulting from type I sacrectomy due to chordoma.

amputation-sacrectomy below S2 *(Figures 4 to 6)*. **Type II.** High sacral amputation–sacrectomy through S1-S2. **Type III.** Total sacrectomy-sacrectomy through L5-S1. **Type IV.** Extended sacrectomy–total sacrectomy combined with excision of the ilium, vertebra, or intrapelvic organs.[35] Hemisacrectomy is the vertical resection of a tumor in half of the sacrum that disrupts the spinopelvic continuity.[36]

A combined anterior–posterior surgical approach allows safe separation of the rectum and blood vessels in the anterior sacral region, and the posterior incision is closed with a rectus flap.[8] Some authors have demonstrated favorable outcomes with posterior–only approach for *en bloc* sacrectomy,[29,37] although others have suggested that the posterior–only approach is most suitable for lesions located at S3 and below[38] *(Figures 4 to 6)*.

The primary goal of any *en bloc* resection is the removal of the tumor in 1 inviolated piece[29] *(Figure 4)*.

In patients for whom surgical resection is not feasible, definitive management with high–dose radiation is reasonable.[7]

The extent of sacral resection impacts the degree of biomechanical instability imparted and therefore the need for spinopelvic fixation.[7] Total sacrectomy causes instability in the pelvis and spine because of the involvement of the sacroiliac joint; thus, it is important that ilio–lumbar stability is restored in these patients.[8] Generally, there are three components in spinopelvic reconstruction : spinopelvic fixation, posterior pelvic ring fixation, and anterior spinal column support;[39] multiple techniques for reconstruction of skeletal defects after sacrectomy have been reported.[39,40] Some authors advocate sacrectomy without reconstruction to reduce complication rate.[17,41,42]

The risk of infection, loss of large amounts of blood, wound complications, and neurological dysfunction are problems associated with sacrectomy.[43]

In patients with diagnosis of chordoma and treated through sacrectomy, the primary prognostic factor is the type of surgical margin attained at initial surgery. Previous intralesional surgery and primary resection with intralesional or marginal margins carries a substantial risk factor for local recurrence.[17]

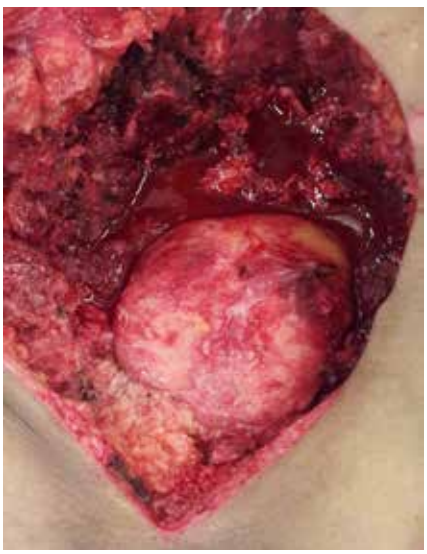

Figure 5: Surgical bed after the type I sacrectomy (relate to *Figure 4)*. Note the close relationship between the tumor and the rectum.

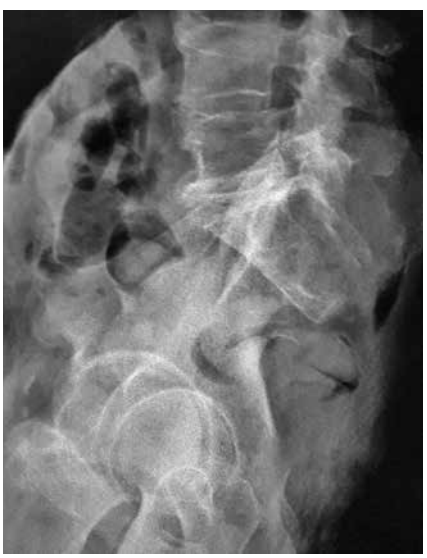

Figure 6: Radiological control by lateral projection after type I sacrectomy.

Post–surgical sequelae

Patient's life quality largely depends on the extent of sacral root resection[43] and the establishment of spinopelvic stability. Sacrectomies are procedures that are associated with neurologic sequelae related to the level of resection and include changes in bowel and bladder function, incontinence, and sexual and walking impairment.[10] Patients facing neurological bladder and fecal incontinence after sacrectomy, require long-term enema, diapers, and urinary catheterization.[10,43] Sometimes colostomy and/or cystostomy are necessary.

Resection of both S3 nerve roots results in sphincter incontinence;[34] in this regard Berra et al. have reported promising results in reconstruction of the sacral nerve roots and consequently in their functional recovery.[10]

Complications

Sacrectomies are complex and have several complications.[33] The complication rate in patients undergoing sacrectomy with reconstruction exceeds 50% and is related to the type of sacrectomy and the volume of the sacral defect.[30,33]

The most common surgical complications after sacrectomy are infection at the surgical site,[33] and wound dehiscence. Soft tissue reconstruction to cover the defect that sacrectomy generates, is an important topic focused on reducing wound complications. In general terms, gluteal advancement flaps are used to cover small defects, and vertical rectus abdominis myocutaneous flaps (VRAM) for the management of larger defects.[30,44] The incidence of failure of internal fixation devices, such as non–healing bone grafts, internal fixation displacement, fracture, and loosening, is high.[45]

Recurrence can be explained by satellite lesions seeding via the tumors pseudocapsule which makes it difficult to achieve disease free surgical margins.[18] Generally the occurrence of metastasis to the lungs, liver and bone is very slow.[10]

Sacrectomy is a complex procedure with high morbidity and mortality rates.[33]

DISCUSSION

Diagnosis of sacrococcygeal chordoma should be present in front of patients with insidious chronic back pain and/or urinary/bowel dysfunction. Early diagnosis can facilitate obtaining negative surgical margins during sacrectomy. The anatomical complexity of the pelvis and the proximity of the sacrum to important anatomical elements, make surgical procedures difficult and thus the possibility of achieving wide surgical margins. Given this scenario, recurrences are frequent. The surgical approach to sacrococcygeal chordoma can be performed in a combined manner (anterior and posterior), or only posterior. The choice of the approach depends of the characteristics of the lesion and the surgical experience of the surgeons. In general terms, a single posterior approach is preferred for tumors located at S3 and below, and a combined approach for lesions located proximally. Total sacrectomies are accompanied by instability, therefore, stabilization after resection is important.

The surgical characteristics of sacrococcygeal resections favor the development of different types of complications that must be addressed as soon as possible to minimize their negative effects on the recovery of patients.

Neurological sequelae, mainly related to sphincter control will depend on the level of resection. Reconstruction of the sacral nerve roots may be a promising alternative in patients undergoing sacrectomy.

Every patient in whom a sacrectomy is indicated, must be fully informed about the possible surgical complications and the functional sequelae of the proposed procedure.

CONCLUSION

Chordoma is a rare bone neoplasm whose sacrococcygeal location is common. Due to their insidious symptoms, they are generally diagnosed when they have already reached large dimensions. It is a lesion that requires surgical treatment through wide or radical resection resorting to some type of sacrectomy. Sacrectomies have the objective of resecting the neoplasia by achieving negative margins, which implies the sacrifice of nerve roots, which in turn will generate neurological sequelae mainly related to sphincter control. These are complex surgical procedures that usually generate musculoskeletal defects and spinopelvic instability. Reconstruction in both directions is generally necessary. The incidence of complications is high and the different sequelae usually require special management. The surgical treatment of sacrococcygeal chordoma must be done in specialized centers to increase the possibilities of controlling the disease.

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