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Clinical Outcome of a FIGO Stage IV Gestational Choriocarcinoma

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Key Words

Metastatic choriocarcinoma · Relapse · EMACO

Abstract

Choriocarcinoma is the most malignant tumor of gestational trophoblastic disease arising from any gestation. It has a tendency toward relapse as well as metastasis. Here, a case of relapsed high-risk choriocarcinoma (FIGO stage IV, WHO score 12) in a 37-year-old female presenting with vaginal bleedings is described. Relapse developed at the site of the surgical scar from hysterectomy that had been performed 2 years earlier. Although the patient was treated with aggressive chemotherapy, she was in a bad general condition and died from infection and liver insufficiency.

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Introduction

Gestational choriocarcinoma usually arises from a prior molar pregnancy or rarely from nonmolar gestation within 1 year of the antecedent pregnancy, usually presenting as an abnormal uterine bleeding [1, 2]. Despite its tendency to cause metastases in other organs, 75% of the FIGO (International Federation of Gynecology and Obstetrics) stage IV choriocarcinoma patients are expected to achieve complete or prolonged remission with a multi-agent chemotherapy [3]. However, metastasis to the brain is considered a poor prognostic indicator. Relapse of the disease is associated with an estimated mortality rate of 30% [4].

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Case Presentation

In October 2012, a 37-year-old female patient presented with a 7-day history of lower abdominal pain, vaginal bleeding and a raised β -hCG level (44,565 IU/l). In anamnesis, she had two normal antecedent term pregnancies. Within 1 year after the second pregnancy, choriocarcinoma developed. In December 2010, the patient was treated for choriocarcinoma with lung metastasis with three courses of EMACO chemotherapy. Hysterectomy with preservation of the adnexa was performed. In May 2011, she developed clinical manifestations of brain metastasis, which was treated successfully through surgery (extirpation of the tumor in the parieto-occipital region of the brain), radiotherapy and 4, 5 and 6 courses of chemotherapy. Thereafter, she was closely followed up by a gynecologist and a neurologist. Her regular therapy was carbamazepine at a dosage of 800 mg daily.

The patient was in remission from July 2011 to October 1, 2012 when she addressed herself to our Institute. A vaginal examination revealed vaginal bleeding and a palpable mass in the lesser pelvis behind the site of the hysterectomy scar. Her physical examination was otherwise normal and, apart from β -hCG units with a tendency to rise, her laboratory analyses were without pathological findings too. An MRI scan of the abdomen and pelvis revealed a tumor of 7.0 × 7.6 × 9.3 cm in size, infiltrating local tissues and indicating a relapse of choriocarcinoma (fig. 1). The MRI scan also showed multiple metastases in the right lung. A computed tomography (CT) of the chest showed multiple metastases (fig. 2), but the brain CT was normal. Previously, the patient was at FIGO stage IV and had a WHO score of 13, both indicating that she was a high-risk patient with poor prognosis [5]. Considering the local tumor infiltration of the tissue, surgery was not an option. Instead, she was introduced to 9 courses of EMACO chemotherapy. Her vaginal bleeding persisted and was stopped by vaginal tamponade. Upon therapy, the patient became highly febrile (39°C). Her laboratory findings revealed elevated enzymes because of an acute-phase inflammation [C-reactive protein 361 mg/l, erythrocyte sedimentation rate 150/mm/h (2–10), fibrinogen 10 g/l (2–4), aspartate transaminase 130 IU/l (14–50), alanine aminotransferase 102 IU/l (21–72) and lactate dehydrogenase 546 IU/l (180–360)]. A blood analysis showed pancytopenia [white blood cell count: 3.7 g/l (0–132); red blood cell count: 1.89 × 10¹²/l (4.10–5.10); hemoglobin 53.5 g/dl (115–165); platelet 125 g/l (150–400)]. The hemostasis tests were within normal ranges. The patient was treated with cephalosporin, ertapenem, metronidazole, ciprofloxacin, neupogen and 4 doses of blood infusion. Three days after the introduction of antibiotics, the patient developed convulsive tonic-clonic seizures, which were partly controlled by carbamazepine. A repeated brain CT did not show metastasis. The patient was transferred to a neurosurgical clinic, where she died from liver failure and infection due to tumor necrosis on the second day after admission.

Discussion

Choriocarcinoma is a highly malignant tumor of the gestational trophoblast of the placenta. Trophoblastic cells have an affinity for blood vessels, and therefore the tumors have a tendency to metastasize through the hematogenous route [6]. The most common sites of metastasis are the lungs (80%), vagina (30%), pelvis (20%) and the liver (10%). Cerebral metastases occur in about 10% of the cases. Despite this aggressiveness, choriocarcinoma is generally highly chemosensitive and carries a much better cure rate than other comparable malignancies. Patients may present with signs and symptoms of bleeding from metastases such as hemoptysis, intraperitoneal bleeding or acute neurologic deficits [7, 8].

Multi-agent chemotherapy is the treatment of choice in high-risk choriocarcinoma. Currently, the most widely used combination regime is EMACO. However, 14% of the high-risk patients who received the EMACO chemotherapy as well as 1% of the low-risk patients who initially received methotrexate followed by the EMACO regimen require further treatment [9, 10].

Our patient presented with clinical signs of vaginal bleeding 15 months after remission (the last EMACO treatment). Several factors indicated poor prognosis, including a preceding normal delivery, an interval between pregnancy and diagnosis greater than 12 months, multiple distant metastases and very high β hCG levels. The patient had a FIGO stage IV tumor and was in complete remission for over 15 months. She was successfully treated with hysterectomy, 8 courses of chemotherapy, craniotomy and brain radiotherapy. The 9th course of chemotherapy was fatal.

Conclusion

In the literature, according to our knowledge, there is no description of recurrent choriocarcinoma at the site of a vaginal scar 2 years after hysterectomy. During chemotherapy, tumor necrosis developed, leading to a fatal general infection invading the central nervous system. The 9th course of chemotherapy was sufficient for liver malfunction.

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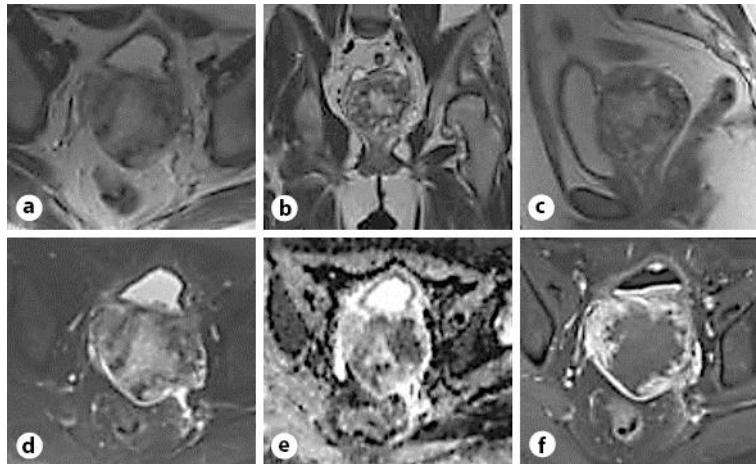


Fig. 1. a–c T2-weighted imaging of the axial, coronal and sagittal plans. d T2-weighted imaging with fat suppression. e Apparent diffusion coefficient map. f Post-contrast T1-weighted imaging with fat suppression on the axial plan shows recurrent choriocarcinoma of the uterus with infiltration of the vagina, posterior wall of the bladder and prevesical part of the left ureter.

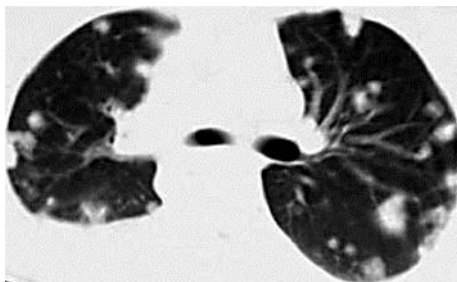


Fig. 2. A chest CT showing bilateral multiple metastases in the lung parenchyma.