

Long-term survival of a patient with multiple abdominal metastasis from endometrial carcinoma treated with multi-portal conformal re-irradiation and chemotherapy

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A patient with recurrent endometrial cancer with multiple abdominal and pelvic tumoral masses was treated with re-irradiation combined with liposomal doxorubicin and oxaliplatin. A multiple field conformal technique was used to deliver a highly accelerated and hypofractionated scheme (15 fractions of 3.5 Gy, within 19 days). Complete response was confirmed four months after therapy. Four years later a lung metastasis appeared and was again treated with a similar course of therapy, once again resulting in a complete response. It is suggested that in the era of modern image-guided radiotherapy patients with endometrial cancer who have relapsed within or outside the loco-regional area, should be carefully assessed for an eventual gross tumor eradication using high-dose localized radiotherapy, leaving as the only target of chemotherapy the microscopic undetectable disease.

Endometrial carcinoma is the most common invasive malignancy of the female genital tract. The typical presentation of endometrial cancer is postmenopausal bleeding and 75% to 80% of women are diagnosed with stage I disease. These patients have a good prognosis and are highly curable with hysterectomy with bilateral salpingo-oophorectomy with or without pelvic node dissection. The use of adjuvant treatment depends on the patients estimated risk of recurrence, mainly tumor grade and depth of myometrial invasion.^{1,2}

In contrast to the early stage of disease, advanced endometrial cancer has poor prognosis. Traditionally, treatment for women with stage III endometrial cancer relies on radio-chemotherapy,^{3,4} while women with stage IV disease are treated with palliative chemotherapy.⁵ Peritoneal metastases from endometrial carcinoma is considered metastatic disease and is treated with chemotherapy, the efficacy of which is low and, even in the case of responsive disease, rapid relapse and death is the rule.

We report a patient with stage IV endometrial carcinoma whose peritoneal and pelvic metastasis showed

long-standing complete remission after stereotactic re-irradiation combined with chemotherapy.

CASE

The patient was a 58-year old woman with a stage I endometrioid adenocarcinoma grade III who underwent total hysterectomy and salpingo-oophorectomy followed by postoperative radiotherapy. She received total tumor dose 50 Gy with a linear accelerator (ELECTA, Stockholm, Sweden) 18 MV using a four-field technique. The patient refused further intracavitary brachytherapy, due to substantial early radiation toxicity.

Three years later she was referred to our department with the diagnosis of peritoneal metastasis and pelvic node relapse. She suffered from sever abdominal pain and cramps and local abdominal sensitivity. At least five discrete tumor masses 2-5 cm were evident in abdominal/pelvic CT-scan. The patient was treated with conformal radiotherapy with multiple fields, combined with chemotherapy. The radiotherapy dose to the tumor masses was 52.5 Gy using an accelerated and hypofrac-

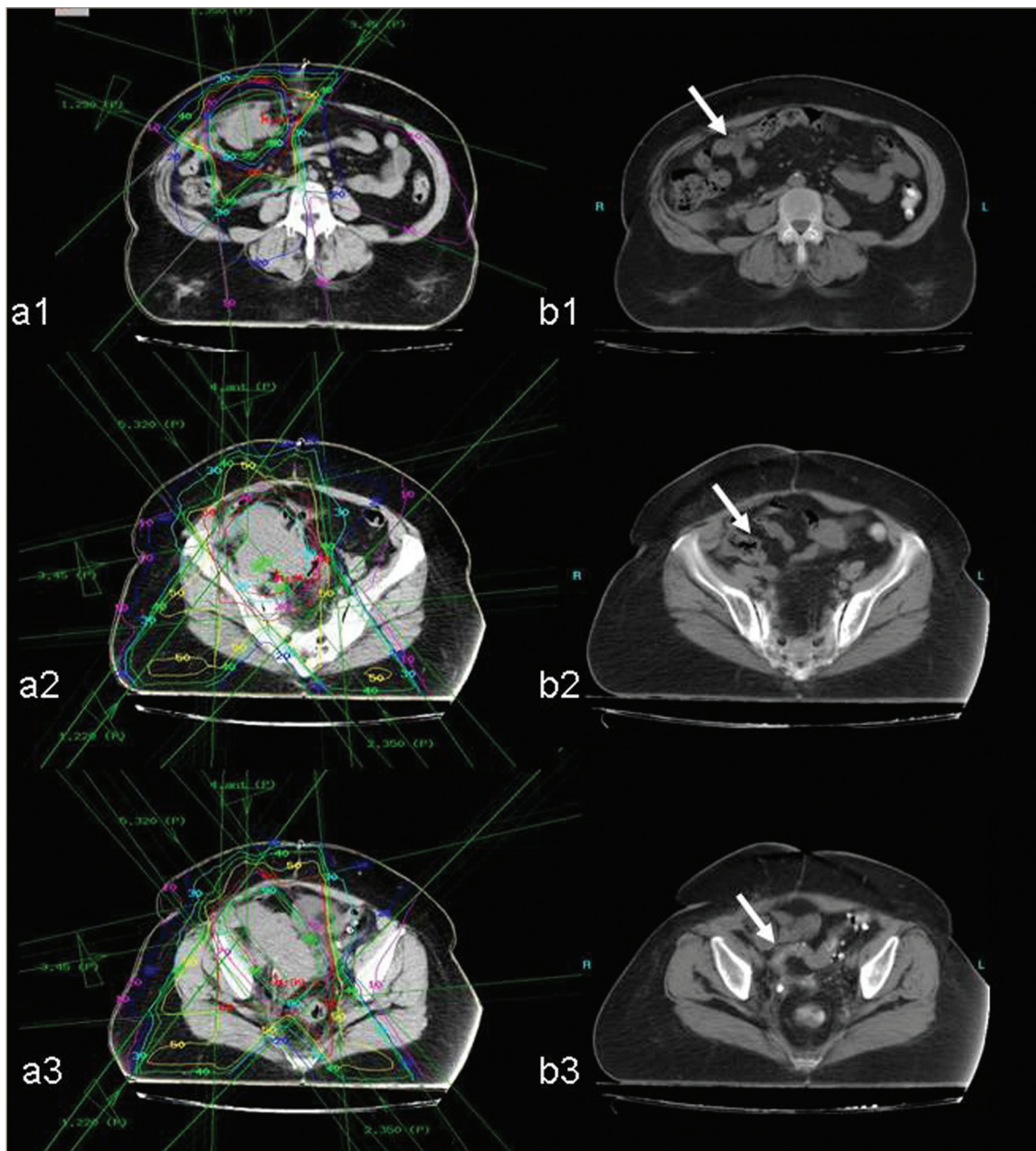


Figure 1. CT-images of abdominal (a1) and pelvic (a2, a3) tumoral masses from recurrent endometrial carcinoma showing the fields and isodose curves of the radiotherapy performed . Complete response of the tumor masses is evident (arrows) at CT-scan performed 4-years after therapy (b1, b2, b3).

tionated technique, delivering 15×3.5 Gy daily fractions within 19 days. This corresponds to a biological tumor dose around 70 Gy. Intravenous chemotherapy consisted of 7 bi-weekly cycles of oxaliplatin (60 mg/m^2) and liposomal-doxorubicin (20 mg/m^2) started on day 1 of radiotherapy. This combination therapy was well tolerated with diarrhea grade 1 and abdominal discomfort

grade 1. No other side effects from chemotherapy or radiotherapy were noted. Four months after therapy, a complete response of the tumoral masses was confirmed in CT scans, leaving remnant scar tissue in the places of former tumors. The patient was alive with no evidence of disease and no severe late radiotherapy sequel (grade 1 abdominal discomfort) for 4 years (**Figure 1**), when

a CT-scan showed a lung metastasis in the right upper lobe that was confirmed with PET-scan. The patients received conformal radiotherapy of the nodule using the same fractionation and chemotherapy as used for pelvic disease. Complete response of the mass was obtained and the patient is now free of disease (10 months after thoracic radiotherapy).

DISCUSSION

Although most patients with early stage endometrial cancer are cured with surgery with or without post-operative radiotherapy, 10% to 15% of them will relapse within the first 3 years after treatment.^{1,2} Radical radio-chemotherapy or re-irradiation (in case of previous radiotherapy) is the treatment of choice for loco-regional recurrence.⁶ Distant metastasis are treated with polychemotherapy (doxorubicin, taxanes, cisplatin) and palliative radiotherapy when necessary, but with poor results as the 5-year survival is less than 5%.⁵ Doxorubicin with cisplatin has long been considered the standard regimen of treating advanced or recurrent endometrial cancer, providing overall response rates of 40%.⁷ The combination of doxorubicin, cisplatin and paclitaxel showed a statistically significant improvement in response rate, progression-free and overall survival but toxicity is

higher with the three drug regimen (thrombocytopenia, neurotoxicity).⁷

This case report stresses the importance of careful evaluation of patients with peritoneal or, eventually limited metastatic disease to other organs, for the feasibility of the delivery of a high dose of radiotherapy localized to the tumoral masses detectable on CT or MRI scans. Indeed, conformal radiotherapy planning and, even better IMRT intensity-modulated radiotherapy techniques, provide the tool for a safe radical treatment of gross disease, leaving it microscopically undetectable. The combination of liposomal doxorubicin with oxaliplatin was well tolerated during and after radiotherapy. The presented case is remarkable for the complete response obtained with such techniques and the long disease-free survival achieved with radio-chemotherapy. Applying the same technique when lung metastasis appeared 4-years after the first treatment, the disease was once again controlled.

We conclude that in the era of modern image-guided radiotherapy patients with endometrial cancer who have relapsed within or outside the loco-regional area, should be carefully assessed for an eventual gross tumor eradication using high dose localized radiotherapy, leaving as the only target of chemotherapy the microscopic undetectable disease.

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