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# Vaginal Recurrence More than 17 Years after Hysterectomy and Adjuvant Treatment for Uterine Carcinoma with Successful Salvage Brachytherapy: A Case Report

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## Key Words

Uterine carcinoma · Late recurrence · Brachytherapy · Salvage treatment

## Abstract

**Purpose:** Although the majority of recurrences occur within the first 3 years of hysterectomy for endometrioid carcinoma, we report herein a successful salvage vaginal brachytherapy in a patient with endometrioid uterine carcinoma which recurred more than 17 years after initial treatment.

**Materials and Methods:** A 61-year-old female was diagnosed with endometrioid adenocarcinoma of the uterus and treated with TAH-BSO, followed by adjuvant external beam radiation therapy (EBRT) to the whole pelvis. After remaining free of any recurrent or metastatic disease for more than 17 years, she was diagnosed with isolated vaginal cuff recurrence and successfully treated with a salvage high-dose-rate intracavitary vaginal brachytherapy.

**Results:** The patient remained disease free until her death from unrelated causes 7 years later.

**Conclusion:** To the best of our knowledge, this case represents the longest time to recurrence of endometrial cancer in someone who had been treated with TAH-BSO and adjuvant pelvic EBRT. This case highlights that even with adjuvant therapy, late recurrences may occur, and successful salvage brachytherapy is very effective.

## Introduction

Endometrial carcinoma is the most common gynecologic malignancy, with 43,470 new cases estimated to have been diagnosed in 2010 [1]. Patients undergoing surgical staging with or without adjuvant radiation therapy have reported disease recurrence rates between 3 and 15% for FIGO stages I–II [2, 3]. Of those malignancies that do recur, 76–87% are evident within the first 3 years of treatment initiation [2, 4]. Here, we report a case of endometrioid uterine adenocarcinoma which recurred 210 months (17.5 years) after treatment. Based on a review of the literature, our patient represents the longest time to recurrence after hysterectomy and adjuvant external beam radiation therapy (EBRT). The case and its treatment are discussed, followed by a review of the relevant literature.

## Case Report

In December 1984, a 61-year-old Caucasian female presented after a routine screening Papanicolaou (Pap) smear revealed cells suspicious for adenocarcinoma. An endometrial biopsy via dilation and curettage showed endometrioid adenocarcinoma of the uterus, FIGO grade II. The patient subsequently underwent surgical staging with TAH-BSO selective lymph node dissection and peritoneal washing on January 15, 1985. A final pathology revealed 1988 FIGO stage IC endometrioid adenocarcinoma, FIGO grade I, with invasion of 16 mm out of the 21-mm thickness of the myometrium. All 16 lymph nodes examined were negative for metastatic disease. Peritoneal washing was negative for malignant cells. The patient was then treated with adjuvant EBRT to the whole pelvis to a total dose of 45 Gray in 25 fractions of 1.8 Gray each, using a 4-field pelvic box technique. Radiation therapy was completed on March 1, 1985.

The patient remained under close follow-up and was without any evidence of recurrent disease until July 2001. At that time, a routine follow-up Pap smear revealed adenocarcinoma. Pelvic examination revealed superficial induration at the vaginal vault. Vaginal cuff biopsy was performed in January 2002, which confirmed recurrent endometrioid carcinoma, FIGO grade 1 with ER/PR-positive stain (fig. 1). Re-staging CT scan of the abdomen and pelvis in January 2002 was negative for any local or metastatic disease. Interim medical history remained non-contributory.

Our patient was treated with a salvage high-dose-rate (HDR) intracavitary vaginal cuff brachytherapy to the upper 4 cm of the vaginal length to a dose of 30 Gray in 5 fractions of 6 Gray each, 1–2 fractions per week, prescribed to 0.5 cm depth, which was completed in September 2002. Treatment was well tolerated with no grade II adverse effects. Subsequently, she underwent routine follow-up with gynecologic and radiation oncology services via clinical examination, routine Pap smear, and routine imaging studies with CT scans of the abdomen and pelvis. For more than 7 years after the salvage treatment, our patient remained free of recurrent or persistent disease. She died in September 2009 from unrelated causes at the age of 88.

## Discussion

After treatment with TAH-BSO, the most common site of endometrioid carcinoma recurrence is the vaginal cuff. Approximately 75% of recurrences occur at this site without adjuvant therapy. Although adjuvant radiotherapy reduces locoregional recurrence, the vaginal cuff still remains the most common site of relapse within the pelvis [2, 5].

The majority of recurrences occur within the first 3 years of treatment. Most initial relapses had occurred within 18 months in the GOG 99 trial [3]. The PORTEC Study Group reported a median time to recurrence of 21 months (range 3–108 months) [2]. A meta-analysis of 12 trials including 2,922 patients, found that 70–100% of recurrences occurred within 3 years of treatment, with a range of recurrences between 2 and 194

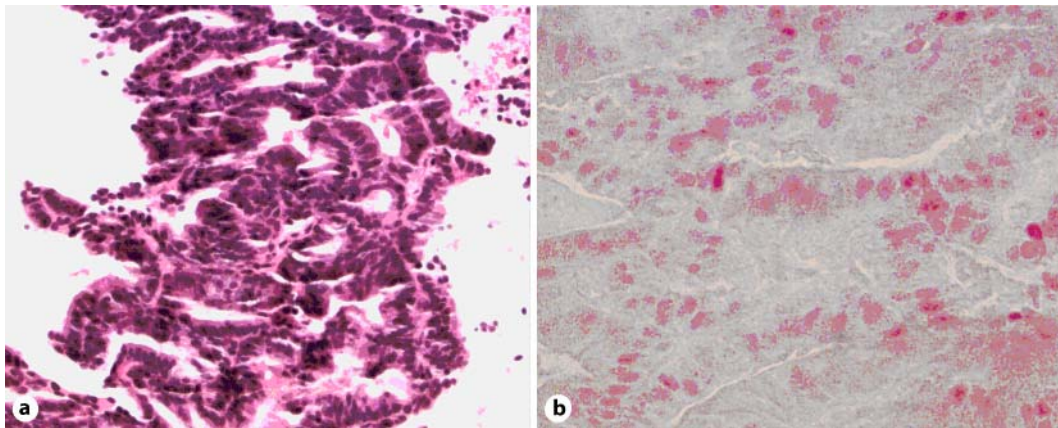
months. It was also described that those at low risk of recurrence (age <60, stage IA, IB disease in 1988 FIGO) had only a 1–3% risk of recurrence, compared to the 13% recurrence rate seen amongst the entire cohort primarily composed of stage I–II patients [6].

Our patient's carcinoma recurred more than 17 years after initial diagnosis and treatment, despite adjuvant radiation therapy to the pelvis. This represents the longest time-to-recurrence reported in the literature after modern treatment with hysterectomy and adjuvant pelvic EBRT. Although rare, recurrences of endometrial carcinoma more than 10 years after initial treatment have been reported. There are 3 reports of endometrial carcinoma recurring more than 10 years after hysterectomy. However, none of these patients received adjuvant EBRT. The first report represents the lengthiest interval to recurrence, 318 months (26.5 years), in a patient originally treated in 1958, with preoperative uterine radium packing, followed by radical hysterectomy [7]. The second report of protracted time-to-recurrence was reported for an endometrial carcinoma recurrence in an abdominal scar 14 years after the initial surgery [8]. The third reported case is of a patient whose malignancy recurred in the upper urinary tract 11 years after hysterectomy. Her relapse was successfully treated with surgical resection and EBRT [9].

Our patient was successfully treated with a salvage intracavitary HDR brachytherapy to the vaginal cuff; she remained disease free until her death 7 years later. HDR brachytherapy, independent of a history of primary adjuvant EBRT, has been shown to be an effective salvage option for those with isolated vaginal cuff recurrences [10]. The etiology of the recurrence may be posited to have been due to the senescence of tumor cells left behind after initial surgery, which survived through adjuvant radiation therapy. Another possibility to consider is the malignant transformation of endometriosis [11]. Our patient had no known history of endometriosis, and no evidence of ectopic uterine tissue was seen on the original pathology following hysterectomy; therefore, this scenario seems less likely.

Later relapse predicts for a better median overall survival. A recent review reported that a disease-free interval of more than 12 months predicted a significantly longer median overall survival of 41 months, as compared to 13 months in those whose carcinoma recurred in less than 12 months [12]. Another review of patterns of relapse reported a difference between those who experienced recurrence after 24 months, with improved 5 and 10 year survival rates, as compared to those relapsing within 24 months [13].

In conclusion, very late recurrence may occur, even after treatment with adjuvant radiation therapy subsequent to hysterectomy for early stage endometrial carcinoma. With appropriate continued surveillance, it is possible to achieve early diagnosis and perform a successful salvage therapy.



**Fig. 1.** **a** Biopsy from the vaginal apex of the recurrence of endometrioid endometrial adenocarcinoma, H&E. **b** DAKO estrogen receptor at 1:100, using EDTA at pH 8 retrieval, with the DAKO LSAB+ detection system and the AEC chromogen on a DAKO Autostainer.

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