

Case Report

Metachronous Cancers

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REZUMAT

Cancerle metacron

Prezentăm cazul unei paciente în vârstă de 33 de ani, fara antecedente personale patologice, nefumatoare, nepotatoare, care a acuzat în noiembrie 2011 dureri pelvine și metroragii. În urma investigațiilor, se pune diagnosticul de carcinom scuamos de col uterin biopsiat stadiul FIGO IIIB. Pacienta a efectuat tratament neoadjuvant (radio-chimioterapie cu Cisplatin), urmat de limfadenocolpohisterectomie totală cu anexectomie bilaterală robotică (martie 2012). Datorită răspunsului parțial la tratamentul neoadjuvant, dar și apariției imagistice a unui bloc adenopatic iliac comun drept, se continuă tratamentul citostatic (Paclitaxel și Cisplatin). Reevaluarea imagistică PET-CT din ianuarie 2013 evidențiază adenopatii supra și subdiafragmatice active metabolic, motiv pentru care se efectuează a doua linie de chimioterapie (Topotecan), examinarea CT din iunie 2013 arătând boală staționară. După 10 luni în care pacienta nu s-a mai prezentat la controlul periodic, revine cu un bloc adenopatic laterocervical stâng de la nivelul căruia se prelevează biopsie, cu rezultat de metastază de carcinom scuamos slab diferentiat. Se continuă chimioterapia cu Paclitaxel și Cisplatin, perioadă în care pacienta prezintă disfonie, rinoree și cefalee. Examinarea imagistică evidențiază adenopatii laterocervicale și o formațiune tumorală nazofaringiană care se biopsiază, rezultatul fiind de carcinom nazofaringian nediferențiat. CT-ul de plan de tratament în vederea radioterapiei nazofaringiene arată metastaze cerebrale. Se efectuează "whole brain radiotherapy". Particularitatea cazului este reprezentată de prezența metastazelor cerebrale, acestea fiind foarte rare atât în cancerul de col uterin cât și în cel de rinofaringe.

Cuvinte cheie: cancer col uterin, cancer nazofaringe, metastaze cerebrale

ABSTRACT

We present the case of a 33 years old female patient with no tobacco and alcohol use patient without any pathological important background who accused in November 2011 pelvic-abdominal pain and metrorrhagia. After the investigation was conducted, it was settled the diagnosis of biopsied squamous cell carcinoma of the cervix staged FIGO IIIB. The patient received concurrent chemotherapy (Cisplatin) with radiotherapy, followed by a robotic total hysterectomy and bilateral pelvic lymphadenectomy (March 2012). Due to partial response to neoadjuvant treatment, but also to the imagistic apparition of a right common iliac adenopatic mass, it is continued the chemotherapy treatment (Paclitaxel and Cisplatin). The imagistic reevaluation done later in January 2013 highlights supra and subdiaphragmatic lymph nodes with metabolic activity, motive for which, it is done a second line of chemotherapy (Topotecan), the CT examination from June 2013 showing stable disease. After ten months in which the patient did not present to the periodic follow-up, she returns with a left latero-cervical adenopatic mass, from which it is performed a biopsy. The histopathological result is a low differentiated squamous cell carcinoma metastasis. The chemotherapy is continued with Paclitaxel and Cisplatin

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period in which the patient presents dysphonia, rhinorrhea and headache. The imagistic examination reveals adenopathies latero-cervical and a nasopharyngeal tumoral mass from which is performed a biopsy; the result obtained being an undifferentiated nasopharyngeal carcinoma. The CT scan for the planned treatment following the nasopharyngeal radiotherapy points out brain metastases. It is done the whole brain radiotherapy. The particularity of the case is represented by the presences of brain metastases, these being seldom in both cervical cancer and nasopharyngeal cancer.

Key words: cervix carcinoma, nasopharynx carcinoma, brain metastases

INTRODUCTION

According to GLOBOCAN, cervical cancer is the fourth most common cancer worldwide touching woman, with approximately around 500000 new cases and 266000 deaths in 2012; in Romania, cervical cancer is the second malignancy diagnosed in women. Cervical cancer is responsible for 7.5% from the whole female cancer deaths and 87% of these cases are encountered in the less developed regions of the world.

The more advanced is the stage of cervical cancer, the worse the prognosis is and the treatment in these cases is mainly palliative with an average survival period of only 7 years as observed in recurrent and/or metastatic cancer. Although IIIB stage is an advanced stage of cervical cancer, favorable results can be obtained with a combined therapy of concomitant chemoradiation with cisplatin.

The confirmation comes from NCCN and ESMO guidelines that stage IIIB of cervical cancer can be successfully treated with neoadjuvant chemoradiation followed by radical hysterectomy, without major complications; in addition the advantage of this staged treatment is represented by the possibility of knowing the effect of chemoradiation through the histopathological result: if in the primary tumor there are still residual cancer cells or if there is lymph node involvement.

Nasopharyngeal carcinoma is a rare form of cancer representing 0.7% of the cancer cases worldwide; the incidence in 2008 was of approximately 80000 new cases per year and 50000 deaths. Nasopharyngeal carcinoma has usually no specific symptoms and many cases are diagnosed at an advanced stage of the disease. Due to the anatomic limitations, chemoradiation with cisplatin followed by adjuvant chemotherapy for loco-regionally advanced disease is the most suitable treatment. (1,2)

CASE REPORT

A 33-year-old Caucasian female presented at a gynecology exam on November 2011 for pelvic-abdominal pain and metrorrhagia. After the clinical examination, cervical biopsy was performed. It revealed poorly differentiated squamous cell carcinoma. The patient did a CT scan that detected a 67/48 mm tumor located in the cervix and bilateral external lymph nodes, staged

FIGO IIIB. Neoadjuvant chemoradiation therapy is initiated (50,4 Gy with a brachytherapy boost until a total dose of 74,4 Gy and cisplatin weekly - 40 mg/m²) followed by robotic type II radical hysterectomy and bilateral pelvic lymphadenectomy (March 2012). The histopathological examination revealed residual lesions of poorly differentiated squamous cell carcinoma in the cervix but no pelvic lymph nodes were involved.

Two months after the surgical procedure, due to partial response to neoadjuvant treatment, but also due to the imagistic apparition of a right common iliac adenopathic mass, the patient was admitted to our hospital for adjuvant treatment. Six cycles of Paclitaxel (175 mg/m²) and Cisplatin (75 mg/2), q3w, were performed. The imagistic reevaluation PET-CT done later in January 2013 (Fig. 1) highlights supra and subdiaphragmatic lymph-nodes with metabolic activity: bilateral axillary with standardized uptake value [SUV(max)] of 3,8, para-aortic lymph nodes of 10 mm with SUV(max) of 3,8, common iliac lymph node of 17 mm with SUV(max) of 7,2 and right hydronephrosis, and right pulmonary micro-nodule of no oncological etiology. We decided to continue the chemotherapy treatment with a second line: 4 series of Topotecan (1,25 mg/m²), q3w. The follow-up

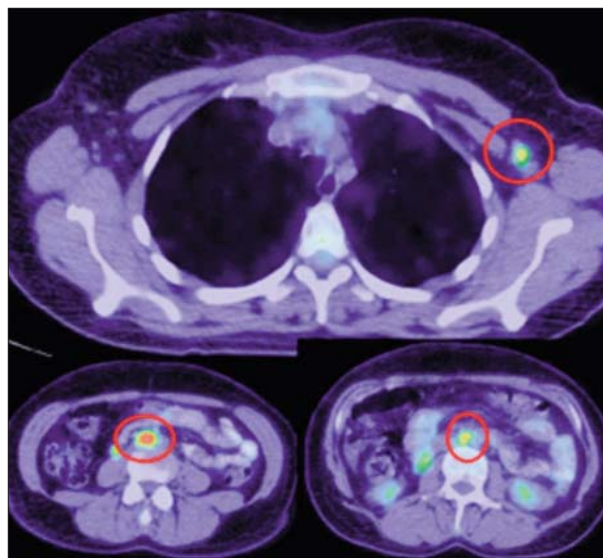


Figure 1. PET-CT show axillary and pelvic lymph nodes metastases

CT from June 2013 showed stable disease.

After ten months (February 2015), in which the patient did not present to the periodic follow-up, she returns with a painful left latero-cervical adenopatic mass (6/3cm), from which it is performed a biopsy. The histopathological result is a low differentiated squamous cell carcinoma metastasis; therefore immunochemistry interpretation confirmed lymph node metastasis of cervix cancer. We decided to continue the oncological treatment with 6 cycles of Paclitaxel (175 mg/m²) and Cisplatin (75 mg/m²), q3w. The otolaryngology consult during this period indicated an important reduction of the submandibular lymph node to 2/2.5 cm. But, the patient presents rhinorrhea, dysphonia and headache.

The imagistic examination reveals a nasopharynx tumor (clinical stage is T4N3) in the left median region, left pterygoid fossa invasion, bilateral cervical lymph nodes, submandibular lymph node with necrotic center, bilateral supraclavicular, mediastinal, para-aortic and bilateral common iliac lymph nodes, bilateral hydronephrosis (accentuated mostly on the left side - grade III-IV), hepatic lesions in the third and seventh segment with a highly suggestive aspect of metastases. A biopsy is performed from the nasopharynx tumor with histopathological and immunochemistry results confirming the diagnosis of undifferentiated nasopharynx carcinoma.

The CT scan from June 2015, for the nasopharynx radiotherapy planning points out multiple frontal lobe brain lesions with suggestive aspect of brain metastases,

an invasive loco-regional nasopharynx tumor without cerebral extension, bilateral cervical (II, III, Vb) lymph nodes, and right apical pulmonary lesion (Fig. 2). Due to the fact that the patient's performance status was poor and the neurologic examination recomanded palliative radiotherapy, a potential biopsy from the brain metastasis was not taken into consideration. Therefor whole brain radiotherapy is performed with a total dose of 18 Gy (3Gy/fraction, twice a day for 3 days).

After one month after radiotherapy, a whole body CT scan is performed revealing progression of the cerebral, pulmonary, hepatic, lymph nodes metastasis, peritoneal macro-nodules of carcinomatosis, left grade IV and right grade III hydronephrosis (Fig. 3). The patient is transferred to palliative care for symptomatic treatment.

DISCUSSIONS

The particularity of this case consists, firstly, in the presence of a secondary cancer developed 4 years after the diagnosis of cervical cancer. Almost all women diagnosed with cervical cancer undergo radiotherapy as a definitive treatment or as a part of a multimodal treatment. It is well known, that, radiotherapy increases the risk of developing a secondary cancer (SC). It has been pointed out that, for the cervical cancer patients, the preferential sites for developing a secondary cancer are situated in the pelvic region (3, 4). However, other studies have highlighted that female patients with cervical



Figure 2. CT scan reveals several cervical lymph nodes, brain metastases, pulmonary metastases and nasopharynx tumor

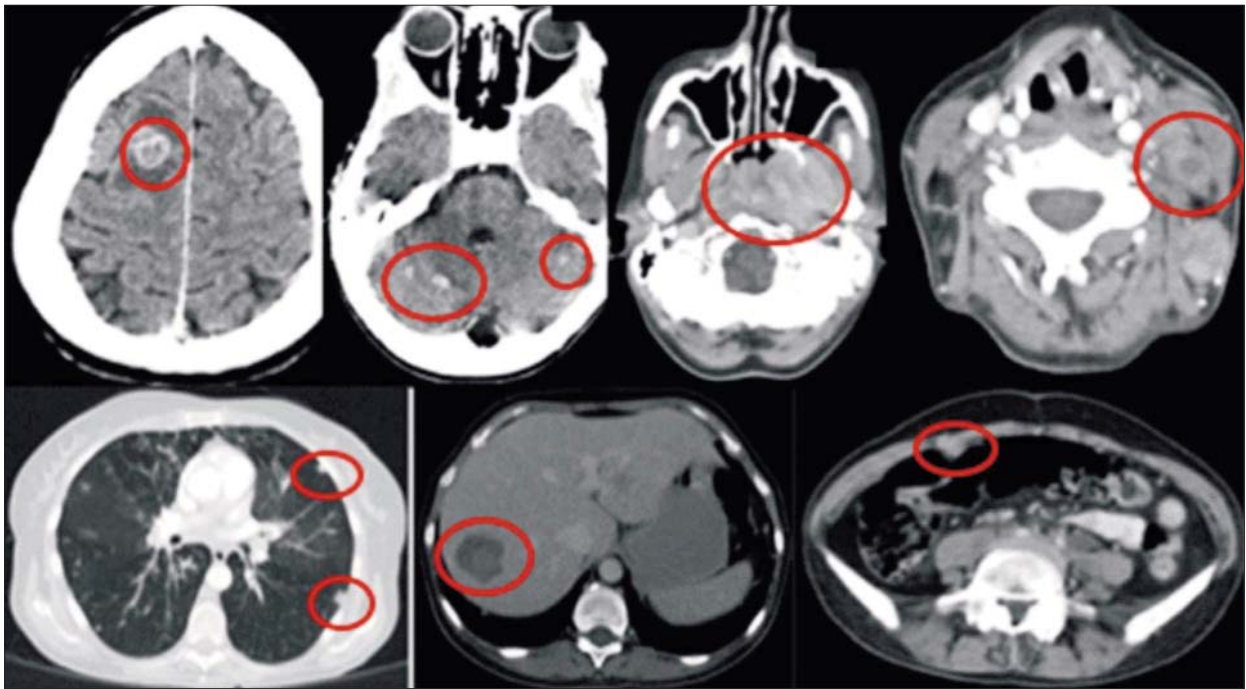


Figure 3. CT scan show progression of disease

cancer develop a SC in the head and neck region with an increased incidence, than the general population. As it was already demonstrated, the HPV infection represents one of the leading causes for both cervical cancer and nasopharyngeal cancer. Further studies are needed to establish if the HPV infection is responsible for the association of these two neoplasia (5). Another study demonstrates the fact that the risk of developing SC is significantly increased in young female patients compared to older patients; these risks are present both for female patients that are treated with radiotherapy or not (6). Former or present smoking female patients are also at high risk of developing SC after intracavitary radiotherapy compared to patients that aren't smokers. However, this study did not evaluate the smoking risk in separate types of secondary cancers (7).

Female patients with stage IIIB FIGO have the worst prognosis. There are some particularities that can be assessed in order to determine what treatment is better to be used. Stage IIIB comes together with an invasion of the pelvic wall and/or hydronephrosis due to the primary tumor or ureteral obstruction (8). Some studies demonstrated the fact that we must differentiate stage IIIB in three different categories: the patients that present pelvic wall invasion, those that additionally have hydronephrosis and finally those that have hydronephrosis without pelvic wall tumor. They compared the progression free survival (PFS) or survival rates at 5 years and data demonstrated that the worst prognosis is when female patients have hydronephrosis without pelvic wall invasion as in our case

(9-12). Also we must emphasize on the difference between unilateral and bilateral hydronephrosis, the latter having a worse prognosis (13).

Another important factor for prognosis is the pelvic lymph node metastases. The extent of pelvic, para-aortic or supraclavicular lymph nodes detected by whole-body FDG-PET is essential for the prognosis of each female patient's survival. (14) Some studies shows that FDG-PET is an important investigation in predicting the evolution of locally advanced cervical cancer (15,16); SUV(max) with a value of more or equal of 3,3 is a criteria for this prognostic. (17)

The presence of brain metastases both in cervical cancer as well as nasopharyngeal cancer is very rare, the statistics shows that the incidence is below 1% of all female patients with cervical carcinoma (18-20). Some authors stress on the importance of the cellular grade, most of them were poorly differentiated type of squamous cell carcinoma (21,22). Also the presence of brain metastases in cervical cancer is often associated with disseminated disease, some studies presented cases like ours with pulmonary metastases (22,23). The literature also reports a few cases of brain metastases from nasopharyngeal cancer; these are extremely rare (24). Many reviews show that brain metastases from nasopharyngeal cancer occur when also others organs present metastases (25-27). It is also important to differentiate direct invasion of the primary nasopharyngeal tumor in the brain with true brain metastases, the first are frequent when the patient has a clinically stage T4 tumor (8,27). In our case, the

patient presented besides brain metastases, also pulmonary and liver metastases; these two regions are more frequent in nasopharyngeal cancer (28), but also in cervical cancer. (29) It is difficult, in this case, to establish the correct origin of these metastases without a proper biopsy. The ideal would have been at least 3 different biopsies performed, but even in this case, it could have been possible that two or more of the biopsies of one of these three organs could have given two different histopathological results and confirm the possibility of both primary cancers to have metastases in a single organ.

Some studies confirm that we can treat radically stage IIIB cervical cancers with neoadjuvant chemoradiation followed by radical hysterectomy, without major complications and with the benefit of knowing after surgery the result of the neoadjuvant treatment, if there were residual cancer cells in the primary tumor or lymph node involved. (30)

CONCLUSIONS

Our case provides an example of complications in setting the diagnosis and treatment of a cervical and nasopharyngeal cancer, this being caused by the fact that the patient did not respect the treatment schedule and follow-ups.

The incidence of brain metastases is a very rare one in cases such as the nasopharyngeal and cervical cancer; also the occurrence of head and neck cancer manifested after a cervical cancer is very rare.

Grade III and IV bilateral hydronephrosis without pelvic wall invasion represent a worse prognosis and are a rare condition in the clinical practice.

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