Adenocarcinoma of Rectum as Second Primary Cancer after Treatment of Endometrium Cancer

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ABSTRACT
Colorectal cancer is the second leading cause of death from cancer in women in the United States. Previous epidemiologic studies have identified a 1.5 – 3 fold increased risk of colorectal cancer in women after ovarian and endometrial cancer. In Pakistan, neither such a study showing relationship of colorectal cancer with gynaecological cancer has been done nor any case has been reported. Here, a case is being reported who developed adenocarcinoma of rectum as the second primary about nine years after completion of treatment for adenocarcinoma of endometrium.

Key words: Colorectal neoplasms. Endometrial adenocarcinoma. Adenocarcinoma rectum.

INTRODUCTION
A woman's lifetime risk for developing colorectal carcinoma is approximately 5%.1 Greater elevations in risk are seen in women with family history of colorectal cancer or polyps or with pre-existing disease like inflammatory bowel syndrome. An analysis done by David et al. has shown that endometrial cancer at 50 years of age or younger and ovarian cancer at 60 years of age or younger should also be considered major risk factor. Elevated risk of colorectal cancer in women 50 years of age or younger with endometrial or ovarian cancer is similar in magnitude to the risk conferred by having a first degree relative with colorectal cancer. Previous cervical cancer does not pose equivalent concerns.2-4 The association is strengthened by studies demonstrating a reciprocal relation of elevated risk of endometrial and ovarian cancer after colorectal cancer.5 Hormonal modulation by unopposed estrogen can be one explanation. Hereditary non-polyposis colorectal cancer is also associated with gynecological cancers. Pelvic radiotherapy for uterine cancer also increases the risk of leukemia and solid malignancies at sites adjacent to uterus.6

Here, a female patient is reported who was treated with pelvic external beam radiotherapy and brachy therapy for endometrial cancer and developed rectal cancer about nine years after completion of treatment.

CASE REPORT
A 35 years old lady with no family history of cancer presented at Nuclear Medicine, Oncology and Radiotherapy Institute (NORI), Islamabad, in November 2000 with the diagnosis of adenocarcinoma of endometrium. She had already undergone total abdominal hysterectomy and bilateral salpingo-oophorectomy a month ago. Histopathology revealed moderately differentiated adenocarcinoma of endometrium, involving more than half of myometrium (grade-II). Sections of cervix showed non-specific cervicitis. There was a simple cyst in left ovary. CT scan abdomen and pelvis showed no lymph node involvement. Hence, the disease was staged as FIGO IC according to UICC TNM Classification of Malignant Tumours, 6th edition. The patient was given adjuvant radiotherapy; the combination of external beam pelvic radiotherapy and brachy-therapy. Whole pelvis was radiated to a total dose of 50 Gy in 25 fractions by four field technique with 6 MV photons on Linear Accelerator. This was followed by 02 fractions of intracavitary brachy-therapy of 06 Gy each at 01 cm depth from the surface. Brachytherapy was performed with high dose rate Varisource with Iridium192. Her treatment completed in March 2001. The patient was kept on regular follow-up with clinical examination, ultrasound / CT abdomen and pelvis, chest X-ray and CA 125. She remained disease-free until December 2009 when she presented with 2 months history of abdominal pain in the left iliac region. There was no history of alternate bowel habits or bleeding per rectum. Her CT scan abdomen showed circumsferential mural thickening of rectal wall with para-aortic lymphadenopathy. On rectosigmoidoscopic examination, she was found having non-negotiable narrowing of rectosigmoid junction with local inflammation and mucosal nodularity at 15 cm from anal verge. Biopsy was taken and histopathologically it was found to be moderately differentiated adenocarcinoma of rectum. Hartmann's procedure was performed in February 2010. Histopathology revealed growth extending to involve subserosa (Figure 1). Metastatic workup was unremarkable. The disease was staged as T3N1bM1a...
(non-regional nodes) according to UICC TNM Classification of malignant tumours, 7th edition. Recurrent disease from endometrial cancer was ruled out with the help of immunohistochemistry which revealed positivity of CEA and CK 20 and negativity of CK7 (Figure 1).

Postoperative CT scan still showed circumferential thickening of rectum (Figure 2). Keeping in view the stage, the patient was started on combination chemotherapy FOLFOXIV (5-Fluorouracil, folinic acid and oxaliplatin). Interval assessment was done in July 2010 with CT scan which showed significant regression in rectal wall thickening (Figure 2) and para-aortic lymph nodes. Chemotherapy was continued for six cycles completed on January 18, 2011. Repeat CT scan done on March 4, 2011 showed complete disappearance of para-aortic lymph nodes, further reduction in rectal wall thickening and no significant luminal narrowing (Figure 2). She has now been planned for abdomino-perineal resection.

![Figure 1: High power view showing adenocarcinoma rectum, positive for CEA and CK 20.](image1)

![Figure 2: CT scan showing rectal wall thickening and marked luminal narrowing pre-chemotherapy (left image) and regression of disease and improvement in luminal narrowing after chemotherapy (centre and right).](image2)

**DISCUSSION**

According to an institution based study in Pakistan, gynaecological malignancies are the second commonest cancers in females in Pakistan and colorectal cancers rank fourth in female patients. Amongst gynaecological malignancies, ovarian tumours are the commonest followed by cancers of cervix and endometrium. Endometrial cancers are usually diagnosed in early stage and hence are cured with long-term survival. These patients are at increased risk of developing second cancers either as a complication of treatment or because of sharing of common risk factors between primary and secondary cancers. Uterine body cancer is the fourth most common cancer among United States women and survival rate is 87% at 5 years. The risk of subsequent primary cancers was evaluated in 115,000 women diagnosed with cancers of ovary or uterine corpus between 1973 and 2000. The risk of developing rectal cancer was found to be 12% in these patients. Elevated risks were limited to younger patients; 25% in women diagnosed at age younger than 50 years and 47% in women diagnosed at age younger than 40 years.

The case reported here was diagnosed with endometrial cancer at the age of 35 years and developed rectal cancer about nine years after completion of treatment thus tallying with the results reported in literature. Dietary, hormonal and genetic factors could have been contributory to the development of rectal cancer in the patient reported. Intake of fatty meals and excess of estrogen can cause both rectal and endometrial cancers. Among genetic factors, women with hereditary non-polyposis colorectal cancer are at increased risk of developing endometrial cancer as well. In the case reported, genetic studies have not been done as this is not possible in Pakistan at the moment.

The patient was treated with both external beam pelvic radiotherapy and brachytherapy. Significant dose of radiation is received by rectum with pelvic radiotherapy. There is strong possibility of developing radiation induced rectal cancer in the patient reported. Literature shows strong association of rectal cancer with radiation. Five patients of radiation induced colorectal cancer were analyzed; each received pelvic radiotherapy 10 years before the development of colorectal cancer. The latent period between radiation exposure and the development of cancer is 2 – 20 years with a peak frequency between 5 and 10 years. The patient reported here developed rectal cancer more than 9 years after completion of pelvic radiotherapy. Association between colorectal cancer and radiation is well documented but cause specific relationship has not been studied in Pakistan. To my knowledge, this is the first case reported in Pakistan where rectal cancer developed after pelvic radiotherapy. As literature shows significant number of radiation induced colorectal cancers and association of gynaecologic cancers with colorectal cancers in the west it is strongly recommended that female patients treated with pelvic radiotherapy for gynaecologic cancer should be strictly followed for second cancers particularly colorectal carcinoma. Moreover, benefit of radiotherapy should be evaluated against the risk of developing cancer in the irradiated bowel.

**REFERENCES**


