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Non-Molar Choriocarcinoma Following Miscarriage: A Rare Clinical Entity

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Abstract: ***This case report presents the rare occurrence of non-molar choriocarcinoma in a 36-year-old female with no documented history of molar pregnancy. The patient presented with recurrent severe bleeding in the first trimester, which led to surgical evacuation. Histological examination revealed non-molar choriocarcinoma, prompting her referral to a regional centre for trophoblastic disease for further management. A retrospective study involving 21 years found the incidence of non-molar choriocarcinoma 1:66 775 relative to live births [1]. Non-molar choriocarcinoma is a rarely reported entity in the literature, emphasizing the diagnostic challenges and need for timely intervention.***

Keywords: Non-molar choriocarcinoma, Miscarriage, Trophoblastic neoplasia, Gestational trophoblastic disease

1. Introduction

A 36-year-old female, gravida 2 para 1, presented at eight weeks of pregnancy with lower abdominal pain and vaginal spotting. Her past medical history included a previous placental abruption at 35 weeks of pregnancy, which necessitated an emergency Caesarean section, complicated post-operatively by postpartum haemorrhage and required a return to the operating room for uterine artery embolization.

In the current pregnancy, the initial ultrasound revealed an irregular 3.2 cm gestational sac with haemorrhagic contents in the fundal endometrium. After a thorough discussion of management options, the patient opted for surgical evacuation (EVAC). The first EVAC procedure was complicated by a blood loss of 800 ml and a suspected uterine perforation. Post-procedure imaging ruled out perforation but indicated the persistence of the gestational sac. A second EVAC was performed, resulting in a further blood loss of 800 ml. The bleeding settled after the second EVAC. After the second EVAC, the human chorionic gonadotropin (HCG) level was 12,606. Antibiotics were administered for seven days, and a plan was formulated to monitor serial HCG levels.

HCG Levels:
HCG 7 days following second EVAC: 12,606
HCG 13 days after the second EVAC: 19,791
HCG 16 days after the second EVAC: 24,859

The histological examination of the first and second EVAC specimens revealed trophoblastic tissue without evidence of a molar pregnancy. As the patient's bleeding had subsided, conservative management was continued. However, the patient returned one month after the second EVAC, presenting with heavy vaginal bleeding and collapse. Imaging indicated a 2 cm mixed echogenic area at the fundus, likely representing retained pregnancy tissue.

A third EVAC was performed under hysteroscopy guidance. Histopathology from the third EVAC revealed coalescent sheets of trophoblastic tissue with a triphasic morphology: cytotrophoblasts, intermediate cells, and multinucleated syncytiotrophoblasts with atypical vesicular nuclei, apoptosis, haemorrhage, and necrosis. Some areas showed apparent invasion of the myometrium, with no chorionic villi identified.

Genetic analysis indicated a bi-paternal pattern with maternal and non-maternal alleles in equal proportion, confirming the tissue as non-molar. This finding raised concerns about the possibility of primary non-gestational choriocarcinoma pre-existing before the patient's pregnancy. This is of particular significance given the patient's history of poor obstetric outcomes and recurrent miscarriages.

The patient was urgently referred to a regional centre for trophoblastic disease. Considering her low FIGO score, she was initiated on single-agent chemotherapy. She was advised to wait for six months after her HCG levels returned to normal before attempting another pregnancy.

2. Discussion

Gestational trophoblastic disease (GTD) encompasses a spectrum of conditions, including complete hydatidiform mole (CHM), partial hydatidiform mole (PHM), invasive mole, choriocarcinoma, placental site trophoblastic tumour (PSTT), and epithelioid trophoblastic tumour (ETT). While CHM and PHM have the potential for malignant transformation, the risk of GTN is higher for CHM than PHM. Advanced maternal age and a history of a previous hydatidiform mole are established risk factors for molar pregnancy. Most cases of GTN occur following molar pregnancies but can also arise after any gestational event, including miscarriage and ectopic or term pregnancies. GTN has a high curability rate, even in cases of metastatic disease.

Modern diagnostics for GTD involve a combination of obstetric history, elevated hCG levels and histopathological analysis of specimens obtained after surgical evacuation. Biopsy is generally avoided due to the risk of haemorrhage. Genetic profiling can differentiate gestational from non-gestational choriocarcinoma, with non-gestational

choriocarcinoma associated with a worse prognosis. Carta et al. described a case of endometrioid carcinoma of the endometrium with a focus on choriocarcinoma-like cells in a 50-year-old woman with a history of abnormal uterine bleeding. Immunohistochemistry showed intense reactivity of tumour cells for CK 7 and AE1/AE3, for beta-human chorionic gonadotropin (beta-hCG), and for HER2, confirming the diagnosis [2].

In summary, this case highlights the challenges of diagnosing non-molar choriocarcinoma, a rare entity that can present without a prior molar pregnancy. Timely diagnosis and management are critical for favourable outcomes in GTD cases.

3. Conclusion

This case report underscores the need for clinicians to consider the possibility of non-molar choriocarcinoma even in the absence of a proven prior molar pregnancy, particularly in patients with recurrent obstetric complications. Timely diagnosis and appropriate intervention are crucial to improving patient outcomes and fertility preservation. Advances in genetic profiling and non-invasive diagnostic techniques continue to enhance our understanding of gestational trophoblastic diseases and aid in their management [3].

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