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Case Report

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Chondrosarcoma of the Pelvis after Radiotherapy for Cervical Cancer: A Case Report

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Abstract

The incidence of bone sarcomas in patients irradiated with cervical cancer who survive 5 years represents only 0.04% of radiation-induced sarcomas (RIS). This rate increases in the first 20 years and decreases thereafter. In this publication, we present the case of a patient who developed a sacroiliac chondrosarcoma 12 years after receiving chemo-irradiation for a cervical cancer.

Case Presentation

47-year-old patient first seen in 2011 for a stage III B adenocarcinoma of the cervix, receiving concomitant chemo-radiation that ended with tumor persistence. She underwent total pelvic exenteration and was kept under surveillance for 12 years. She consulted for lumbosacral pain and the computed axial tomography (CT) study showed a tumor lesion in the left sacroiliac joint with extension to the soft tissues. An incisional biopsy of the lesion was proposed, but the patient did not undergo the procedure. She returned 7 months later with severe sacroiliac pain and inability to ambulate, with increased volume in the region. A new CT scan showed in the left iliac bone a lesion of 13.8 x 13.4 x 9.4 cm compatible with chondrosarcoma and in the thorax, pulmonary metastasis. The biopsy reported chondrosarcoma grade 3 radium induced by radiation, so it was sent to medical oncology for palliative treatment without the patient attending her treatment.

Introduction

Reports on radiation-induced sarcomas were first documented in the early 20th century by Martland, who described the development of bone sarcomas in Swiss watchmakers exposed to radioactive phosphorus [1]. In 1929, Beck published the case of a patient who developed sarcoma sometime after receiving radiotherapy for a benign lesion [2,3] .Radiation-induced sarcoma (RIS) is a late and rare event, with an incidence ranging from 0.03-0.9% [1,4-8]. RIS accounts for 3-6% of all sarcomas, with the most frequent locations being the chest and pelvis [1,7-9]. 79% are soft tissue sarcomas, and 21% are bone sarcomas [2,7]. The latency period ranges from 7 to 40 years, with an average of 16.8 years [1,4-6,7,8], and its frequency has increased in recent years attributed to the longer lifespan of patients and the use of concomitant chemotherapy, which significantly shortens the time to presentation [1,4,6,7]. Chemotherapy has been reported to potentiate the effects of tissue damage produced by radiotherapy, interfering with DNA repair processes, reducing the time to development of RIS, and increasing its incidence [1]. Regarding cervical cancer (CC), RIS typically occurs late after receiving radiotherapy. It has been reported that 10-40% occur before the age of 50, and 22.8% occur after the age of 50 [3,10,11]. According to the Globocan 2022 platform, [12] cervical cancer presents the 4th position in the incidence of any type of cancer in woman (considering absolute numbers, incidence in females, and age 5-85+) with 14.1 cases for every 100,000 women and represents the 3rd position in mortality induced by any type of cancer with a rate of 7.1 per every 100,000 women.

In Mexico, cervix cancer is the 2nd cause of death for any type of cancer and also is in the 2nd position in incidence (15 cases per 100,000 women considering both, rates in women 5-85+ years). For the group from 50 to +85 years, the incidence is in the 3rd position but has increased to 36.3 cases per 100,000 and is the 2nd cause of death by cancer with 21.4 cases per 100,000 [12]. While isolated cases of RIS in CC, such as leiomyosarcomas [13], cutaneous angiosarcomas [14], and rhabdomyoblastic sarcomas [4], have been the most common sarcomas reported in some series are undifferentiated pleomorphic sarcoma, angiosarcoma, and leiomyosarcoma [2,4]. The incidence of bone sarcomas in patients irradiated for CC who survive 5 years represents only 0.04% [3], significantly increasing in the first 20 years and decreasing thereafter [11,15]. The most common are osteosarcoma, undifferentiated pleomorphic sarcoma, and chondrosarcoma [3].

This publication presents the case of a patient who developed a sacroiliac chondrosarcoma 12 years after receiving chemo radiation for stage IIIB cervical cancer. Her evolution is discussed, along with a review of the literature.

Case Presentation: The patient was first seen in June 2011 at the age of 47 with a history of sexual debut at 17 years old, one sexual partner, 2 births, one cesarean section, and menopause at 46 years old. Her condition started 6 months before admission with genital bleeding, leading to a positive biopsy for cervical adenocarcinoma. Gynecological examination revealed a cervix with infiltrating ulcerous lesions, bleeding, extending to two-thirds of the upper vagina and both parametria, with the right infiltrating to the pelvic wall and the left to its internal third. It was classified as Stage IIIB (FIGO-2009), and the slide review reported poorly differentiated cervical carcinoma (Figure 1). With negative staging for metastasis (computed tomography), she was administered concurrent chemoradiation (External Beam Radiotherapy 50 Gy plus 4 cycles of chemotherapy with cisplatin 50 mg per m2 of body surface area), plus 30 Gy of low-dose rate brachytherapy, which ended on 05-10-2011.One month after completing treatment, locoregional examination showed tumor activity in residual cervical tissue with positive biopsy for cancer, along with residual tumor in the upper half of the vagina and parametria with suspected tumor activity. On 30.01.2012, exploratory laparotomy revealed a uterus measuring 10x4x6 cm, left hydro ureter, and bilateral parametrial fibrosis. Total pelvic exenteration was performed with total colpectomy supported by a perineal procedure, along with partial resection of both levator ani muscles and pelvic floor reconstruction with a rectus muscle flap from the left side.

Intraoperative examination of the surgical specimen showed no residual tumor at surgical margins, and she had a satisfactory postoperative course, discharged 10 days after surgery. The pathology reports of the surgery indicated residual poorly differentiated endocervical adenocarcinoma (Figure 2) and in the lower uterine segment (1cm), plus high-grade cervical intraepithelial neoplasia with histological changes associated with HPV infection. The bladder, rectum, sigmoid colon, and anus were negative for neoplastic cells, and there was no tumor at surgical margins.

The patient remained under periodic follow-up without evidence of disease until 28-01-22 (12 years after completing treatment for cervical cancer), when she presented with severe lumbosacral pain requiring a CT scan, which reported a tumoral lesion in the left sacroiliac joint. Periosteal reaction towards soft tissues, incipient involvement of the left iliopsoas and gluteal muscles were noted (Figure 3). With a diagnosis of left sacroiliac bone neoplasia, it was decided to perform an incisional biopsy of the lesion under general anesthesia, which the patient did not undergo. She returned 7 months later with severe sacroiliac pain, inability to ambulate, and increased volume and consistency in the left iliac fossa, gluteal region, and inguinal region (Figure 4). A CT scan revealed a lesion in the left iliac crest with a blastic appearance, wide transition zone, brush-like bone destruction pattern, and popcorn-like cartilaginous matrix, with interrupted periosteal reaction extending into soft tissues and involvement of the ipsilateral iliopsoas, quadratus lumborum, and gluteus Maximus and medius muscles, measuring 13.8 x 13.4 x 9.4 cm with a volume of 909 cc and involvement of

ipsilateral sacral neuroforamina (Figure 5). On the sagittal view, a blastic lesion with bone destruction and popcorn-like cartilaginous matrix was observed, along with periosteal reaction and extension into soft tissues, with greater prominence in the gluteal region (Figure 6). In the thorax, pleural thickening and multiple diffuse sub pleural nodules were observed, with the largest showing a cartilaginous matrix (Figure 7).

On October 7, 2022, under general anesthesia, an incisional biopsy of the lesion was performed, which reported conventional chondrosarcoma. Histological grade: 3, absent lymphovascular invasion, poorly differentiated. Tumor necrosis: <50% (2 points); histological grade 3 (high grade). Conclusion: Due to the history of radiotherapy, a radiation-induced chondrosarcoma is considered (Figures 8 and 9). With a diagnosis of grade 3 radiation-induced chondrosarcoma in the left iliac bone with pulmonary metastases, she was referred to Medical Oncology for palliative treatment, which the patient declined due to potential deterioration in quality of life. She was referred to palliative care and pain clinic, last seen on January 13, 2023.

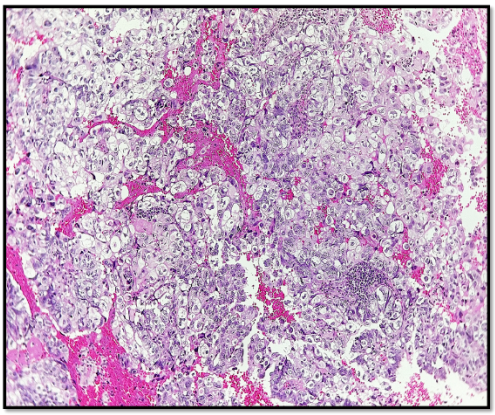

Figure 1: Microphotography in H-E technique at 100x. Malignant epithelial neoplasia is observed, of an invasive type, with a solid growth pattern, with large, round cells, with abundant cytoplasm with some vacuoles, the nuclei present marked atypia, with hyperchromatic and/or vacuolated nuclei, with evident nucleoli.

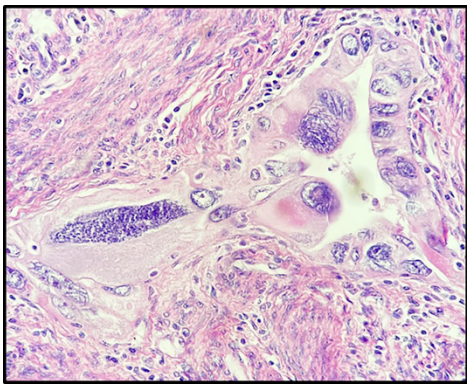

Figure 2: Photomicrograph in H-E technique at 400x, where malignant epithelial neoplasia is observed, with a glandular, invasive growth pattern; The cells are large, with abundant cytoplasm with some vacuoles, eosinophilic, the nuclei present atypia and marked pleomorphism (anaplasia). This "monstrous" change.

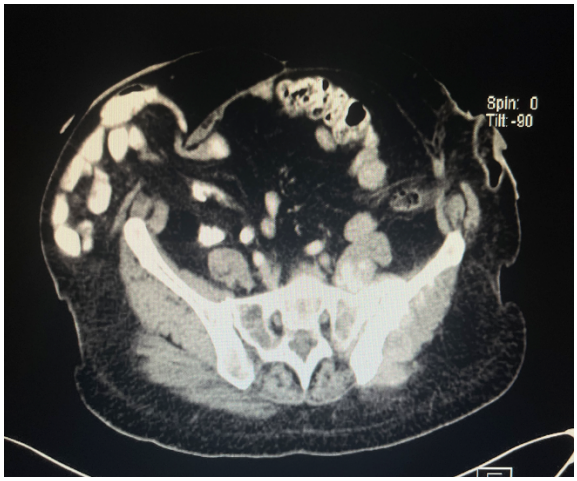

Figure 3: CT scan of the pelvis with tumor lesion in the left sacroiliac joint. Periosteal reaction towards soft tissues, incipient involvement of the left iliopsoas and gluteus.

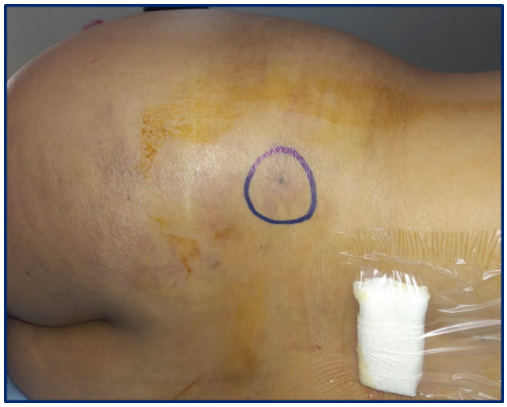

Figure 4: The increase in volume and consistency presented by the patient in the left gluteal region with the tattoo point of the previous irradiation is shown. The lesion extended to the left iliac fossa and inguino-crural region.

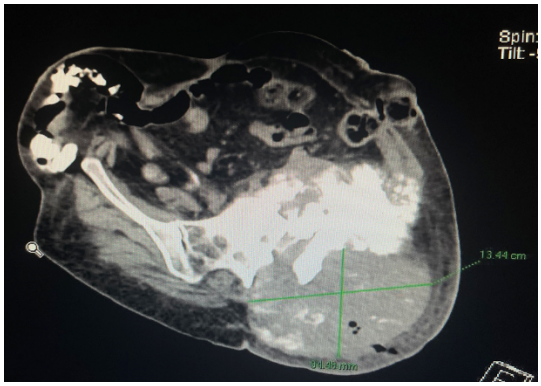

Figure 5: Lesion in the left iliac crest with a blastic aspect with bone destruction and cartilaginous matrix in a popcorn shape; periosteal reaction plus extension towards the soft tissues, involving the ileopsoas, quadratus lumborum, gluteus maximus and medius muscles ipsilateral, and affecting the ipsilateral sacral neuroforamina with dimensions.

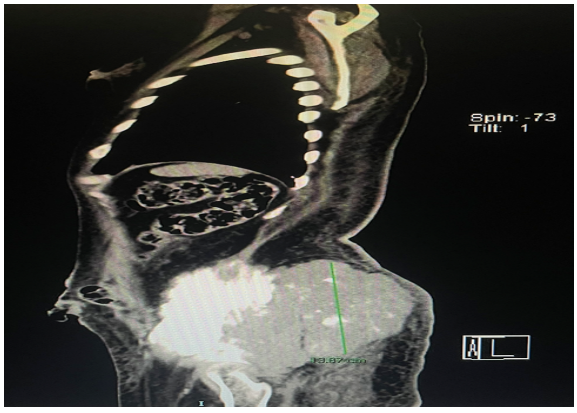

Figure 6: CT scan sagittal section showing blast-like lesion, bone destruction and cartilaginous matrix in popcorn shape, periosteal reaction; extension into the soft tissues.

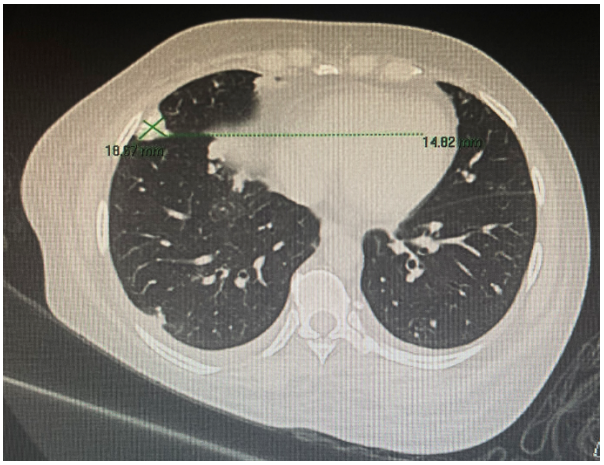

Figure 7: CT scan pulmonary window showing pleural thickening and multiple subpleural nodules of diffuse location, the largest of which has cartilaginous matrix.

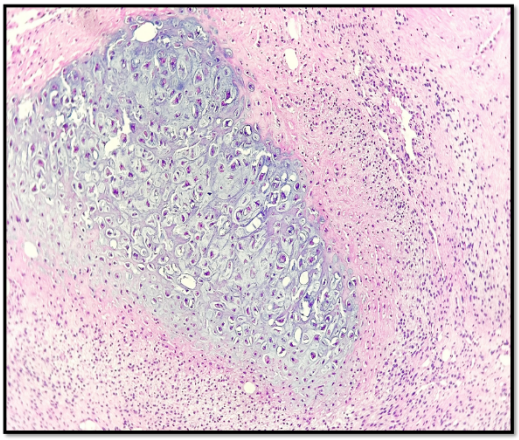

Figure 8: Bone biopsy of the pelvis. Microphotography in H-E technique at 100x. Malignant mesenchymal neoplasm is observed, with chondroid aspect with solid growth pattern, with invasion to adjacent soft tissues and desmoplastic reaction. The cells have a "lacunae" appearance. No bone is observed.

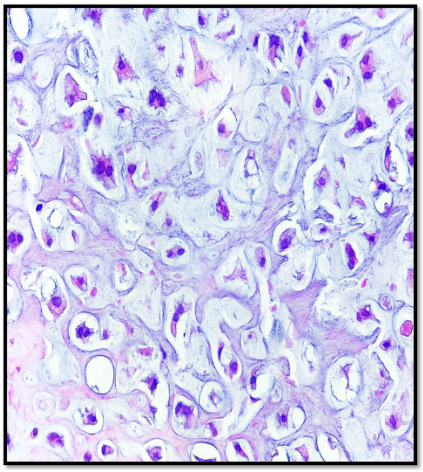

Figure 9: Microphotography in H-E technique at 400x, showing malignant mesenchymal neoplasm, chondroid aspect with solid growth pattern. The cells show marked atypia, hyperchromatic nuclei arranged in the center of the myxoid matrix; irregularity of nuclear membranes and some atypical mitosis figures.

Discussion

The development of second malignant neoplasms in previously irradiated patients is led by breast cancer [9], followed by CC [5], where second primaries occur in both the uterine body and neighboring sites: rectum, bladder, vagina, or even bones of the pelvis [3,5-7,11,15,16,17]. In the Surveillance, Epidemiology, and End Results (SEER) database of the United States for CC patients who survived radiotherapy treatment spanning 9,092 patients from 1973-2008, 54 patients (0.6%) developed second primaries in the uterine body [17]. This figure was 33 (0.9%) among the 3,674 CC patients included in the National University College of Medicine Registry in Seoul, Korea [8].

The reported frequency for bone sarcomas in CC patients irradiated is 0.04% [3], and their risk for development significantly increases in the first 20 years and decreases thereafter, with osteosarcoma, undifferentiated pleomorphic sarcoma, and chondrosarcoma being the most common [3, 11]. Regarding the pathogenesis of secondary sarcomas, it is estimated that radiation-induced oncogenesis is linked to DNA damage repaired incompletely in cells retaining their mitotic potential, as well as genomic instability such as abnormal intracellular signaling, cytokine production, free radical generation, and inflammatory response [13,16].

Regarding radiation-induced bone sarcomas, some authors consider that sporadic osteosarcomas developed in irradiated territory are not specifically different genetically from radiation-induced sarcomas, while others believe they are, showing more chromosomal aberrations such as losses on chromosome 1p and specific loss of material on chromosome 3p [12,15,18]. Clinical presentation in the series by Nakanishi K. et al, with 5 cases [3], showed that bone sarcomas in CC patients irradiated clinically presented as large round or oval masses mainly in the sacroiliac joint, extending into gluteal soft tissues, or in the ileum location, with extensive extension into both anterior and posterior soft tissues. The authors concluded that the diagnosis of radiation-induced pelvic sarcomas should be considered in CC patients when a mass is observed in the soft tissues of the previously irradiated field, especially if the mass is posterior to the sacroiliac joint and the latency period is over 5 years [3].

Our patient received chemoradiation treatment for advanced cervical cancer that persisted after treatment, requiring total pelvic exenteration, remaining under follow-up without evidence of disease for 12 years, after which she presented severe lumbosacral pain that evolved 7 months later to ambulation inability due to tumoral lesion involving the left iliac fossa, ipsilateral gluteal region, and left inguinal region. CT scans showed a blastic lesion in the left iliac crest with extensive soft tissue involvement and sacral neuroforamina involvement. Thoracic study showed pulmonary metastases. The incisional biopsy reported a secondary high-grade chondrosarcoma, and the patient discontinued follow-up without accepting palliative chemotherapy. Consulted literature refers to RIS being commonly diagnosed late, being of high grade, and having a poor prognosis; surgery, when feasible, constitutes the treatment of choice, and overall survival rarely exceeds 2 years [2,3,6-8,14].

In the series from the Maria Sklodowska-Curie National Oncology Institute in Poland, overall survival in 58 patients was 21 months [7], and the median follow-up period was 23.1 months in the series of 33 patients reported by Kyung Su Kim, et al from the Department of Radiation Oncology, Seoul National University College of Medicine, Seoul, Korea [8]. Rebecca A. Gladd et al from Memorial Sloan-Kettering Cancer Center, New York, NY, reported that adverse prognostic factors in 130 RIS patients were related to high histological grade of the neoplasm, size larger than 5 cm, and positive surgical margins [6].

Lagrange JL and J Thariat [16] refer to the development of a sarcoma not always implying that long-term survival is impossible, for which early diagnosis and aggressive, appropriate strategy are necessary. This should all be done in specialized centers. WirbeL JR et al [19] based on their experience with 51 chondrosarcomas of the pelvis,refer that the incidence of local recurrences was influenced by the surgical margin achieved, whereas the incidence of distant metastases was influenced by the tumor stage. Lagrange JL and J Thariat [16] suggest the following recommendations In patients with cancer, the risk of radiation is low compared to the curative and palliative benefits it provides. The risk of developing a sarcoma in irradiated territory should always be considered to ensure early diagnosis. When, to achieve the same outcome,

it is possible to choose between strategies that include or do not include radiation, the strategy without radiation should be favored.
• Patients treated with radiation should be monitored for life.

Conflict of Interest: The authors declare no conflict of interest in the present publication.

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