DOI: 10.69729/aogp.v20i2a07

Successful pregnancy after invasive mole and choriocarcinoma: A case report

Desfecho reprodutivo favorável após uma mola invasiva e um coriocarcinoma: Caso clínico

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Abstract

Choriocarcinoma is a very rare but highly malignant epithelial tumor. Gestational choriocarcinoma most commonly develops following a molar pregnancy. Most lesions begin in the uterus, although it can develop in ectopic pregnancies. The most common metastatic sites are lungs, brain, liver, pelvis and vagina. The treatment of gestational choriocarcinoma is chemotherapy and survival rate varies between 91-100%. Chemotherapy may accelerate the onset of natural menopause, but in young women rarely causes permanent ovarian failure or infertility. We describe a case of a successful pregnancy after a cornual choriocarcinoma in a woman previously treated for an invasive molar pregnancy.

Keywords: Ectopic pregnancy; Choriocarcinoma; Hydatidiform mole.

Resumo

O coriocarcinoma é uma neoplasia trofoblástica rara com elevado potencial de malignidade, que surge frequentemente após uma gravidez molar. Na maioria dos casos, desenvolve-se no útero, embora possa ter origem em gestações ectópicas. A metastização é mais frequente nos pulmões, cérebro, fígado, pélvis e vagina. O tratamento é quimioterapia e a taxa de sobrevivência varia entre 91-100%. A quimioterapia pode antecipar a menopausa em cerca de três anos, mas em mulheres jovens, raramente provoca insuficiência ovárica permanente ou infertilidade. Apresentamos o caso de uma gravidez sem intercorrências após um coriocarcinoma numa gravidez ectópica, numa mulher com antecedentes de mola hidatiforme invasiva.

Palavras-chave: Gravidez ectópica; Coriocarcinoma; Mola hidatiforme.

INTRODUCTION

Choriocarcinoma is a rare and highly aggressive malignant tumor of trophoblastic origin, most commonly developing within one year after a gestational event, although it may occur anytime between 5 weeks and 5 years after a pregnancy[1]. Choriocarcinoma arises from an abnormal trophoblastic cell population undergoing hyperplasia and anaplasia and can either be gestational and non-gestational, which have very distinct biological activity and prognosis. The former arises following a hydatidiform mole, normal pregnancy or, most commonly, spontaneous abortion. In Europe and North America its incidence is estimated to be around 1 in 40,000 pregnant patients and 1 in 40 patients with hydatidiform moles[2]. Besides a prior complete mole hydatidiform (a 100-fold increased risk), other risk factors include advanced age, long-term oral

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contraceptive use and blood type A[2]. It is estimated that only 0.76 – 4% cases of choriocarcinoma develop in ectopic location, although they are more aggressive and associated with distant metastasis. The prognosis is affected by the time of diagnosis and initiation of chemotherapy[3]. Given that gestational trophoblastic disease predominantly affects women of reproductive age and is associated with an excellent overall prognosis, post-treatment reproductive potential is a key consideration. Relevant concerns include the gonadotoxic effects of chemotherapy, such as impaired fertility, unfavourable obstetric outcomes and premature menopause. Herein, we describe a case in which a woman achieved a spontaneous and uncomplicated pregnancy and delivery after being diagnosed with a cornual choriocarcinoma, surgically managed, and having a history of invasive mole.

CASE-REPORT

A 20-year-old female presented to the obstetrics emergency department of a tertiary hospital, approximately one year after her last delivery, with complaints of uterine bleeding and pelvic pain, for two hours prior to admission. The vital signs were pulse rate 65 bpm, temperature 36ºC and blood pressure 79/35 mmHg. Her obstetric history included three spontaneous abortions, two induced abortions, an invasive mole diagnosed in 2018 and treated with uterine evacuation and methotrexate chemotherapy, with complete remission, and an uncomplicated vaginal delivery in 2020. She had no other past medical history, no history of taking medicine and was not using any contraception. On physical examination she had diffuse abdominal pain, but no signs of peritoneal irritation. Gynecologic examination revealed a hematic vaginal discharge in small quantity and bimanual pelvic examination revealed pain on cervical mobilization but no palpable masses. A transvaginal sonography was performed which demonstrated an empty uterine cavity. Left adnexal area showed a hyperechoic structure with 26×19 mm. There was also free fluid in the anterior and posterior *cul-de-sac*. Laboratory findings indicated anemia (hemoglobin 11.1 g/dL, hematocrit 33%) and an elevated β-HCG titter (43225 mUI/mL). The first diagnostic hypothesis was an interstitial/cornual ectopic pregnancy. An abdominal laparotomy was performed which showed a hemoperitoneum and a cornual mass, suggestive of a cornual ectopic pregnancy. Both ovaries showed no lesions. A left cornual wedge resection and a left salpingectomy were performed. The mass was macroscopically completely removed. Histology examination showed fragments of an infiltrative neoplasia with syncytial and cytotrophoblast tissue, with cellular atypia and immunohistochemistry positive for p53, β-hCG and Ki67 of 90%. These findings were compatible with gestational choriocarcinoma. The patient was discharged three days after surgery in a stable condition. Sixteen days post-surgery, β-hCG titers decreased to 17528 mUI/mL. A thoraco-abdomino-pelvic staging CT scan performed one month after surgery demonstrated the presence of pulmonary nodules suspicious for metastatic disease. No metastatic masses were found on brain computed tomography. According to the International Federation of Gynecology and Obstetrics (FIGO) classification, the cancer was assigned stage III. A regimen with methotrexate was initiated, as well as a subcutaneous contraceptive implant. After 4 cycles, β-HCG titters reached a plateau, 7065 mUI/mL, 8082 mUI/mL and 7714 mUI/mL on first, second and third weeks of follow-up, respectively. Due to methotrexate resistance, a regimen with EMA-CO (a combination of methotrexate, dactinomycin, cyclophosphamide and vincristine) was initiated. She completed 5 cycles of EMA-CO. After a significant fall on β-HCG titters, a raise was noticed from 32 mUI/mL to 283 mUI/mL. A new thoraco-abdomino-pelvic scan showed signs of an asymptomatic pulmonary embolism without evidence of cardiac overload and oral anticoagulation was started. Also, the pulmonary metastasis were growing (from 16 mm to 24 mm; from 10 mm to 18 mm). For this reason, treatment with BEP (bleomycin, etoposide, cisplatin) was initiated. Three months later, β-HCG titters were negative. Follow-up CT scans showed stabilization in size of the 2 pulmonary nodules previously described. Those nodules were removed 15 months after the diagnosis of choriocarcinoma and no tumoral cells were found. Almost two years after the diagnosis, no metastatic lesions were seen on the CT scan. Follow-up care was maintained, although the patient did not attend several scheduled

follow-up appointments and laboratory monitoring was not performed as recommended. Nearly three years after the diagnosis of choriocarcinoma, the patient conceived spontaneously for the ninth time. This pregnancy progressed uneventfully and a caesarean section was performed at 38 weeks, without complications. No signs of uterine dehiscence were found. Placental histology was normal and one month postpartum, β-HCG titters were negative.

Written informed consent was obtained from the patient for publication of this case report.

DISCUSSION

Gestational choriocarcinoma is a trophoblastic tumor that mostly occurs in women of reproductive age. The clinical manifestations are variable but can be quite identical to those of an ectopic pregnancy, such as amenorrhea, vaginal bleeding, pelvic pain and increases in serum β-HCG levels. Histopathological examination of an ectopic pregnancy is essential for its confirmation or exclusion of any trophoblastic pathology. These tumors, like other trophoblastic tumors, produce much more β-HCG than a normal pregnancy, as reported in this case. This serum marker is also used for follow-up and detection of any recurrence. On ultrasound, no specific imaging findings have been described for extra-uterine choriocarcinoma[5]. Although, choriocarcinoma is 1000-fold more likely to occur after a complete hydatiforme mole than after another pregnancy[6], the long interval between the invasive mole and the diagnosis of choriocarcinoma and the occurrence of an intervening normal term pregnancy suggest that the cornual choriocarcinoma was more likely related to a subsequent gestation rather than representing persistent or recurrent trophoblastic disease. Nevertheless, a definitive causal relationship between the prior invasive mole and the later development of choriocarcinoma cannot be entirely excluded, highlighting the complex and heterogeneous nature of gestational trophoblastic neoplasia. Until 2017, only 4 cases of women with choriocarcinoma arising in the cornua have been previously reported in the literature[7,8,9,10], highlighting the rarity of this medical condition. Kazemi *et al.*[1] did a review on the case reports published in the last 10 years concerning choriocarcinomas that were first diagnosed as an ectopic pregnancy. In this review, the predominant presentation was tubal ectopic pregnancy, followed by ovarian ectopic pregnancy. Of all 24 patients, 14 had metastasis at the time of diagnosis, with the lung being the most common site of metastasis. In our case, the tumor had already metastasized to the lungs and after initial therapy with methotrexate, it was proven resistant and chemotherapy with EMA-CO and BEP was needed. Despite treatment with a combined chemotherapy regimen, including an alkylating agent known to impair ovarian function, the patient subsequently achieved a successful pregnancy and delivery. Several authors have investigated reproductive outcomes following the conservative management of choriocarcinoma. However, these studies are limited by small sample sizes and significant heterogeneity in chemotherapy protocols[11,12]. Regarding perinatal outcomes after choriocarcinoma chemotherapy, Madi *et al.* suggest that available data indicate good perinatal results in pregnancies after GTN treatment[13]. According to the American Society of Clinical Oncology, cyclophosphamide and cisplatin are classified as intermediate risk (20-80%) of amenorrhea in women aged 30-39 years[4]. After EMA-CO, the incidence of secondary infertility is estimated to be around 4-5%[4]. A cornual wedge resection increases the risk of uterine rupture as it involves loss of myometrium and significant uterine scarring. Rune Svenningsen *et al.*[14] compared the fertility outcomes in women treated surgically with cornual resection for an interstitial pregnancy compared to women treated with salpingectomy for non-interstitial pregnancy and no detrimental effect on subsequent pregnancy rates was found. Liao *et al.* analyzed 29 cases of interstitial pregnancies treated with cornual resection and found that 2 women presented with uterine rupture and the incidence of subsequent uterine rupture and dehiscence was 30%[15].

To conclude, this case report underscores the challenges in diagnosing ectopic pregnancy, emphasizing the critical role of histological examination combined with serial β-HCG monitoring. Furthermore, besides the rarity of this case, it highlights the potential for successful pregnancy outcomes after cornual resection and gonadotoxic chemotherapy.

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AUTHOR CONTRIBUTIONS

All authors contributed significantly to the conception, development and review of the present work. Rita Nunes and Ana Dagge were responsible for drafting the initial version of the manuscript. Anabela Colaço, Ana Rodrigues and Maria Pulido Valente contributed to the critical review of the content and to improving the final structure of the document.

CONFLICT OF INTEREST

None.

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RECEIVED: 16/03/2025
ACCEPTED: 03/04/2026