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Pelvic Chondrosarcoma. Case Report and Literature Review

Carlos Hernández Brito[1], Indalecio Barcelata Rodríguez[2], Arturo Hernández Reyes[3], Omar Josué Herrera López[4], Óscar Mauricio López Gil[5], Luis Ángel Amezcua Toledo[6], Brenda Paola Sáenz Dávila[7], Luis Eduardo Méndez Turrubiates[8], Pedro Arredondo Ruiz[7]

[1]Surgical Oncology Department, IMSS UMAE, Veracruz, Mexico
[2]Orthopedic and Traumatology Department, IMSS UMAE, Veracruz, Mexico
[3]Plastic and Reconstructive Surgery Department, IMSS UMAE, Veracruz, Mexico
[4]Anatomical Pathology Department, IMSS UMAE, Veracruz, Mexico
[5]Anesthesiology Department, IMSS UMAE, Veracruz, Mexico
[6]Radiology Department, Centro Oncológico Onkolid, Veracruz, Mexico
[7]Clinical Oncology Department, Centro Oncológico Onkolid, Veracruz, Mexico
[8]Radiaton Oncology Department, Centro Oncológico Onkolid, Veracruz, Mexico
Email: carlosincan@hotmail.com

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Abstract

Background: 30% of chondrosarcomas develop in the pelvis making it the most common malignant bone tumor in this location. Unlike other locations, it has a less favorable functional and survival outcome. **Aim:** Describing the importance of multidisciplinary management and the complexity of the procedures required for a successful outcome. **Case Presentation:** A 32-year-old male with a pelvic chondrosarcoma measuring 25 × 30 cm in the iliac bone region with extension to the soft tissues of the lumbar region treated by a type I internal hemipelvectomy as a limb-sparing surgery. **Conclusion:** Pelvic chondrosarcoma presents less favorable oncological and functional outcomes due to the complexity of its surgical treatment and the lack of useful adjuvant treatments to reduce the risk of recurrence and/or disease progression.

Keywords

Chondrosarcoma, Pelvic Chondrosarcoma, Hemipelvectomy, Pelvic Sarcoma, Limb-Sparing Surgery, Bone Sarcoma

1. Introduction

Chondrosarcoma (CS) accounts for 15% to 30% of all malignant bone tumors and is the second most common malignant bone tumor in adults [1]-[7]. Histological

subtypes include conventional type (cCS), clear cell type, mesenchymal (mCS), and dedifferentiated (dCS) [8]-[10].

Approximately 30% of chondrosarcomas develop in the pelvis, making it the most common malignant bone tumor in this location, followed by osteosarcoma (less than 10% occur in the pelvis), with the chondroblastic variety being the most frequent, and Ewing sarcoma being the third most frequent [2] [11]. Unlike other locations, pelvic CS has a less favorable functional and survival outcome due to multiple factors, including late onset of presenting symptoms, larger tumor size and/or extracompartmental spread, higher likelihood of metastatic disease at diagnosis (up to twice as likely compared to limb chondrosarcoma) [3] [11], a higher rate of high-grade tumors, and especially greater difficulty in achieving a wide resection margin due to pelvic content and adjacent neurovascular structures [3] [11], particularly in pelvic chondrosarcomas located in the periacetabular and ischial regions, and in those that extend to more than one pelvic region [2] [3] [5]. In addition, surgical procedures are also associated with a higher risk of complications and a higher rate of local recurrence [3] [4] [6].

We present the case of a patient diagnosed with pelvic CS, describing his clinical evolution, diagnostic approach, and surgical treatment, emphasizing the importance of multidisciplinary management and the complexity of the procedures required for a successful outcome.

2. Case Presentation

A 32-year-old male with no history of other diseases presented with a tumor in the right iliac region that had been growing progressively for 11 months, with subsequent development of pain in the tumor site radiating to the buttock and thigh, and progressive limitation in mobilization until only assisted standing is achieved for short periods remaining on prone position for most of the day. Tumor growth continued until it invaded the skin, spreading to the lumbar soft tissues and reaching large dimensions. He was evaluated by the surgery department, which performed an incisional biopsy with a histopathological report of CS, for which he was referred to surgical oncology. On initial physical examination, the patient presented an irregular, fungating, abscessed tumor measuring 25 × 30 cm fixed to the pelvis in the iliac bone region with extension to the soft tissues of the lumbar region (**Figure 1**), with ipsilateral pelvic limb muscle strength 3/5, achieving assisted standing, and with limb sensitivity intact. The pathologist review confirmed the diagnosis of a grade 1 cCS, and the chest, abdomen, and pelvis computed tomography (CT scan) revealed a solid, hypodense, heterogeneous tumor with a chondroid bone matrix and areas of air density inside, extending to the skin and infiltrating the paravertebral muscles, right posterior abdominal wall, psoas, and gluteal muscles, and at the bone level with erosion and cortical destruction of the transverse processes of L3, L4, and L5, and the iliac bone (**Figure 2**) without distant metastasis.

Due to the patient did not present with neurovascular compromise of the ex-

tremity and the tomographic findings showed tumor extension without compromise of the iliac vessels or invasion of the sacrum and/or lumbar spine, and with tumor involvement of only one pelvic area, a multidisciplinary meeting with the orthopedic and reconstructive plastic surgery departments decided on a limb-sparing approach.

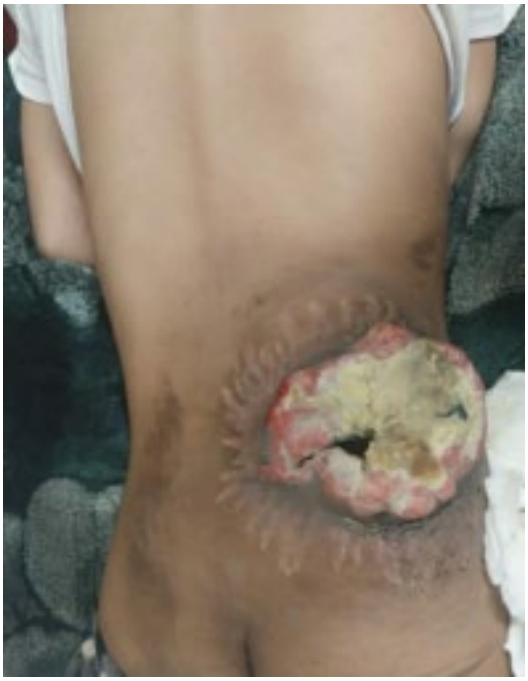

Figure 1. An irregular, fungating and abscessed tumor measuring 25 × 30 cm in the iliac bone region with extension to the soft tissues of the lumbar region.

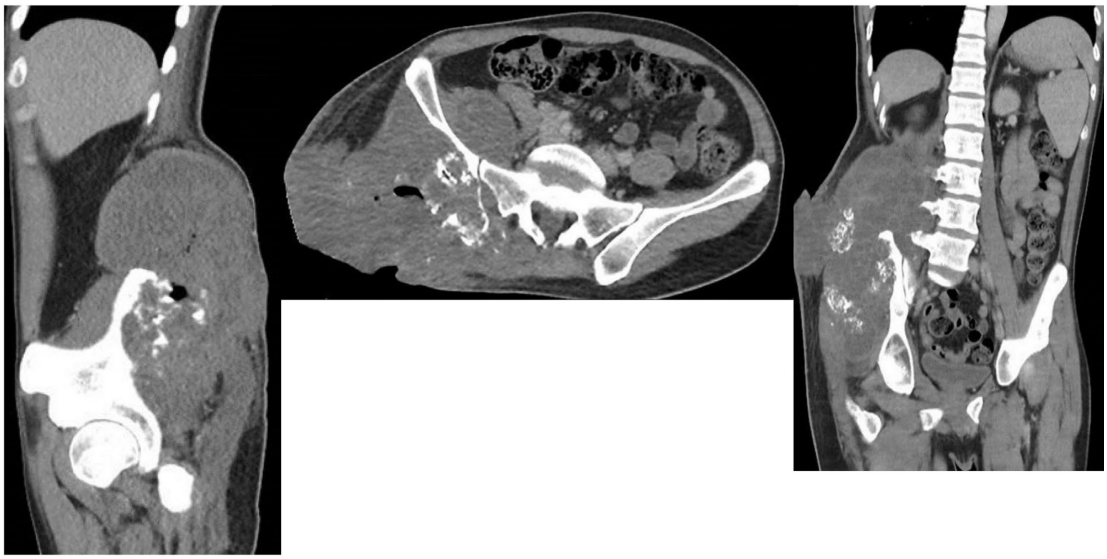

Figure 2. CT scan: A large, solid, hypodense, and heterogeneous tumor with a chondroid bone matrix and areas with air density inside in the the iliac bone. It infiltrates right paravertebral muscles, right posterior abdominal wall, psoas muscle and the gluteal muscles, extending to the skin. At bone level it causes erosion and cortical destruction of transverse processes of L3, L4, and L5.

The patient underwent tumor resection by a type I internal hemipelvectomy, which required resection of the lumbar, paravertebral, and psoas muscles (the latter partially, preserving the genitofemoral nerve along its path), as well as the right transverse processes of the L3, L4, and L5 vertebrae due to their proximity to the tumor, and the right sacroiliac joint (without compromising the sacral foramina) to achieve a wide resection margin (**Figure 3**). The intraoperative finding was a tumor approximately 30 cm in diameter with no vascular or pelvic organ involvement and no compromise of the lumbar plexus, which was preserved. Subsequently, under fluoroscopic guidance, the orthopedic team placed pedicle screws with a connecting rod in the pedicles of L5 and L4, and in the supraacetabular region via the posterior route, completing a lumbopelvic fixation that provides greater stability in the event of injuries to the pelvic ring and spine (**Figure 4**). Due to the length of the surgery, the volume of blood lost, and the need for vasopressors support and blood transfusions with a good response, the surgical wound was protected with a negative pressure system and closure was deferred to a second intervention after the patient's hemodynamic stabilization. There were no postoperative complications. The reconstruction phase was performed in three surgical stages by the reconstructive plastic surgery team using a latissimus dorsi flap, a vertical rectus abdominis myocutaneous (VRAM) flap, and two keystone island flap (**Figures 5(A)-(E)**).

The histopathological study concluded a grade II cCS measuring 22 cm in diameter with cortical rupture and extension to soft tissues, abscessed in its center with liquefactive necrosis, and with resection planes free of neoplasia (**Figures 6(A)-(F)**). After postoperative recovery, the patient was sent to rehabilitation, where he progressed favorably, achieving assisted ambulation, and is currently disease-free for 3 months (**Figure 7**). Given the histological subtype and the status of the surgical margins, adjuvant treatment was not considered beneficial. We will continue with surveillance every three months for two years with clinical check-ups and serial imaging studies (CT scans and X-rays). Subsequently, the periods between surveillance may be longer.

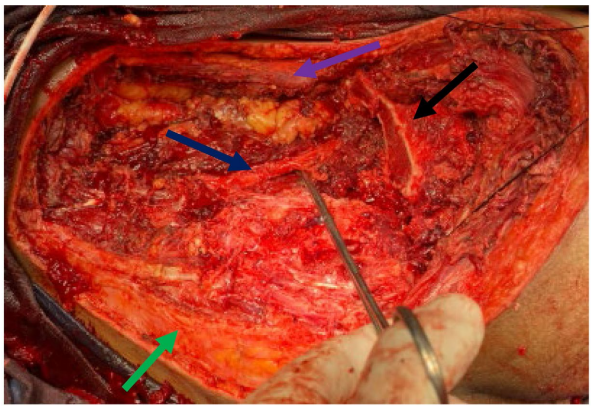

Figure 3. Resection site with preservation of lumbar plexus (blue arrow), bone margin near the acetabulum (black arrow), spine (green arrow) and abdominal wall muscles (purple arrow).

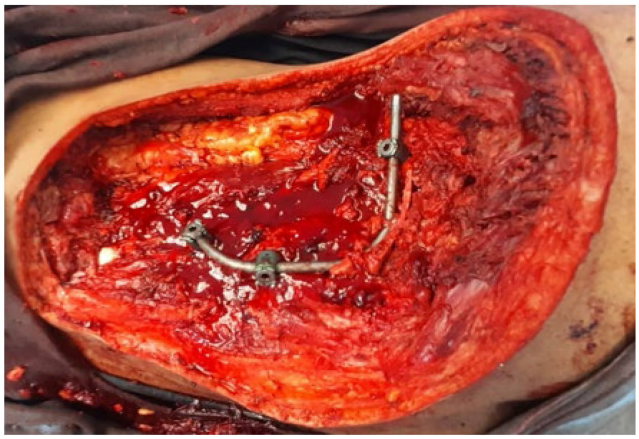

Figure 4. Lumbopelvic fixation on pedicles of L5 and L4 and in the supraacetabular region.

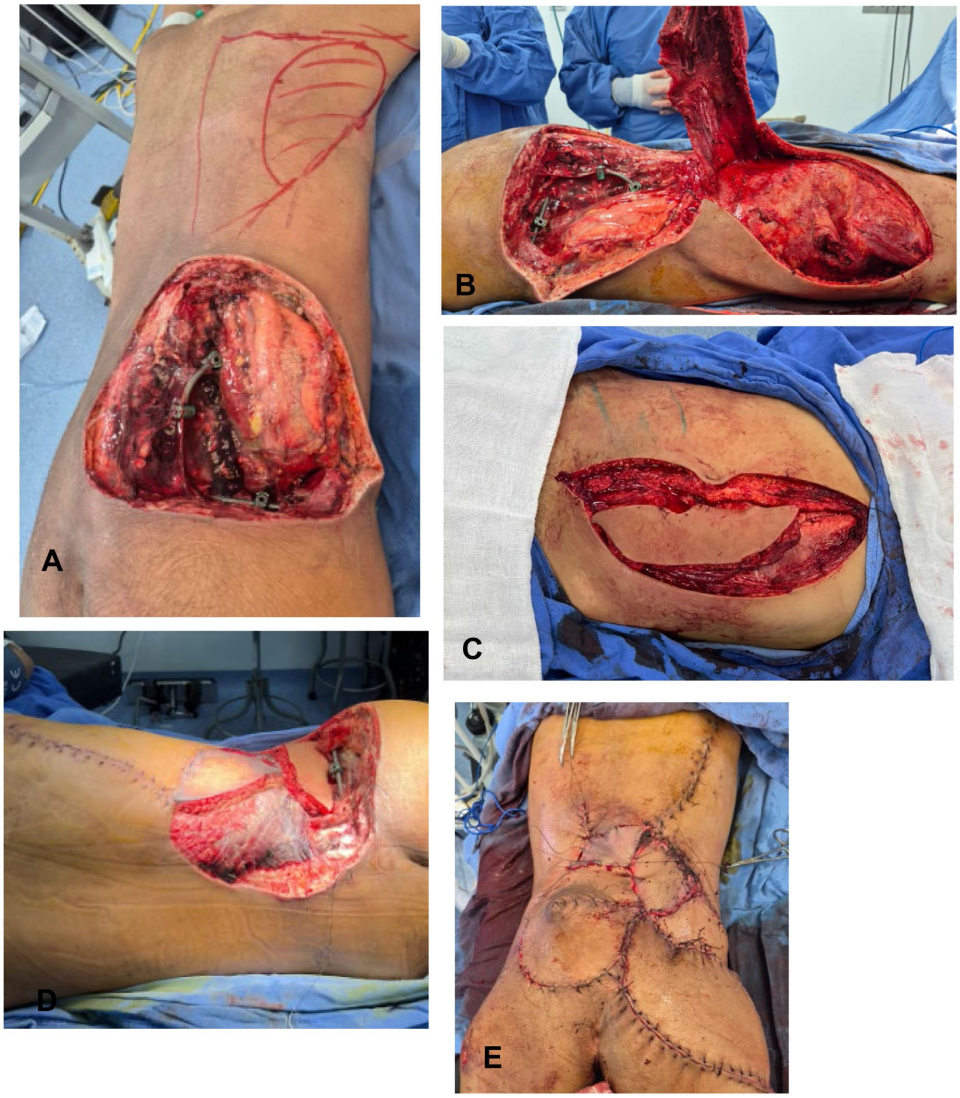

Figure 5. First stage of reconstruction. (A) Resection site with donor site marking. (B) Latissimus dorsi flap. Second stage of reconstruction. (C) Vertical rectus abdominis myocutaneous (VRAM) flap. (D) Residual defect. (E) Third stage of reconstruction with two keystone island flaps.

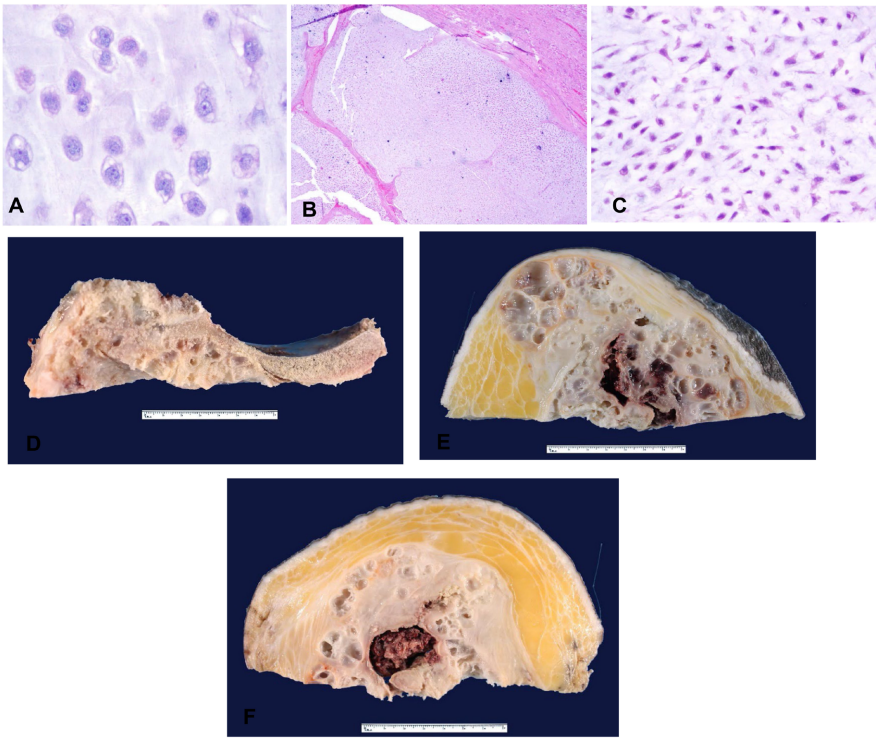

Figure 6. (A) Low magnification photomicrograph of tumor, 5X H&E, hyaline chondroid neoplasm surrounded by fibrous tissue replacing striated muscle and adipose tissue. (B) High magnification photomicrograph, 40X H&E, pleomorphic chondrocytes with irregular nuclei of dispersed chromatin and evident nucleoli are identified. (C) Medium magnification photomicrograph, 10X H&E, showing basophilic chondroid matrix with dense cellularity, loss of polarity, no isogenic groups, and marked pleomorphism. (D) Macroscopic section: the lesion is whitish with a chondroid appearance, cystic degeneration, cortical rupture, and extension to soft tissues. (E) Anterior two-thirds of the bone are affected by the neoplasm. (F) Cortical rupture due to the tumor is identified.

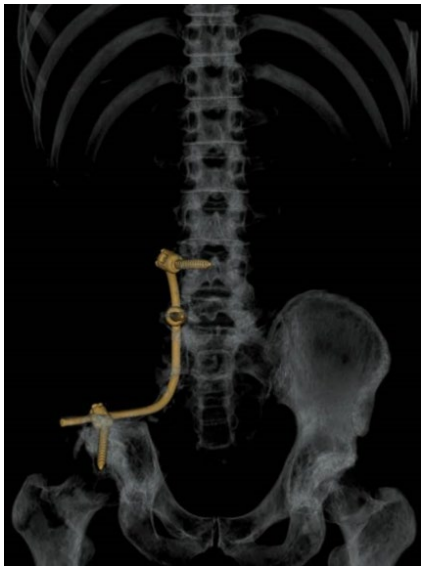

Figure 7. 3D reconstruction CT sacn with surgical changes due to type I internal hemipelvectomy with the lumbopelvic fixator.

3. Discussion

CS predominates in adults, especially in males (61%), with a median age of presentation of 54 years and unlike our patient, up to 70% of cases occur in people over 40 years of age [1] [3] [4] [6] [7] [12]; it can develop intramedullary or grow on the bone surface [13], and although it usually develops primarily in healthy bone (primary chondrosarcoma) [14], up to 5% can originate from the malignant transformation of enchondroma and/or osteochondroma (secondary chondrosarcoma) [3] [6].

Most secondary chondrosarcomas are low-grade tumors; the risk of malignant transformation of a solitary osteochondroma is approximately 1%, and when they are multiple, it can increase to 5%, furthermore, this risk appears to be even higher when they are located in the pelvis [6] [12]. In Ollier's disease and Mafucci syndrome, the risk of malignant transformation of enchondroma is 46% and 57% respectively [13].

In tumor development 50% to 70% of CS have mutations in the IDH1 and IDH2 genes which are normally involved in the Krebs cycle enzymatic process [6]. These mutations are currently considered to be an early event in pathogenesis, as they are present in both solitary and multiple enchondromas and in the dedifferentiation of conventional CS to dedifferentiated CS [9].

CS generally develops in the proximal portions of long bones and/or joints, with the most common site of presentation being the proximal femur [1] [4] [6]; in the axial skeleton the most frequent site is the pelvis [1] [13]. Other less frequent locations (especially of the mesenchymal subtype) include the bones of the craniofacial region, the meninges and the spinal cord [6], and a small percentage may develop in soft tissues [6].

Like other bone sarcomas, CS presents as persistent and progressive bone and/or joint pain, predominantly at night, with the subsequent development of a palpable tumor and progressive limitation of limb movement [6] [11], this sequence was the clinical presentation of our patient. As it is generally a slow-growing tumor, symptoms may be present for up to 15 months before the tumor is detected, and progressive weakness of the limb may culminate in a pathological fracture, especially in high-grade CS [6] [11].

The typical finding suggestive of CS on conventional radiography and tomography is a "ring-and-arc" pattern representing the presence of sclerosis and chondroid matrix [6] [13], and high-grade tumors may have a moth-eaten appearance secondary to bone destruction. MRI is useful for ruling out bony lesions and delineating the extent of the tumor to soft tissues and its relationship to neurovascular structures [6].

cCS is the most common type accounting for 85% - 90% of cases [1] [4] [6] [13]. Based on its location in the affected bone it is classified as central (85% of cases), periosteal, and peripheral [13] [14]; most are grade 1 and 2, and given their behavior the WHO classifies them based on their location as atypical cartilaginous tumors when located in the extremities [12] [14], and as grade 1 chondrosarcomas

when located in the axial skeleton [6] [13]. Based on grade, the reported incidence is 35.4%, 42.6%, and 12.9% for grades I, II, and III respectively [7].

dCS accounts for 10% of all chondrosarcomas, and up to 20% of patients present with metastatic disease at the time of diagnosis [9] [13]. It is a high-grade biphasic tumor with a conventional CS component and a high-grade non-cartilaginous sarcoma component generally showing histological features of osteosarcoma, fibrosarcoma, or pleomorphic undifferentiated sarcoma [13]. Molecularly it shares the same p53 and IDH1/2 mutations as cCS indicating a common origin, and PD-L1 expression has been reported in up to 50% of cases [13].

mCS presents a bimorphic histological pattern consisting of an undifferentiated component of small round cells and a well-differentiated cartilage component [13] [15]; up to 10% of patients with this variant present with metastatic disease [9], and unlike the other variants, mCS occurs at an earlier age, with a peak incidence in the second and third decades of life [6], and presents with the high-grade translocation (11; 22) (q24; q12) that distinguishes it from other variants, suggesting a different origin and that it may belong to the group of small round cell tumors [13].

Due to its slow growth, low mitotic division, and the production of hyaline cartilage by tumor cells which leads to low vascular and lymphatic circulation restricting drug penetration, CS is considered a chemoradiation-resistant tumor [1]-[4] [6] [7] [11] [13] [16] [17]. Other factors associated with their chemoradioresistance include the presence of the p-glycoprotein, the multidrug-resistance-1 gene (MDRI), a high expression of Bcl-2 family proteins, and a dense extracellular matrix [14].

Prognostic factors include age, gender, tumor size, histological subtype, tumor location, and the presence of pathological fracture; all of these must be taken into account when choosing treatment [1] [7] [13]. Two other extremely important prognostic factors include histological grade and resection margin achieved [4] [7]; regarding the former it is important to mention that although image-guided core needle biopsy has high diagnostic accuracy for bone tumors and CS, the classification of its histological grade is difficult and can even vary by up to 52% when compared to the final grade of tumor resection [5] [12]; in our patient the initial biopsy revealed data compatible with grade 1 CS, and after resection the final result was grade 2. Regarding the resection margin, it should be noted that this is the only modifiable prognostic factor [5] [6] [11]. Currently the reported 5-year survival rates are 83%, 53% - 74%, and 7% - 31% for low-grade, high-grade, and undifferentiated chondrosarcoma respectively [11] [13] [14], the reported local recurrence rate is 18% to 45% [2], and the most common site of metastatic disease is the lung [14].

Like other primary malignant bone tumors, CS is staged using the TNM system by the American Joint Committee on Cancer International Union Against Cancer (AJCC/UICC) and/or the Enneking System [12]. The latter is based on histological grade (I = low and II = high grade) and compartmental spread (A = intracompartmental, B = extracompartmental); if the bone cortex is intact and there is

no soft tissue invasion, the tumor is intracompartmental [12]. Finally, stage III corresponds to metastatic disease [12]. Our patient corresponded to an Enneking IB and a T2b N0 M0 G2 (tumor confined to one pelvic segment with extraosseous extension greater than 8 cm); currently, the AJCC prognostic stage groupings for the spine and pelvis have not yet been described.

The treatment of low-grade CS is controversial [3]; in long bones it can be treated with intralesional extended curettage with or without local adjuvant therapy such as phenol or cryotherapy, and reconstructed with cement or bone graft [6] [10] [16], however many recent studies recommend wide resection due to high recurrence rates [3] [14], especially in the pelvis, where it is not considered a treatment option for low-grade chondrosarcoma [11].

For all grade 2 and 3 chondrosarcomas, and all pelvic chondrosarcomas and on the rest of the axial skeleton regardless of grade, the main treatment is wide surgical resection with limb-sparing surgery [1] [3] [6] [7] [9] [10]-[14] [16]; it offers the best results in overall survival and disease-free survival (37% versus 18% with other therapeutic modalities) [1] [4].

The recommended resection margin is ≥1 mm [3]; however in high-grade chondrosarcomas has been reported that a resection margin >2 mm further reduces even more the risk of local recurrence [11] [12], and in the series by Stevenson *et al.* a surgical margin of 4 mm was recommended for pelvic chondrosarcoma [5]; the resection margins achieved with our patient were between 1 and 2 mm. It is important to mention that this margin was possible because even with advanced reconstruction flaps, the secondary defect could be restored. As for adjuvant treatment (radiotherapy and/or chemotherapy) it does not seem to improve overall survival and disease-free survival rates, especially in the conventional subtype [1]; given our histological subtype and the negative resection margins we do not consider adjuvant treatment to be beneficial.

Enneking and Dunham developed a classification system for pelvic resection based on the section or sections of bone to be resected in four types: type I the iliac wing, type II the periacetabular region, type III the pubic rami, and type IV the sacrum [18]; given the tumor location, the tumor-free status of the rest of the pelvis, and the preserved function of the limb, our patient was a candidate for a type I pelvic resection. If the extent of the tumor or the resection procedure requires the removal of two of the three critical pelvic structures necessary for the lower limb function (the sciatic nerve, the femoral neurovascular bundle and the periacetabular region) an external hemipelvectomy should be recommended [18] [19].

Currently there are several alternatives for pelvic reconstruction; iliofemoral pseudarthrosis or arthrodesis, grafts (allograft, free vascularized fibular graft, vascularized fibular autograft, or autoclaved autograft), prosthetic reconstruction and customized prosthetic reconstruction [19]. The pelvic reconstruction should be individualized to each patient because certain anatomic resections lend themselves more easily to a functional reconstruction whereas some are better left unreconstructed, the most common pelvic resection that needs reconstruction is

type II as well as the combined resections in which the continuity of the lumbopelvic articulation is compromised [18] [19]; generally type I and type III resections often are left unreconstructed with minimal functional compromise and the outcomes are favorable with most patients achieving ambulation [18] [19]. Patients undergoing internal hemipelvectomies usually have favorable functional results [20].

dCS can be treated with neoadjuvant and/or adjuvant chemotherapy [16], and the National Comprehensive Cancer Network guidelines report the use of the treatment regimen for osteosarcoma (doxorubicin, ifosfamide, cisplatin, metrotexate) [1] [4] [8] [10] [12] [16] [21], however given the rarity of this histological subtype there are only retrospective studies about the role of chemotherapy with controversial results [13] [14] [21]. A systematic review compared the 5-year survival rate between patients treated with surgery alone and patients treated with surgery + chemotherapy reporting no differences between the two treatments, however the studies analyzed were retrospective [21]. For mCS chemotherapy with regimens similar to those used for Ewing sarcoma may be considered, especially as neoadjuvant treatment [12] [13] [15] [16], and as adjuvant treatment it has been associated with reductions in the risk of recurrence and death [9] [10].

PD-L1 expression has been reported exclusively in patients with dCS, in approximately 40% of cases. A phase II study (SARC 028 study) investigating the role of pembrolizumab in advanced bone and soft tissue sarcomas reported that of the five patients enrolled with dCS, one achieved a partial response [9]. Similarly, the phase I/II ImmunoSarc study investigating the use of nivolumab and sunitinib in advanced bone and soft tissue sarcomas demonstrated activity in dCS [9].

In terms of targeted therapies, the multitargeted tyrosine kinase inhibitor (MTKI) pazopanib has been reported to prolong disease stabilization in progressive chondrosarcomas, with a median progression-free survival (mPFS) of 7.9 months in a phase II study [9]. Another MTKI that has been evaluated in the management of chondrosarcoma is regorafenib, which in the REGOBONE study showed an improvement in mPFS of 19.9 weeks compared to placebo (8 weeks) [9].

Another therapeutic target to consider are IDH1 and IDH2 mutations; in the CS cohort of the phase I study of ivosidenib, mPFS was reported to be 5.6 months [9]. Currently the IDH1 inhibitor olutasidenib, the IDH2 inhibitor enasidenib, and the dual inhibitor of IDH1/2 vorasidenib are under investigation [9].

Radiotherapy may be useful in incomplete resections due to close or positive margins [12], especially in high-grade tumors [14], or as palliative treatment in unresectable tumors or those involving unacceptable morbidity (invasion of the spinal cord or beyond the midline of the sacrum), and/or in inoperable patients [3] [11] [12] [15]. Although adjuvant radiotherapy could be effective for mCS given its aggressiveness and high recurrence rate, while some articles have reported improvements in survival, others have not concluded a benefit [15] [17],

and the NCCN in its latest edition does not recommend the use of adjuvant radiotherapy in cases of R0 resection.

4. Conclusion

Unlike other chondrosarcomas, pelvic chondrosarcoma presents less favorable oncological and functional outcomes due to the complexity of its surgical treatment which makes it difficult to achieve wide resection margins, and the lack of useful adjuvant treatments to reduce the risk of recurrence and/or disease progression. To achieve the best therapeutic outcome in these patients, the diagnostic and therapeutic approach must be multidisciplinary.

Consent

Written informed consent was obtained from the patient for publication of this case report.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviation

Chondrosarcoma (CS)
Conventional type chondrosarcoma (cCS)
Mesenchymal chondrosarcoma (mCS)
Dedifferentiated chondrosarcoma (dCS)
Multitargeted Tyrosine Kinase Inhibitor (MTKI)
Median progression-free survival (mPFS)