



Locally advanced cervical cancer treated with chemo-radiotherapy: a case report of a particular recurrence

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Background: Adenocarcinoma of uterine cervix is usually treated with concurrent chemotherapy and external beam radiotherapy (EBRT), eventually followed by brachytherapy that can provide a good tumor control rate, although approximately one-third of the patients can develop further recurrence. The most common recurrence sites are the pelvis and the para-aortic nodes, with few patients having a single metastatic deposit. In this regard, precise definitions of recurrences and optimal treatment strategies are still to be clearly defined and currently there are no guidelines for the treatment of patients with oligometastatic cervical cancer.

Case Description: We present a case of an 81 years old patient with Stage IIB adenocarcinoma of uterine cervix, that was successfully treated with concurrent chemoradiotherapy with definitive intent. Six months later, she developed a solitary abdominal nodule for which she underwent resection followed by chemotherapy. At the present time there are no signs of local recurrence or distant metastasis after 3 years. In the case reported, the use of different strategies (radiotherapy, chemotherapy and surgery), as well as the correct choice and the timing of the different approaches has provided a great benefit for the patient.

Conclusions: The use of surgery and chemotherapy in patients with recurrent cervical cancer is safe even in older patients with atypical localizations.

Keywords: Cervical cancer; radiotherapy; chemotherapy; surgery; case report

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Introduction

The incidence of invasive cervical cancer is declining due to screening programs and HPV vaccination, although the relative survival rate has remained unchanged over the last 40 years (1).

Concurrent chemo-radiotherapy or surgery represent the treatment of choice, depending on the stage of disease. Also, there is still a large proportion of patients who develop distant metastases, and few of them present with an oligometastatic disease (2). The clinical management of recurrence cervical cancer usually depends on previous treatments, site of recurrence and burden of disease.

At the present time, there are no guidelines for such patients, although a small proportion of patients can still be

cured if treated aggressively (3).

We present a case of a woman, who completed curative treatment with chemoradiotherapy and later on developed a peritoneal metastasis that was successfully treated with surgery and chemotherapy.

The following case was presented in accordance with the CARE reporting checklist (available at <https://gpm.amegroups.com/article/view/10.21037/gpm-20-49/rc>).

Case presentation

Our patient is a 81 year old female who was diagnosed with a locally advanced cervical cancer in January 2017. The family history was negative for cancer disease, the patient had an history of COPD (chronic obstructive pulmonary

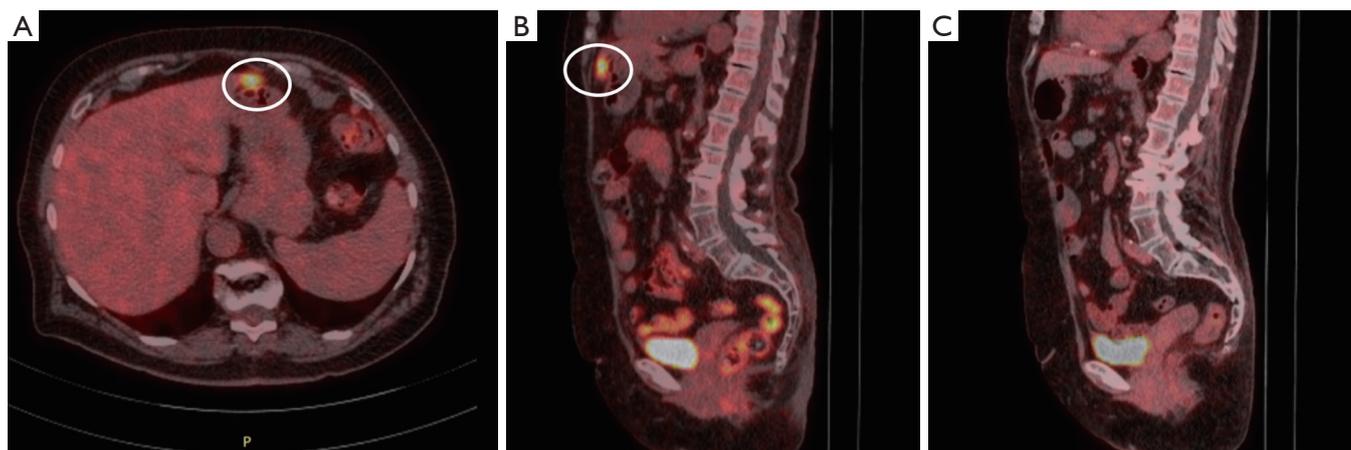


Figure 1 The PET/CT scan. (A) Peritoneal recurrence (transverse view); (B) peritoneal recurrence (sagittal view). The cervical area shows no signs of persistence of disease, whereas the bowel shows radiation-induced inflammation; (C) the last follow up PET/CT examination, showing no signs of recurrence of disease. Bowel inflammation is resolved.

disease) due to smoking, and diabetes.

She presented to the hospital with complaints of fatigue and vaginal bleeding in menopause and the gynaecological examination showed the presence of a vegetating mass inside the uterus cavity.

Hysteroscopy with biopsy confirmed the diagnosis of mild differentiated cervical adenocarcinoma. The patients underwent staging with CT scan, cystoscopy and colonoscopy. Unfortunately, no MRI was done for the extreme claustrophobia of the patient.

The lesion was a 3 cm inhomogeneous mass on the uterine neck that extend posterior to both vaginal fornices and to the parametrium bilaterally, no clear cleavage plane between bladder wall and uterus, no pathological lymphadenopathies, presence of a 3 cm lesion in the left adrenal gland that was deemed as non-pathological.

Cystoscopy as well as Colonoscopy showed no clear sign of tumor infiltration.

The clinical staging was a IIB cervix carcinoma and external beam radiotherapy (EBRT) concomitant with chemotherapy (weekly carboplatin) was planned, followed by brachytherapy treatment (BRT).

The planned target volume 1 (PTV1) comprehended both parametrium, the dose prescribed was 59.36 Gy with a daily fraction of 2.12 Gy/die with 5 days treatment a week for a total of 28 fractions.

The PTV2 comprehended common iliac lymph nodes, internal and external iliac lymph nodes, obturator and pre-sacral lymph nodes and the cervix: the dose prescribed was

50.40 Gy with a daily fraction of 1.8 Gy/die with 5 days treatment a week for a total of 28 fractions.

The patient during the radiation therapy received a weekly infusion of concomitant CHT AUC2 carboplatin with the dose of 100 mg, the patient was able to receive all the 6 planned administrations with the manifestation of only low grade side effects (nausea, haematological toxicity).

At the end of the EBRT+CHT treatment she completed BRT boost treatment on the GTV (total dose 21 Gy in 3 fractions).

The patient was then admitted to a strict follow up to monitor the treatment results and the disease control.

The first restaging exams (CT total body) in August 2017 showed a considerable reduction of the mass of the uterus body and neck and of the endometrium, with no more sign of infiltration of both parametria. Unfortunately the exams showed a peritoneal lesion of roughly 2 cm situated on the transverse mesocolon, that a PET/CT examination confirmed as highly suspicious (*Figure 1*).

The patient was then referred to the Surgery Department and underwent abdominal surgery to remove the lesion. The pathological exam confirmed that it was a cervical metastasis and the patient underwent adjuvant chemotherapy with Carboplatin till January 2018.

The patient reported no acute or sub acute toxicity, after surgery and during adjuvant chemotherapy.

The subsequent imaging (PET/CT and CT scans) showed no signs of other recurrences of disease and after three years since recurrence the patients is still with no

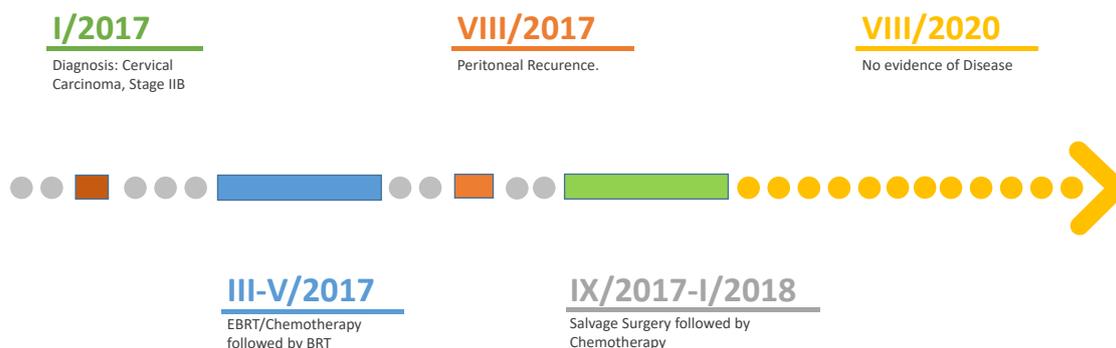


Figure 2 Timeline of the reported case.

evidence of disease (*Figure 2*).

Due to the anonymous use of clinical data, the current study is in accordance to the Italian Legislation Personal Data Protection Law 196/2003. All procedures performed in studies involving human participants were in accordance with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this study and any accompanying images.

Discussion

Chemoradiotherapy in locally advanced cervical cancer can provide a good tumor control rate, although approximately one-third of the patients can develop further recurrence (2,4). The most common recurrence sites are the pelvis and the para-aortic nodes (2).

In this regard, precise definitions of recurrences and optimal treatment strategies are still to be clearly defined. Recently, Bendifallah *et al.* developed a proposal for a classification based on anatomical dissemination pathways and prognosis (5). In their work, single site recurrences showed a trend towards a better prognosis.

The Moore Criteria, conversely, have been used to predict outcomes in patients undergoing chemotherapy for recurrent or metastatic cervical cancer (6). African American race, performance status > 0, pelvic disease, prior cisplatin exposure and time interval from diagnosis to first recurrence < 12 months were poor prognostic factor. Our reported patients would have at least three criteria.

The follow up after chemoradiotherapy in locally advanced cervical cancer can include either conventional surveillance or completion hysterectomy (7). The addition of hysterectomy may be associated with better outcomes in retrospective series (7), but is associated with high risks of

surgery in an irradiated pelvis (8).

Radiotherapy represent one of the keystone treatment for cervical cancer, although radioresistance remains a clinical challenge (9,10). Weichselbaum *et al.* performed an interesting study regarding the relationship between intrinsic tumor radiosensitivity and the immune system, named radiation-induced tumor equilibrium (11). In the context of cervical cancer, the chemoradiotherapy can induce an immunosuppressive environment increasing Treg cells in the circulation (12).

Peritoneal metastasis can occur during surgery (13) and some surgical techniques are adopted to prevent tumor spillage during the procedure (14,15).

In the reported case, although, it's highly likely that the peritoneal metastasis was present since onset of disease. Recently, Lin *et al.* performed a retrospective analysis on a sample of 607 patients with cervical cancer treated with radiotherapy and found that an isolated pelvic failure was detected in 11% of the patients (16). The presence of pelvic and para-aortic nodes at onset was associated with worse progression free survival and the salvage surgery approach was associated with prolonged survival in comparison to systemic therapy or no therapy (16), with a 5 year survival rate of 32%.

One third of the patients developed subsequent distant failure within 2 years of pelvic relapse, thus a strict follow up is strongly recommended in the first period.

The role of systemic therapy in recurrent or metastatic cervical cancer has been investigated in several clinical trials. Gynecologic Oncology Group (GOG) trial 179 demonstrated a benefit of cisplatin and topotecan versus cisplatin alone (17). GOG 204 trial showed no differences among 4 combinations of platinum doublets (18) and more recently the GOG 240 demonstrated the benefit in

survival with the addition of bevacizumab to combination chemotherapy (19).

The strength of the care reported is the successful use of surgery for recurrent cervical cancer in an old patient. The limitations are the lack of MRI at the beginning and in the follow up, due to the claustrophobia of the patient.

Concluding, the use of different strategies (radiotherapy, chemotherapy and surgery) seems to be useful in terms of outcomes in the management of cervical cancer patients.

A multidisciplinary approach is mandatory in order the choice the correct approach in the different setting of this disease. Older patient, at the same time, can be considered even for aggressive approaches, with the correct combination of radiotherapy, chemotherapy and even surgery, as they can aim to be cured in selected settings.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at <https://gpm.amegroups.com/article/view/10.21037/gpm-20-49/rc>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://gpm.amegroups.com/article/view/10.21037/gpm-20-49/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Due to the anonymous use of clinical data, the current study is in accordance to the Italian Legislation Personal Data Protection Law 196/2003. All procedures performed in studies involving human participants were in accordance with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this study and any accompanying images.

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