Clinical Case Report

Sacral chordoma with metastatic dissemination in a child: case report

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Introduction: Chordoma is a rare pathology in the pediatric age group, especially when located in the sacral region. Despite the local infiltrative character, some cases of metastasis are reported. The prognosis of these patients depends on early diagnosis and tumor resection.

Case Report: 13 y-o girl transferred with a huge mass lesion in the lumbosacral area. In the primary hospital, she was submitted to a biopsy, whose anatomopathological report showed chordoma. The patient started with pain in the lumbosacral region a year ago, which rapidly evolved to a significant bulging in the area, pain in the posterior region of the left lower limb, urinary retention, and difficulty in walking. A surgical approach, both anterior and posterior, was performed en block resection of the tumor. During the procedures, there was evidence of metastatic dissemination to the ovary and peritoneum. The pathological examination confirmed the initial diagnosis. Due to the late recognition of the condition and the fast evolution of the disease, there was not enough time to perform adjuvant radiotherapy and the patient died.

Discussion: From notochordal remnants, chordoma manifests in less than 5% of patients in the first two decades of life and is occasionally found in the sacral region, but rarely with metastatic dissemination at presentation. These patients open up with the manifestation of local pain and, when not diagnosed early, progress with bulging of the sacral region and tumor dissemination. Management is based on primary resection, for the complete removal of the lesion, followed by radiation therapy.

Keywords: Chordoma, sacral, dissemination, metastasis

INTRODUCTION

Chordoma is a rare pathology in the pediatric age group, especially when located in the sacral region. Lothar Henninh described the first sacrococcygeal chordoma in a seven-month-old child in 1900, however, as the patient was very young, the case was considered a birth anomaly [1]. The general incidence of chordoma is 0.08 cases per 100,000 individuals, while less than 5% of cases are represented by children and adolescents [2]. The clinical presentation varies according to its location. Pain is usually the main symptom in sacral chordomas, and it may advance in accordance with the disease progression. Despite the local infiltrative character, some cases of metastasis are reported in the literature and these tumors' level of aggressiveness still imposes difficulty in the treatment. The prognosis of these patients depends on several factors such as early diagnosis and extensive tumor resection.

The authors describe the case of a child presenting an extensive sacral chordoma associated with metastatic dissemination to the peritoneum and ovary, who underwent en bloc surgical resection using a combined anterior and posterior approach in a single surgical procedure.

CASE REPORT

A 13-year-old girl transferred with a huge mass lesion in the lumbosacral area. In the primary hospital, she was submitted to a biopsy, whose anatomopathological report presented chordoma. One year ago, the patient started with pain in the lumbosacral region, which rapidly evolved to a significant bulging in the area, pain in the posterior region of the left lower limb, urinary retention, and difficulty in walking. In the physical examination, the bulging in the sacral region involving the gluteal and right gluteal lines, measuring approximately 15 cm (FIGURE 1) was evident, in addition to hyperemia in the center of the lesion and pain on local

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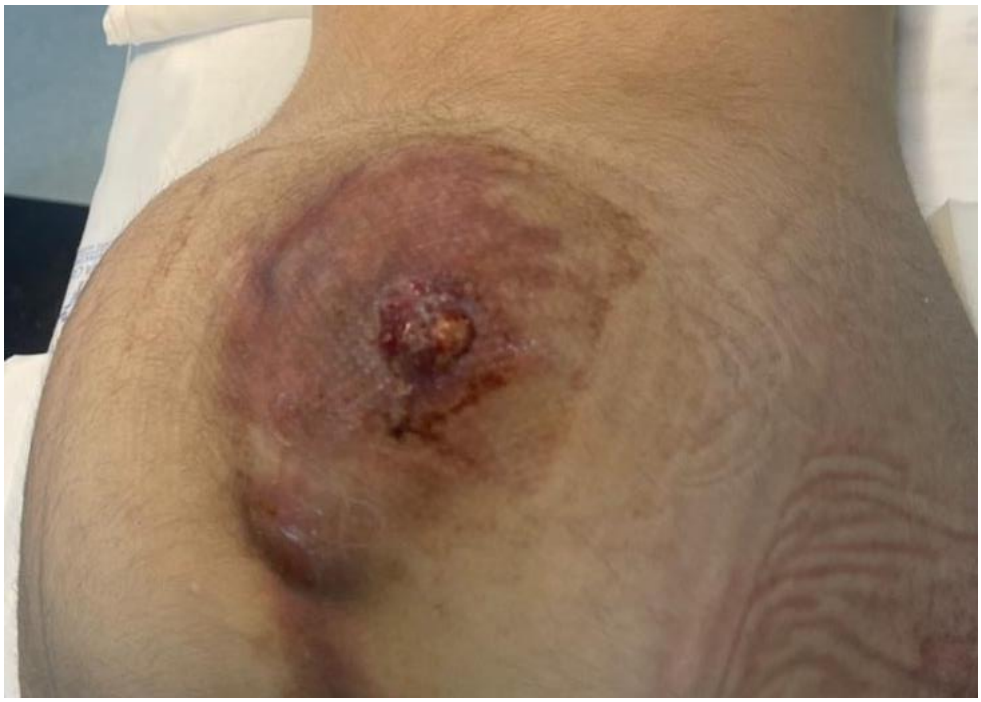

Figure 1- Preoperative image: patient with the presence of an ulcerated mass in the midline of the lumbosacral region.

superficial palpation. Muscle strength was impaired, with grade III in the left lower limb, worse distally (grade II).

Allodynia in the posterior region of the left thigh, gluteus, and pubic region were also present, in addition to bilateral patellar and Achilles hyporeflexia and urinary retention. Magnetic resonance imaging (MRI) of the lumbosacral spine showed a massive expansive lesion involving the sacrum and lumbosacral roots, with extensive infiltration of the surrounding soft tissues (FIGURE 2). Gadolinium T1-weighted image shows a honeycomb pattern corresponding to areas of intratumoral hemorrhage and calcifications. The analysis of adjacent structures allows the identification of significant urinary retention, in addition to an increase in the dimensions of the right ovary.

A combined anterior and posterior surgical approach was performed by teams from pediatric surgery, spine surgery, and neurosurgery. Initially, the anterior approach was performed to detach the lesion from the pelvic structures. At the same surgical time, the posterior access in the lumbosacral spine was performed for en bloc resection of the expansive lesion (FIGURE 3) from a sacrectomy inferior to S2, with sacrifice of the roots surrounded by the tumor, and the infiltrated part of the gluteus maximus and medius. During the procedure, there was evidence of metastatic spread to the ovary and abdominal lymph nodes with excision of the lesions and anatomopathological (AP) analysis.

The AP examination confirmed the diagnosis of conventional chordoma with extensive areas of necrosis, angiolymphatic invasion, and impairment of adjacent structures (FIGURE 4). The immunohistochemical analysis presented Brachyury, CKM (pan cytokeratin), EMA (epithelial membrane antigen), and INI-1positive and S100, PAX8, and CK (cytokeratin) 8/18 negative. Ki-67 positive in about 90% of neoplastic cells. In the postoperative period, the patient initially presented a satisfactory evolution, however, the previous deficits remained. Control exams showed extensive resection of the lesion (FIGURE 5) and the plan to refer the patient to conventional radiotherapy continued. However, during the vesicostomy performed 15 days after the surgical resection, peritoneal metastatic dissemination was observed and the patient died within a few weeks.

LITERATURE REVIEW

Chordomas are rare malignant tumors arising from primitive notochordal remnants, corresponding to less than 5% of primary bone neoplasms and 1% of primary spinal tumors [2,3]. They represent the most common primary sacral tumors, accounting for more than 50% of cases [2]. This kind of tumor is characterized by its slow growth, but it is extremely locally aggressive, with high rates of recurrence. It occurs in less than 5% in patients under 20 years of age [3,4,5]. Ridenur III et al. (2010) described 37 cases of chordoma occurring in pediatric patients and young adults under the age of 25 years: 66% in spheno-occipital location, 20% in mobile spine, and 17% in sacrococcygeal location. All sacrococcygeal tumors in this study presented histological atypia and aggressive behavior with worse survival [6]. The rest of the literature also emphasizes the aggressiveness and clinicopathological differences of chordomas in childhood,

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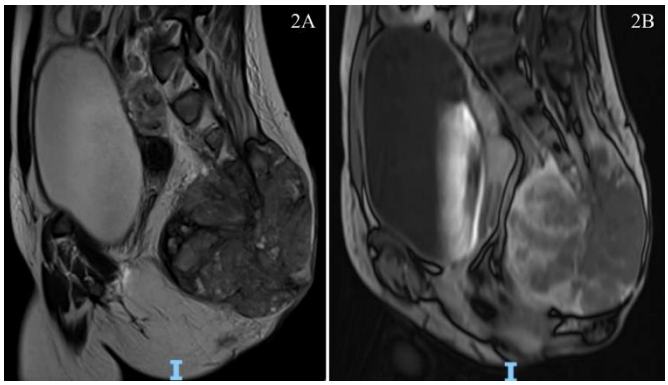

Figure 2 – Preoperative examination. (2A) Sagittal T2-weighted MRI showing an expansive lesion with small areas of hyperintensity in the lumbosacral spine with invasion of adjacent structures: lobulated appearance of the lesion and multiple hypointense septa. (2B) Sagittal gadolinium T1-weighted MRI reveals a "honeycomb" pattern of the septa, with hypodense areas of necrosis or mucus.

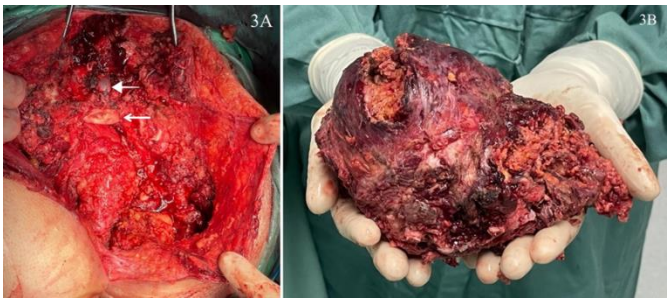

Figure 3 – Intraoperative images. (3A) Extensive surgical cavity after chordoma removal: sacrectomy (arrow) and cauda equina amputation (full arrow) are observed. (3B) En bloc resection of the chordoma.

unlike their adult equivalents, especially when located in the sacrococcygeal region. [3.5]

The clinical presentation of this tumor is varied, specifically when located in the sacral region. The patient usually starts the condition with local pain, which becomes progressive as the lesion grows and invades adjacent structures [7]. The wrapping of the lumbosacral roots, either by compression or by invasion, promotes muscle strength loss and radicular pain in the lower limbs, bladder and bowel dysfunction, perineal pain, and other changes in sensitivity. When not diagnosed early, there may be the occurance of a subcutaneous mass in the presacral space, eventually ulcerated and massive, with bone destruction and extension to the soft tissues [3,8]. Lumbosacral spine computed tomography (CT) characterizes the extent of this bone destruction, however magnetic resonance imaging (MRI) provides an accurate assessment of the involvement of adjacent structures [2,8]. The chordoma appears hyperintense on T2-weighted MRI with a lobulated appearance and multiple hypointense septa. When gadolinium is injected, most show a "honeycomb" pattern of the septa, while areas of necrosis or mucus remain iso/hypointense. Some studies suggest that the increase in contrast intensity is related to a more aggressive tumor behavior and risk of recurrence [2,3].

Macroscopically, chordomas are gelatinous and encapsulated tumors that may contain areas of hemorrhage, cyst, and necrosis [3]. Its history begins in 1846 with Virchow. This pathologist was the pioneer in performing the histological description of chordoma from previous autopsy findings. He used the word "physaliphora" in reference to the cytoplasmic vacuoles found on microscopic examination [1]. This cellular finding is reported to the present day and was considered a characteristic of chordomas [3]. In addition to physaliferous cells, the presence of abundant myxoid matrix also composes the architecture. The presence of intratumoral heterogeneity, with varying degrees of mitosis, nuclear atypia, and pleomorphism, raised the need for histological subdivision of chordomas: conventional, chondroid and undifferentiated. The first group is found in most patients and is characterized by low cellularity and minimal cellular atypia. The second presents a matrix similar to hyaline cartilage. The third group has foci of cellular atypia and a high-grade lesion equivalent to sarcoma, conferring greater aggressiveness [2,3,5,6,9]. Research directed at biomolecular markers is currently under emphasis in order to comprehend the biological behavior of the chordoma. Immunohistochemical complementation expresses epithelial markers such as cytokeratins (CK), epithelial membrane antigen (EMA), vimentin (VIM) and Brachyury. The latter is the most sensitive and specific marker in the identification of the chordoma, as it corresponds to the transcription factor in the embryonic development of the notochord. Therefore, reactivity to brachyury became essential in the diagnosis [1,2,3,9].

In 1907, Fisher and Steiner drew attention to the probable malignant nature of chordoma after the death of a boy with neurological symptoms resulting from the tumor [1]. Nonetheless, it was only 63 years later that en bloc surgical resection was proposed. At the same time, studies showed that surgical contamination of the wound with tumor cells would be responsible for recurrence, which supports the need for en bloc excision [9]. Despite medical progress, complete chordoma resection remains the standard treatment advocated in the literature [1,2,3,7,9,10].

Complete surgical resection poses enormous surgical challenges and therefore the rate of complete resection remains unsatisfactory, between 0% and 36.4%, which requires re-operations [3]. Chordomas caudal to the

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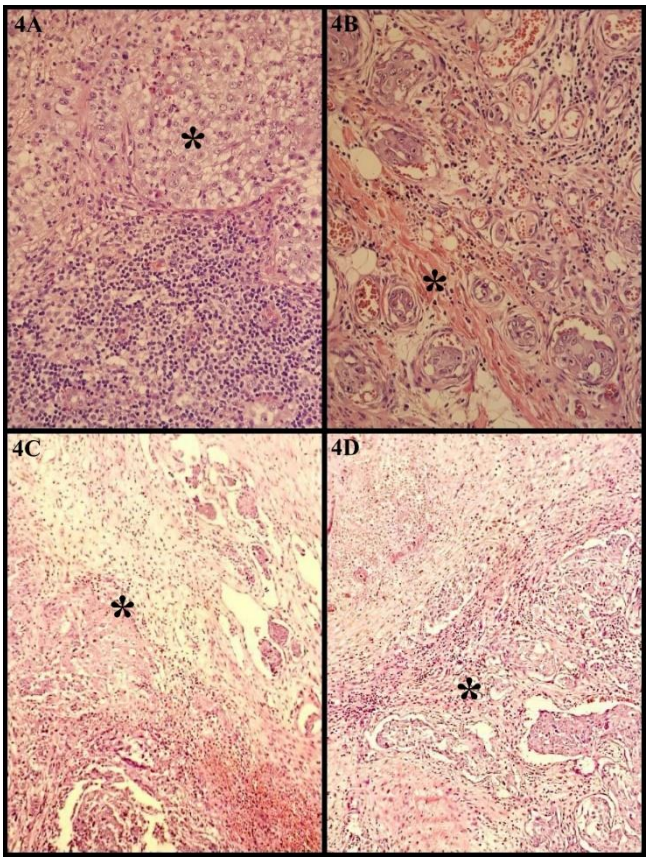

Figure 4 – Slide stained with HE (hematoxylin and eosin), 200x. (4A e 4B) Poorly differentiated malignant neoplasm of epithelioid cells of intermediate size, solid architectural pattern, with occasional mitotic figures (asterisk). Implantation of poorly differentiated malignant neoplasm compatible with lymph node (4C) and ovary (4D) metastasis of chordoma. Tumor tissue marked by asterisk on images to differentiate from normal tissue.

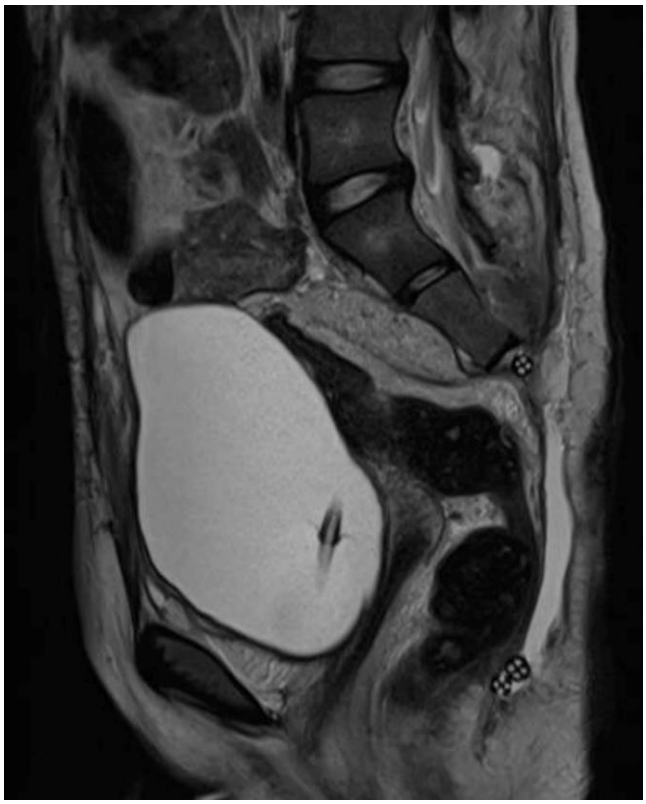

Figure 5 – Postoperative T2-weighted MRI showing radical resection of the previous expansive lesion.

sacroiliac joint are technically laborious and may require multiple specialties to combine anterior and posterior surgical access [2,9]. Low sacral amputations often sacrifice local roots in order to achieve the desired margins, causing neurological deficits [2]. The main purpose of this aggressive resection is to prevent recurrence. Patients undergoing total sacral chordoma removal had local recurrence in 2.27 years after surgery, compared to 8 months in patients with partial excision of this tumor [9]. The overall median survival after total chordoma resection is 6.29 years: 67.6% of patients survive for 5 years and 39.9% for 10 years [2].

Unfortunately, treating chordoma remains a challenge. After tumor resection, adjuvant radiotherapy is advocated by most authors [3,7]. The report of a series of intracranial chordomas showed that total or partial surgical resection followed by radiotherapy has a better result than surgical excision alone [3]. The need for high-dose radiation imposed the development of a method that is less harmful to children's development. Proton beam (particle) radiation therapy has become a choice in adjuvant therapy for chordoma in pediatric patients due to its ability to reduce the radiation dose to adjacent structures and concentrate on the tumor area [3,11]. The attempt to reconcile radiotherapy and safety has encouraged some research in this area. Iannalfi et al. conducted a study that evaluated the results and safety of particle beam therapy, specifically protons (PrT) and carbon ions (CIRT), in patients with chordoma at the base of the skull. In this series, of 135 patients treated with PrT or CIRT, 5-year local disease control was 84% and 71%, respectively. In addition, they were able to verify that the local control (LC) of the tumor with radiotherapy is directly related to the postoperative residual tumor volume (RTV): in the CIRT group, the 3-year LC rate was 81% and 56% for patients with RTV <= 23.1 cm3 and > 23.1 cm3, respectively; while in the PrT group, the 3-year LC rate was 94% and 71% for patients with RTV <= 10.4cm3 and >10.4cm3, respectively. Therefore, low doses and inhomogeneity of radiation within the tumor are reasons for local recurrence. It is believed that, in short, the choice of particle therapy tends to be defined by the postoperative

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residual volume of the chordoma [11]. However, despite promising studies in this area showing the benefits of radiation with protons when compared to radiation with photons (radiotherapy with linear accelerators), this technique is still very expensive and poorly available, with no equipment in Latin America. As for chemotherapy, there is still no obvious benefit [1, 2, 3, 4, 5, 7]. Molecular therapy has been studied for its benefit in chordoma tumor cells, but with limited evidence [12].

The first case of metastatic chordoma was described in 1919 by Pototschmig, whose patient developed metastasis to abdominal lymph nodes [1]. Currently, the incidence of metastasis is estimated at 3 to 48% [3,6,10,13,14,15]. Lungs, bones and lymph nodes are the preferred structures of tumor cells that spread via the hematogenous route. [3,10] Ozkal et al. (2015) describe the first case of sacral chordoma with peritoneal metastasis, in which the author opted for palliative treatment [7]. This metastatic disease is considered to be indolent in most cases. [10] The rate of local recurrence of chordoma after surgery is 30-75%, which is directly related to a higher incidence of metastases and reduced survival [8,10,13,15]. McPherson et al. (2006) followed 37 patients with chordoma over a period of 10 years, of which 23 had a sacral location. Tumor recurrence was the only significant factor for the development of metastatic disease, as no patient with controlled local disease showed metastasis and 28% of cases with local recurrence had distant tumor spread [10]. Akiyama et al. (2018) describe a unique infiltrative pattern of chordoma called “micro-skip” metastasis, referring to a small nodule of tumor cells around the main lesion and undetectable on imaging tests. In this study, of the 40 cases of sacral chordoma treated with total resection, there was 45% recurrence – of which 77.8% were micro-skip. All micro-skip metastases were found in gluteus maximus, where the distance from the main tumor to the metastasis was 0.3mm to 20mm. This type of tumor implant was associated with an increased risk of local recurrence ($p = 0.023$). Another important data computed by the study was the survival rate of these patients: local recurrence-free survival in patients without micro-skip metastases was 71.2% both at 5 and 10 years; however, survival in those who had these metastases was 51% at 5 years and 25.5% at 10 years [15]. The main prognostic factors related to chordoma are histologic type, patient age, and primary tumor site [2,3,4,12,13]. Ridenour III et al. (2006) reported that the mortality rate in their study was 67% for patients with atypical chordomas versus 27% for the other two subtypes. In addition, it also inferred that the chordoma located in the sacrum had a worse prognosis in young patients (80% mortality for mobile spine versus 35% for skull base). Late presentation of sacral tumors would be the main reason for this high mortality rate, because at the time of diagnosis the lesion already has a significant size, which influences the degree of resection and, consequently, local recurrence and metastases [6]. Survival is better in children than in adults, remaining around 56.8-81% and 23-66%, respectively. The exception can be found in aggressive chordomas whose predilection is for pediatric patients, especially in the age group below 5 years, making the prognosis dismal [3]. Almost 200 years after the first histological description, this disease remains a therapeutic challenge, as its uncertain behavior and limited therapy keep the mortality rates high.

The clinical case presented by the authors shows that the behavior of the chordoma cannot be based only on histology. The anatomopathological examination concluded that it was a patient with conventional chordoma, but the tumor had characteristics with a proliferative index (ki-67) of 90%, consistent with the evolution of a malignant tumor similar to the undifferentiated subtype. The same pattern of behavior has already been reported in the literature by Iwasa et al. (1995) who presented two pediatric cases of sacral chordoma with malignant evolution similar to sarcoma, but with histology not consistent with the evolution [5]. Late diagnosis of sacral chordoma also directly influenced the treatment perspective. Surgical resection, although extensive, had no impact on the survival of the patient whose case was described by the authors, since the metastatic spread considerably shortened her life.

CONCLUSION

Chordomas are rare and aggressive tumors that have a high recurrence rate. They are found mostly in the adult population, but pediatric patients develop more aggressive forms of the tumor, especially when located in the sacral region. Total surgical resection and radiotherapy are the mainstay of treatment for this disease. Proton radiation appears to be superior to photon treatment. Despite the progress in medicine, the mortality rate of this disease is still high. This is justified by the still uncertain behavior of the chordoma, which may not be consistent with the histological subtype. Molecular markers have been studied in order to obtain targeted therapies. Therefore, early diagnosis is essential in order to offer the currently most appropriate therapy and provide better living conditions for these patients.

DISCLOSURES

Ethical approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the local Ethics Committee

Consent to participate

The patient gave consent to use his information and images for research proposes.

Consent for publication

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The patient gave consent to use his information and images for publication.

Conflict of interest

The authors declare no conflicts of interest with respect to the content, authorship, and/or publication of this article.

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