Rapid Fatal Progression of Cervical Cancer during Pregnancy Treated by Neoadjuvant Chemotherapy

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Abstract

Background: Cervical cancer is the most commonly diagnosed gynaecological malignancy in pregnant women. The prognosis of this cancer does not seem to be influenced by the pregnancy. However, the cancer management comes into competition with maternal and foetal outcomes, especially during the 2nd trimester of pregnancy. Challenging issues lie in the cervical screening during pregnancy, the evaluation of lymph node status and the indication of neoadjuvant chemotherapy to avoid foetal prematurity without comprising maternal prognosis.

Case: We report a case of locally advanced cervical cancer diagnosed during the second trimester of pregnancy with rapid progression and fatal maternal outcome despite neoadjuvant chemotherapy.

Conclusion: Chemotherapy for cervical cancer during pregnancy is not always effective and maternal outcome could potentially be compromised.

Keywords
Cervical cancer, Pregnancy, Neoadjuvant chemotherapy

Teaching Points

- To evaluate lymph node status for patient with cervical cancer diagnosed during pregnancy is a main prognostic issue.
- The efficiency of neoadjuvant chemotherapy during pregnancy for patient diagnosed with cervical cancer remains debated.
- Identifying predictive factors of chemo-sensitivity of cervical cancer is necessary to perform a better selection of candidate for neoadjuvant therapy.

Introduction

Cervical cancer is the first gynaecological cancer diagnosed during pregnancy [1] but most cases (70%) are diagnosed at an early stage thanks to routine cervical screening in prenatal care.

Abnormal cervical cytology is encountered in around 5% of pregnant women whereas invasive cervical cancer affects only 1 to 2 women among 10 000 pregnancies [2,3]. Some authors report that maternal outcome is not worsened by pregnancy in particular for squamous cell types [2,4].

As in other cancers that occur during pregnancy, mother and child outcomes are weighed against each other. In this context, the management of patients with locally advanced cervical cancer remains controversial especially in the second trimester of pregnancy. Treatment is mainly influenced by the risk of lymphatic spread and distance metastases, gestational age, previous pregnancies and the parents’ decision [1]. Termination is often recommended due to the poor prognosis of the disease. However, a few cases of neoadjuvant chemotherapy with preservation of the pregnancy have recently been reported suggesting that this option might be an alternative to systematic pregnancy termination.

We report a case of squamous cell carcinoma diagnosed during the second trimester of pregnancy with a rapid progression and a fatal maternal fatal outcome despite neoadjuvant therapy.

Case

A 30-year-old woman, gravida 1 para 0, was referred to the expert centre of pregnancy associated cancers (CALG) at Tenon Hospital for a cervical cancer diagnosed at 19 weeks of pregnancy. The Papanicolaou (Pap) smear test carried out at the first prenatal visit because of vaginal bleeding was negative although only endocervical cells were detected. Hence, vaginal bleeding during the first trimester of pregnancy was attributed to cervical ectropion.

At the visit corresponding to the 19th week of gestation, the physician diagnosed an exophytic cervical lesion measuring at least 4 cm without invasion of parametrium corresponding to IB2 FIGO stage. A cervical biopsy was performed and histology revealed an undifferentiated squamous cell carcinoma. Immunohistochemistry showed that cervical lesion was positive for p16 and p63 protein as well as for KL1 and CD 5/6 cytokeratin confirming the diagnosis of squamous cell carcinoma. No chromogranin, CD 56 neither synaptophysin expression was observed ruling out the neuroendocrine origin.

Magnetic Resonance Imaging (MRI) confirmed a 65 mm cervical lesion without nodal involvement (Figure 1).

As the couple wished to conserve the pregnancy, neoadjuvant chemotherapy with carboplatin (5 AUC, 1160 mg/m²) and paclitaxel (175 mg/m², 360 mg) was recommended. Fetal ultrasound during the first and second trimester showed no fetal malformation or...
intra-uterine growth restriction. After two cycles of chemotherapy, physical examination found an increase in tumour size confirmed by MRI showing a tumour of 8 cm of diameter with bilateral ureteral dilatation (Figure 2). In this context, preterm birth by caesarean section was organized at 29 weeks of gestation after foetal lung maturation (betamethasone, 12 mg per day during 2 days). The infant girl weighed 1525 grams and had an Apgar score of 10 at 1 minute which decreased to 2 at 5 minutes justifying intubation for respiratory assistance. She remained in the hospital intensive care unit until she was 27 weeks old. Today the child is 4 months old and healthy.

PET-FDG performed on the mother during the early postpartum period revealed a suspicious pelvic node but no uptake in the para-aortic areas. An extraperitoneal para-aortic lymphadenectomy was performed 2 weeks after the caesarean section and histology revealed metastases in 6 of the 16 lymph nodes. Exclusive concomitant radiochemotherapy was consequently recommended (external beam radiotherapy: 45 Grays on the pelvis and a complement of 10 Grays on each iliac site associated with Cisplatin 30 mg/m² weekly during 2 weeks then Topotecan, 4 mg/m², one cycle).

However, despite treatment, the patient developed intraperitoneal carcinomatosis with ascites, hydrodrionephrosis and pulmonary embolism 11 weeks after the birth. The patient died of tumor progression 5 months after the initial diagnosis and 11 weeks after giving birth.

Discussion

Several studies have reported that pregnancy does not affect prognosis or survival of patients with early stages of cervical cancer justifying postponing treatment until after delivery [5-7]. However, this case report suggests that neoadjuvant chemotherapy administered during pregnancy is not always effective and can affect thus the prognosis compared to non pregnant patient.
For pregnant patients with a tumour stage greater than IB1, guidelines for treatment differ from country to country [1,8] (Figure 3). The trimester during which the cancer is diagnosed and lymph node status are essential to determine therapeutic strategy. In the case reported here, two major arguments justified the decision to delay surgical lymph node staging: MRI did not detect the para-aortic lymphadenectomy that was required as the scan was negative. This underlines quality criteria of Pap smear imposing effectively an ectropion and Pap smear did not note the presence of glandular cells. This underlines quality criteria of Pap smear imposing detecting both the presence of glandular and squamous cells.

The current case report highlights that, although neoadjuvant chemotherapy is an option to treat cervical cancer during pregnancy, chemotherapy is not always effective and maternal outcome could potentially be compromised. There is hence a need to identify predictive factors of chemo-sensitivity of cervical cancer to better select patients that could benefit from this therapeutic strategy.

References