Available online at www.sciencedirect.com

SciVerse ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology 51 (2012) 89–92

www.tjog-online.com

Case Report

Uterine carcinosarcoma associated with pelvic radiotherapy for sacral chordoma: A case report

Korhan Kahraman [a,*], Fırat Ortac [a], Duygu Kankaya [b], Gulsah Aynaoglu [a]

[a] *Department of Obstetrics and Gynecology, Ankara University School of Medicine, Ankara, Turkey*
[b] *Department of Pathology, Ankara University School of Medicine, Ankara, Turkey*

Accepted 28 December 2010

Abstract

Objective: Postirradiation sarcoma of the female genital tract is rare, but a recognized event. Most reported cases have been associated with history of radiotherapy for various gynecologic conditions, particularly cancer of the uterine cervix and abnormal uterine bleeding. The occurrence of uterine sarcoma secondary to radiotherapy for a non-gynecologic tumor and, furthermore, this condition being simultaneous with the recurrence of primary tumor is unique.
Case Report: A 67-year-old woman presented with a uterine mass which was diagnosed as a sarcoma by endometrial curettage and history of pelvic radiotherapy 23 years previously for sacral chordoma. Surgical staging procedure for uterine malignancy was performed. The final pathologic diagnosis was carcinosarcoma of the uterus.
Conclusion: In uterine masses seen in patients with history of irradiation to the pelvic field, the probability of uterine sarcomas should always be kept in mind. These tumors may occur simultaneously with recurrence of primary tumor previously treated by adjuvant radiation therapy.

Keywords: carcinosarcoma; radiation-associated neoplasm; sacral chordoma; uterine sarcoma

Introduction

Carcinosarcoma of the uterus, also referred to as malignant mixed Müllerian tumor, is a rare neoplasm composed of epithelial and mesenchymal malignant elements. These tumors accounting for 40–50% of all uterine sarcomas usually occur in postmenopausal women with a peak incidence at the ages of 60–70 years [1,2].

Previous pelvic irradiation is a recognized predisposing factor for uterine carcinosarcoma which has been estimated to occur in approximately 15% of cases [3]. Despite this defined relationship, no specific clinical or histopathological features distinguish between radiation-associated and *de novo* uterine sarcomas.

Chordoma is a rare, slowly growing, locally aggressive, malignant bone tumor that originates from notochordal remnants and occurs exclusively in the axial skeleton. The sacrum is the most common location of the chordomas [4].

Herein we present a unique case of uterine carcinosarcoma and recurrent sacral chordoma occurring simultaneously in a 67-year-old woman who had a history of pelvic irradiation for sacral chordoma 23 years previously. The clinical, radiographic, and pathologic features of this case are discussed.

Case report

A 67-year-old, multiparous woman was referred to our clinic with the diagnosis of uterine sarcoma in November 2009. Eleven days before she was referred, an endometrial curettage was performed because of postmenopausal uterine bleeding and revealed a sarcomatous malignancy at another center, but differential diagnosis between high-grade leiomyosarcoma and carcinosarcoma could not be done. She was

* Corresponding author. Department of Obstetrics and Gynecology, Ankara University School of Medicine, 06100 Ankara, Turkey.
E-mail address: korhankahraman@hotmail.com (K. Kahraman).

1028-4559/$ - see front matter
doi:10.1016/j.tjog.2012.01.018

operated because of sacral chordoma in 1986 with follow-up radiation therapy [posterior and anterior pelvic fields of 13×17 cm delivering a dose of 5000 rad (50 Gy) in 25 fractions between March and May 1986]. In addition, repeated surgeries were performed for the recurrence of sacral chordoma in 1989, 1999, and 2002. She had been menopausal since the age of 44 years and had never used hormone replacement therapy. She had no history of tamoxifen use. Her medical history was significant for diabetes mellitus and hypertension. In April 2009, a magnetic resonance imaging (MRI) scan was performed at another hospital because of a painful swelling in the lumbo-sacral region, and showed a mass indicative of sacral chordoma recurrence (Fig. 1A, B). The same MRI scan also showed a uterine mass measuring $62 \times 42 \times 38$ mm that completely filled the uterine cavity (Fig. 1A, B). Despite these MRI findings suggesting a uterine tumor, further diagnostic interventions to demonstrate or rule out uterine malignancy had not been performed at the same center. With a possible diagnosis of recurrent sacral chordoma, she had been treated with radiotherapy according to the following schedule: a total of 2600 cGy (26 Gy) in 13 fractions between April and May 2009. Follow-up MRIs did not show a significant reduction in the size of the sacral mass.

Tumor markers were normal except mildly elevated serum cancer antigen 125: 71.6 U/mL (reference range <35 U/mL). A chest radiograph and computerized tomographic scan of thorax and upper abdomen were negative for metastatic disease.

With a diagnosis of uterine sarcoma, exploratory laparotomy was performed at our clinic. Laparotomy revealed an enlarged uterus totally with a mass probably representing sarcoma. The uterine tumor invaded the bladder and the uterus was adherent to the recto-sigmoid colon, omentum, and peripheral structures. Minimal serous-hemorrhagic ascites was observed. Both ovaries were atrophic. Other pelvic and abdominal structures and peritoneal surfaces were all grossly normal. A staging procedure was performed including a peritoneal washing for cytological evaluation, total hysterectomy, bilateral salpingo-oophorectomy, para-aortic lymph node dissection, infracolic omentectomy, multiple peritoneal biopsies, and partial resection of the bladder invaded by the tumor. Pelvic lymphadenectomy was not performed because of technical difficulties resulting from the excessive fibrosis at the pelvic lymph node regions secondary to previous radiotherapy.

Macroscopic evaluation showed a polypoid mass filling the uterine cavity, 7 cm long in diameter, with a hemorrhagic, necrotic, fleshy cut surface. Histopathological evaluation of the uterine mass revealed a neoplasm composed of an admixture of malignant epithelial and mesenchymal components. The epithelial component was endometrioid type adenocarcinoma (Fig. 2A, B) and the sarcomatous areas were poorly differentiated with highly atypical spindle cells and numerous atypical mitotic figures (Fig. 2C). Areas of osteosarcoma were detected as heterologous element (Fig. 2D). Vimentin expression was strong and extensive in sarcomatous areas and focally in epithelial component (Fig. 3A). Epithelial component showed diffuse and strong cytokeratin expression immunohistochemically (Fig. 3B). Scattered smooth muscle actin (SMA) expression was detected in a few cells of sarcomatous areas indicating poorly differentiated leiomyosarcoma (Fig. 3C). There was extensive myometrial invasion exceeding the inner half. Bilateral paraovarian tissues and urinary bladder were infiltrated. Lymph node involvement was confined to only one (1/12) para-aortic lymph node. Omentum and both ovaries showed no evidence of malignancy. The cytology of peritoneal fluid was negative for malignant cells. Therefore, the final diagnosis was a FIGO (*Federation Internationale de Gynecologie et d'Obstetrique*) stage IVA uterine carcinosarcoma. She recovered uneventfully and was discharged on the 13th postoperative day in a stable condition. She received adjuvant chemotherapy consisting of six cycles of paclitaxel (80 mg/m^2) and carboplatin (2 AUC). The first three cycles were given at

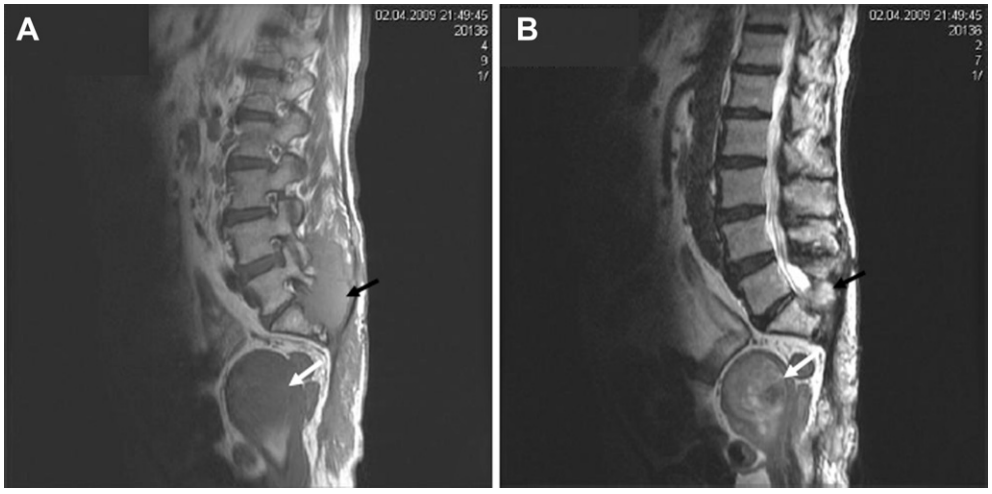

Fig. 1. (A) T1-weighted sagittal image; a hypointense recurrent sacral chordoma (black arrow) and a heterogeneous hypointense mass filling the endometrial cavity of the uterus (white arrows). (B) T2-weighted sagittal image; the relatively hyperintense uterine mass (white arrows). Hypointense areas within the endocavitary mass denote hemorrhage. The sacral chordoma (black arrow) is also seen as a relatively hyperintense mass partially filling the spinal canal and abutting the filum terminale.

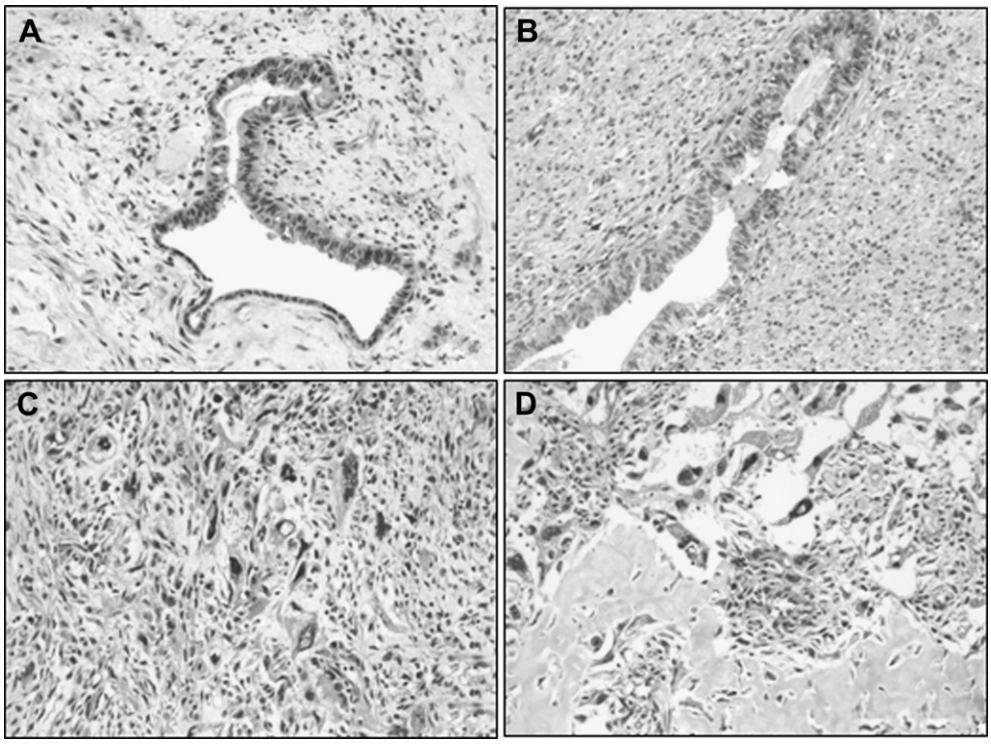

Fig. 2. Histological and immunohistochemical findings. (A, B) Glands lined by atypical pseudostratified columnar epithelium dispersed in sarcomatous areas (H&E, ×20, ×20). (C) Poorly differentiated sarcomatous areas with marked nuclear atypia and numerous atypical mitotic figures (H&E, ×20). (D) Osteosarcoma as heterologous sarcomatous element with highly atypical spindle cells in an osteoid matrix (H&E, ×20).

weekly intervals. There was a 2-week interval between the third and fourth cycle, and the last three cycles were again given weekly. Currently, at the 9th postoperative month, the chemotherapy courses were completed and the patient was well and disease-free in terms of uterine sarcoma.

Discussion

Postirradiation sarcoma of the female genital tract is rare, but a significant long-term complication of pelvic radiotherapy. The uterus is the most common site of irradiation-associated sarcoma in the genital tract. These uterine sarcomas have been mostly reported in patients treated with radiotherapy for malignancies of the uterine cervix, and for benign conditions such as menorrhagia in early reports [5,6], but to the best of our knowledge, a case of uterine sarcoma after radiation therapy for sacral chordoma has not previously been reported in the English literature.

To consider a sarcoma to be irradiation-associated, some criteria must be met, including: (i) the development of sarcoma must be within a previously irradiated field; (ii) patients should have received a significant amount of radiation; (iii) a latency period of several years (at least 3–5 years) must elapse between the time of radiation and the development of the sarcoma; (iv) the diagnosis of the sarcoma must be histologically proven; and (v) the secondary sarcoma should

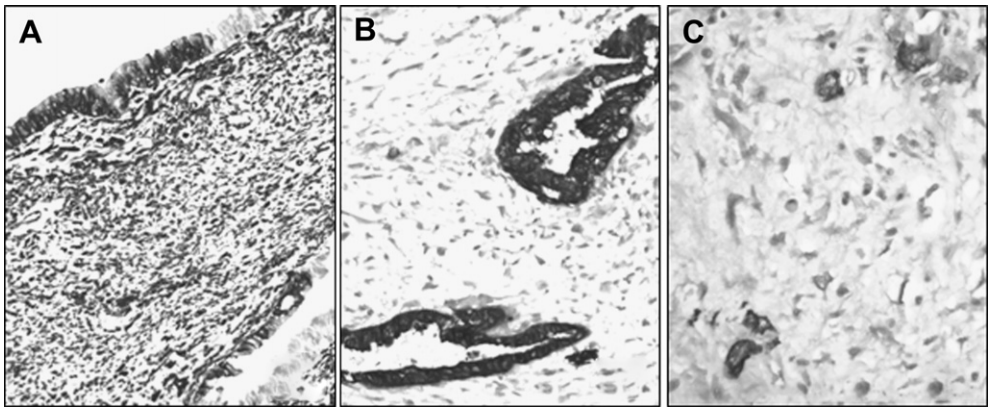

Fig. 3. (A) Diffuse vimentin expression in sarcomatous areas and focally in epithelial component (×20). (B) Cytokeratin expression of epithelial component (×20). (C) Scattered expression in a few cells of sarcomatous areas with SMA (×40).

be histologically different from the primary neoplasm [7]. The present case satisfies all the above criteria. In the published cases of uterine sarcoma seen in patients with history of irradiation to the pelvic field, the interval between the time of irradiation and the diagnosis of uterine sarcoma varies between 3 and 30 years, with the total radiation doses ranging from 2400 to 8000 cGy, and the most common type of secondary uterine sarcoma is the carcinosarcoma [5,6]. In the present patient, considering that the tumor arose within the irradiation field after a long latency period (23 years), a diagnosis of irradiation-associated sarcoma was made. By contrast, there are no specific clinical or histopathological features distinguishing between irradiation-associated and irradiation not associated uterine sarcomas. Therefore, it cannot be completely ruled out that the occurrence of uterine carcinosarcoma in this patient may be *de novo*.

Comprehensive surgical staging is the primary treatment modality of uterine carcinosarcomas. Although there is little evidence to support the benefit of adjuvant treatment in advanced disease, the use of adjuvant chemotherapy and/or radiotherapy is generally recommended. Adjuvant radiotherapy for uterine carcinosarcoma has not been evaluated adequately, but a study has demonstrated the advantage of radiotherapy for local control in advanced disease [2]. However, considering the possibility of significant adverse effects, pelvic radiotherapy was not performed as the present patient had been exposed to prior pelvic radiotherapy twice, and she received only chemotherapy as an adjuvant treatment.

Surgical stage and depth of myometrial invasion have been suggested as very important prognostic factors. At presentation, extrauterine extend is found in up to one-third of patients with uterine carcinosarcomas and their survival is very poor [1,2]. A history of pelvic irradiation is more frequently associated with extrauterine disease at clinical presentation. It has been suggested that the reason extrauterine disease is more frequent in patients that were exposed to pelvic irradiation is due to cervical stenosis, which develops as a result of past radiotherapy, hindering uterine bleeding, which is the most common presenting symptom of uterine sarcoma; thus, if the disease presents itself with symptoms other than uterine bleeding it is at a more advanced stage [8]. This is supported by a study, comparing spontaneous uterine carcinosarcoma with irradiation-associated sarcoma, stating that uterine bleeding was the most common presenting symptom of spontaneous carcinosarcoma, whereas the most common presenting symptom of irradiation-associated uterine carcinosarcoma is abdominal distension and pain [5]. However, proof of this theory requires further clinicopathologic studies evaluating the possible fibrosis and stenosis of the cervical canal histopathologically. In the present case, we re-evaluated the patient's previous MRI scans, when she applied to our clinic with the results of her probe curettage that was performed at another medical facility, as she presented with postmenopausal bleeding 5 months after her first MRI was taken in April 2009 and the uterine mass was diagnosed, for which no previous intervention was performed. It is difficult to interpret the relation of this delay in diagnosis and the effect of radiotherapy as re-irradiation for recurrent sacral chordoma on the prognosis of uterine carcinosarcoma. In addition, although the post-radiotherapy MRI revealed no significant reduction in the size of uterine mass, the lesion had changes in accordance with necrosis and bleeding. This necrosis and bleeding, developing after radiotherapy, may hinder a further delay in diagnosis by leading to uterine bleeding; however; it is difficult to explain why this uterine bleeding developed 5 months later, instead of occurring relatively earlier.

In two large studies on post-irradiation uterine sarcoma [5,6], most patients were exposed to radiation, performed as a primary treatment modality for cervical cancer. Furthermore, in these studies, patients that were exposed to radiation for abnormal uterine bleeding were second in rank; however, radiotherapy for the treatment of abnormal uterine bleeding does not currently include this method. None of these studies included patients with non-gynecologic radiotherapy indications.

In conclusion, the probability of uterine sarcomas should always be kept in mind in a uterine mass seen in a patient with a history of pelvic field radiotherapy. Furthermore, another point to be considered is that irradiation-associated neoplasm and recurrence of primary tumor previously treated by adjuvant radiation therapy may occur simultaneously.

References

[1] D'Angelo E, Prat J. Uterine sarcomas: a review. Gynecol Oncol 2010;116:131–9.
[2] Gonzalez Bosquet J, Terstriep SA, Cliby WA, Brown-Jones M, Kaur JS, Podratz KC, et al. The impact of multi-modal therapy on survival for uterine carcinosarcomas. Gynecol Oncol 2010;116:419–23.
[3] Ho SP, Ho TH. Malignant mixed Mullerian tumours of the uterus – a ten-year experience. Singapore Med J 2002;43:452–6.
[4] Bergh P, Kindblom LG, Gunterberg B, Remotti F, Ryd W, Meis-Kindblom JM. Prognostic factors in chordoma of the sacrum and mobile spine: a study of 39 patients. Cancer 2000;88:2122–34.
[5] Duran JV, Nochomovitz LE, Prem KA, Dehner LP. Postirradiation mixed Mullerian tumors of the uterus. Cancer 1980;45:1625–31.
[6] Mark RJ, Poen J, Tran LM, Fu YS, Heaps J, Parker RG. Postirradiation sarcoma of the gynecologic tract. A report of 13 cases and a discussion of the risk of radiation-induced gynecologic malignancies. Am J Clin Oncol 1996;19:59–64.
[7] Hsieh TC, Kao CH, Wu YC, Hsu CN, Wang CH, Lin YY, et al. Fulminant postirradiation soft tissue sarcoma. Clin Nucl Med 2009;34:811–4.
[8] Sutton G, Kavanagh J, Wolfson A, Tornos C. Corpus: mesenchymal tumors. In: Barakat RR, Markman M, Randall ME, editors. Principles and practise of gynecologic oncology. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009. p. 733–61.