

Does Cancer Therapy Causes Cancer? A Case Report and Mini Review of the Literature

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The subject of whether cancer treatment causes cancer is less widely recognized but obviously not insignificant. Although previous studies have attempted to address the concept of "postradiation carcinoma" there is no direct evidence that these tumors are caused by radiation or simply present incident malignancies in an at-risk population. The risk of second primary cancer in women with cervical cancer in previously irradiated fields remains still unclear.

We present an atypical case of endometrial cancer formerly submitted to pelvic irradiation because of cervical carcinoma and we discuss the eventual association of pelvic radiation with a subsequent endometrial carcinoma.

Key Words: Endometrial cancer, Cervical cancer, Post radiation malignancy

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Case Report

A 56 years old woman, gravida 4, para 2, was admitted to our department because of vaginal bleeding. She was in a very good general condition and did not complain for any major symptoms.

Her first menstrual period was at 12 years old, while her last menstrual period was at 43 years old with normal ovulatory cycles until then. Her BMI was 27 and she was taking medication for blood hypertension. Thirteen years ago (43 y.o.) she underwent a dilatation and curettage because of vaginal bleeding due to cervical polyps of the uterus. At that time, histology showed squamous cell cancer of the cervix and she was treated with pelvic chemoradiation and brachytherapy for cervical cancer clinical stage IIb. From that time, she was closely followed up with annual clinical examination and CT scans every 6 months for the first 2 years and then annually, with no evidence of disease until the day of presentation to our department.

Thorough clinical examination and laboratory evaluation

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(MRI, U/S, tumor markers), did not show any evidence of disease, therefore it was decided to perform a dilatation and curettage. Histology revealed serous adenocarcinoma of the endometrium and the patient underwent full surgical staging including cytology of free peritoneal fluid, total abdominal hysterectomy (TAH), bilateral salpingoophorectomy (BSO), omentectomy, pelvic lymphadenectomy and removal of one bulky node between the aorta and the inferior vena cava. The patient made an uneventful recovery and was released from our hospital on the 7th postoperative day. All histology specimens were free of disease and multidisciplinary (MDT) meeting decided that no additional treatment was required for serous endometrial cancer stage Ia.

Discussion

Our patient represents a case of a second primary cancer of the endometrium following treatment for cervical cancer. Pelvic radiation therapy has been reported to increase the risk of ovarian, vaginal and endometrial cancer.^{1,2} In a study by Evans et al, women with invasive cancer of the cervix, most of whom received pelvic irradiation, had an increased risk of bladder, rectal, vulval and vaginal carcinomas.³ Radiation in the pelvis has also been associated with the development of endometrial adenocarcinoma.⁴ An increased incidence of carcinomas of the breast and ovary has been reported in atomic bomb survivors in Japan.^{5,6} Although there are many references in the literature about the concept of postradiation carcinoma, there is not enough evidence to adequately support this theory.

On the other hand, the concept of postradiation sarcoma is well defined and appreciated. Postradiation sarcomas occur more commonly in women because of the use of radiation therapy for the treatment of cervical and breast cancers. The frequency seems to be dependent on the dose of radiation and the standard latent period (time between radiation therapy and postradiation sarcoma) is between 10 and 20 years.⁷ It is important to mention that the histological spectrum of postradiation sarcomas is more limited than that of sarcomas in general (fibrous histiocytoma in 70% of cases).⁷ In fact, in most series, most of the postradiation sarcomas have been carcinosarcomas.^{8,9} For that reason, some cases previously reported as postradiation sarcomas, may actually be carcinomas.

In an original article by Seidman et al, 4 cases of postradiation carcinomas of the endometrium are reported.¹⁰ Of these, 2 were grade III endometrioid carcinomas stage Ic, one was a serous carcinoma stage IIb, and one was a carcinosarcoma stage Ib. Only 2 of these patients had received pelvic irradiation for cervical cancer in the past, (one with endometrioid endometrial cancer and one with carcinosarcoma) with the latent periods reported, being 20 and 15 years, respectively. The other 2 patients (one with endometrioid endometrial cancer and one with serous endometrial cancer) had received pelvic irradiation for ovarian ablation (because of breast cancer) and colon cancer, respectively.

In a study by Parkash et al, uterine papillary serous carcinomas after radiation therapy of the cervix have been reported,¹¹ while another study of 23 patients with endometrial cancer after pelvic irradiation for cervical cancer suggested that more aggressive subtypes of endometrial carcinomas (such as serous, clear cell) were more common in irradiated patients.¹² Our patient was also a case of a serous adenocarcinoma.

From the data presented, there is not enough evidence to support the concept of postradiation endometrial cancer and the direct effect of pelvic irradiation on the disease. It is likely that some of these cases are sporadic. However, the Gynecologist Oncologist should be aware of this potential increased risk of carcinogenesis in this group of patients. Pelvic irradiation has been widely used for many years and for that reason we have a large population at risk.

References

1. Kleinerman RA, Curtis RE, Boice JD Jr, et al. Second cancers following radiotherapy for cervical cancer. *J Natl Cancer Inst* 1982; 69:1027-33.
2. Pride GL, Buchler DA. Carcinoma of the vagina 10 or more years following pelvic irradiation therapy. *Am J Obstet Gynecol* 1977;127:513-7.
3. Evans HS, Newnham A, Hodgson SV, et al. Second primary cancers after cervical intraepithelial neoplasia III and invasive cervical cancer in Southeast England. *Gynecol Oncol* 2003;90:131-6.
4. Meredith RF, Eisert DR, Kaka Z, et al. An excess of uterine sarcomas after pelvic irradiation. *Cancer* 1986; 58:2003-7.
5. Thompson DE, Mabuchi K, Ron E, et al. Cancer incidence in atomic bomb survivors. Part II: solid tumors, 1958-1987. *Radiat Res* 1994;137(2 Suppl):S17-67.
6. Ron E, Ikeda T, Preston DL, et al. Male breast cancer incidence among atomic bomb survivors. *J Natl Cancer Inst* 2005;97:603-5.
7. Weiss SW, Goldblum JR. *Enzinger and Weiss's Soft Tissue Tumors*, 4th edn. Philadelphia, PA: Mosby, 2001:3-4.
8. Norris HJ, Taylor HB. Postirradiation sarcomas of the uterus. *Obstet Gynecol* 1965;26:689-94.
9. Ronnett BM, Zaino RJ, Ellenson LH, et al. Endometrial carcinoma. In: Kurman RJ, ed. *Blaustein's Pathology of the Female Genital Tract*, 5th edn. New York: Springer Verlag, 2002:501-9.
10. Seidman JD, Kumar D, Cosin JA et al. Carcinomas of the female genital tract occurring after pelvic irradiation: A report of 15 cases. *Int J Gynecol Pathol* 2006;25:293-7.
11. Parkash V, Carcangiu ML. Uterine papillary serous carcinomas after radiation therapy for carcinoma of the cervix. *Cancer* 1992;69:496-501.
12. Pothuri B, Ramondetta L, Martino M, et al. Development of endometrial cancer after radiation treatment for cervical carcinoma. *Obstet Gynecol* 2003;101:941-5.