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Case Report

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Cesarean Scar Choriocarcinoma Following a Cesarean Scar Molar Pregnancy: A Case Report

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ABSTRACT

Gestational choriocarcinoma, a rare variant of gestational trophoblastic disease, typically arises from abnormal trophoblastic cell proliferation post-pregnancy, often associated with a hydatidiform mole. While most choriocarcinoma cases develop within the uterine cavity, an exceedingly rare manifestation occurs within a previous cesarean section scar. In our study, a 31-year-old woman with a history of hydatidiform mole presented with amenorrhea and spotting. Initial assessments revealed elevated beta-human chorionic gonadotropin (βhCG) levels and a heteroechoic mass at her prior cesarean section scar in sonographic examination. Histopathologic findings and the metastatic workup categorized the patient as FIGO stage I, indicating no metastasis. Due to the absence of metastasis, adjuvant chemotherapy was omitted. Total abdominal hysterectomy confirmed choriocarcinoma. Post-surgery, βhCG levels notably decreased, remaining negative during the two-year follow-up with no reported symptoms. Our findings suggest that surgical resection and meticulous βhCG monitoring may be a promising treatment strategy for non-metastatic choriocarcinoma.

Introduction

Gestational choriocarcinoma is a rare variant of gestational trophoblastic disease, typically arising from an abnormal trophoblastic cell population undergoing hyperplasia and anaplasia after a pregnancy, most commonly a hydatidiform mole [1]. While its usual location is within the uterine cavity, sporadic occurrences have been noted in the cervix, ovary, and fallopian tube [2]. Primary choriocarcinoma within a cesarean scar defect is an exceedingly rare phenomenon, with only seven documented cases to date [2]. Notably, cesarean scar choriocarcinoma (CSC) often mimics cesarean scar pregnancy, frequently resulting in misdiagnosis [3]. This misclassification can lead to delayed treatment, ineffective interventions, or metastasis [2]. Consequently, early identification and prompt lesion removal constitute pivotal elements in CSC management. In this study, we provide insights into the diagnosis and therapeutic strategies employed in a case of CSC at the Imam Khomeini Hospital Complex in Tehran, Iran.

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Case Presentation

The case involves a 31-year-old woman with gravida 3, parity 2 (the first delivery was vaginal, and the second was a cesarean section), and one abortion. She presented to the Obstetrics and Gynecology Clinic in 2021 with complaints of amenorrhea and spotting. During her third pregnancy in 2019, she was diagnosed with a molar pregnancy within the cesarean scar at another center. Her beta-human chorionic gonadotropin (βhCG) level was 27112mIU/mL. Initially, she underwent hysteroscopic resection of pregnancy products, followed by four doses of methotrexate (MTX) due to persistently elevated βhCG levels. Subsequently, five doses of actinomycine D were administered in 2020, resulting in a notable reduction in βhCG levels. However, they did not reach a negative pregnancy status (< 5mIU/mL). Over the following months until three months before referral to our clinic, her βhCG levels fluctuated between 12-30mIU/mL (Fig. 1). Despite these elevated levels, the patient's management at the previous center was insufficient. Due to her preference to preserve fertility, a hysterectomy was not performed, and only close monitoring of βhCG level was conducted. During this time, she used condoms and oral contraceptives intermittently as her contraception method.

On December 4, 2021, the patient presented to our clinic with complaints of delayed menses and spotting. There was no available ultrasonographic data from her follow-up period at the previous center. During our initial evaluation, her βhCG level notably elevated to 3992mIU/mL. Furthermore, a transvaginal

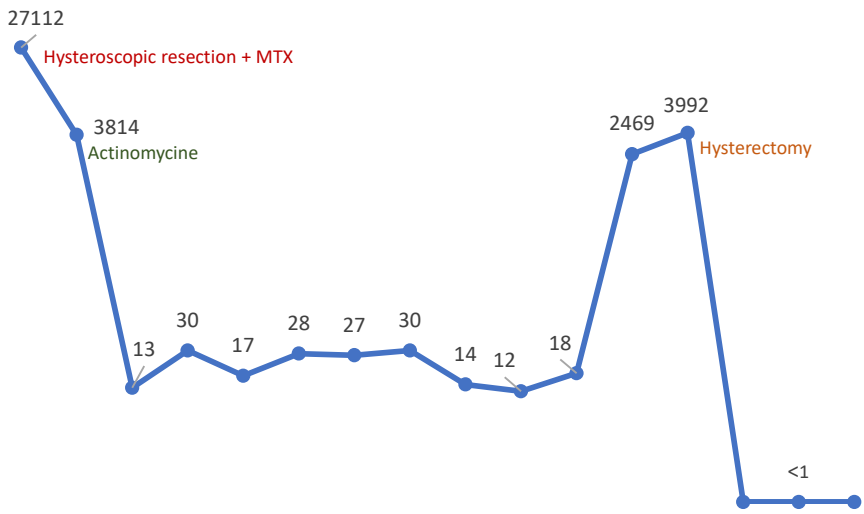


Fig 1. Dynamic changes of βhCG levels and administrated treatments from 2019.

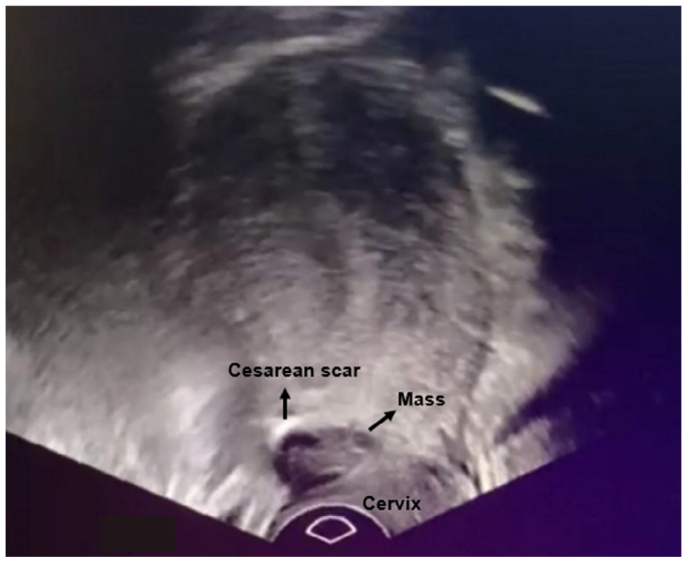
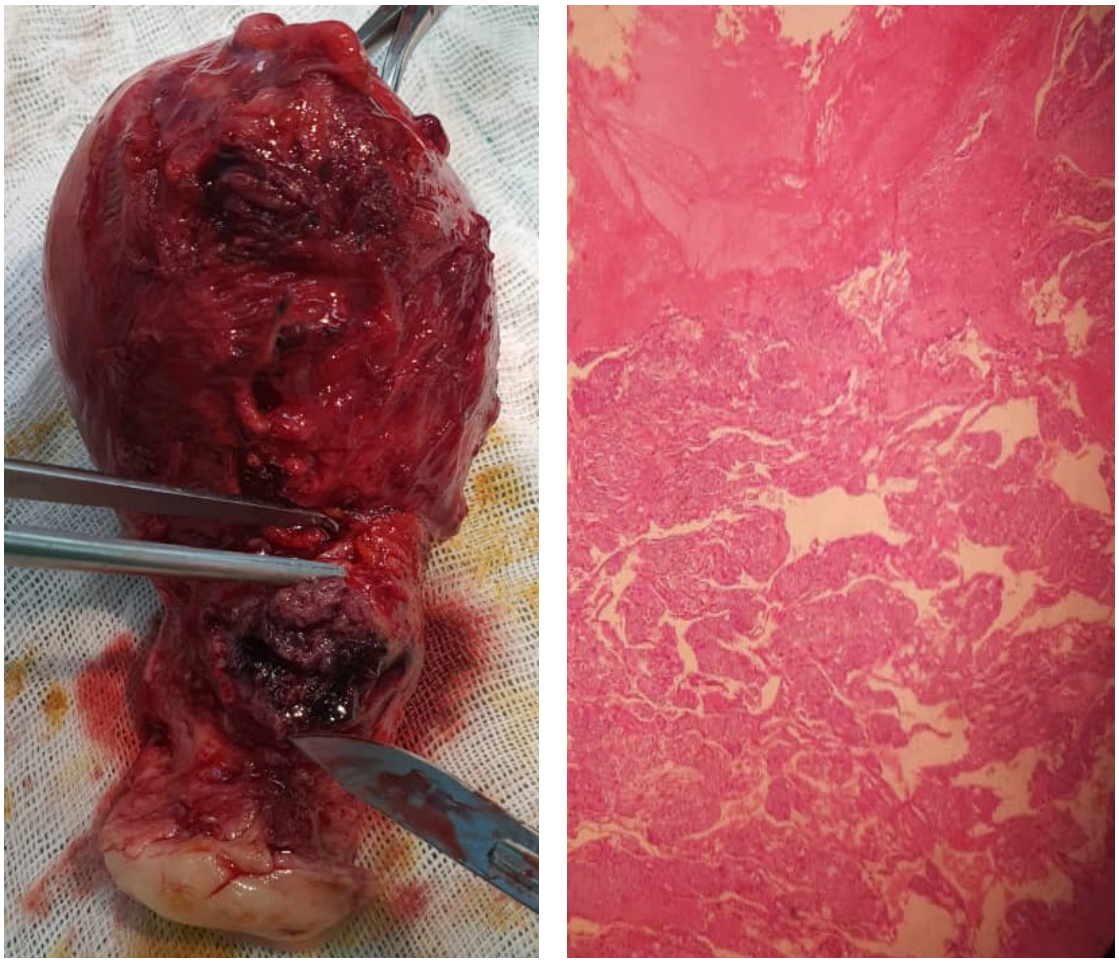


Fig 2. Transvaginal sonography demonstrated a round, heteroechoic, and hypervascular mass located on the cesarean section scar defect (isthmus).



(a) (b)

Fig 3. (a) The uterus isthmus contained a 2*1.5*1cm^3 mass at the right side of the cesarean scar defect, exhibiting both lymphovascular invasion and peripheral margin involvement, (b) Microscopic view of the specimen confirming the pathology of choriocarcinoma.

ultrasonographic examination revealed a 2.3*2.0cm^2 round, heteroechoic, and hypervascular ectothrix mass on the right side of the cesarean scar defect. This mass had also penetrated the myometrium (Fig. 2).

Considering the clinical, laboratory, and sonographic data, two primary differential diagnoses were considered: cesarean scar ectopic pregnancy and CSC. Due to the suspicion of CSC and the patient's preference to avoid further pregnancies, a total abdominal hysterectomy was performed. Specimens were subsequently submitted for histopathologic examination, which confirmed a 2.0*1.5*1.0cm^3 tumor within the isthmus of the anterior uterine wall, diagnosed as choriocarcinoma (Fig. 3). According to the histopathologic findings and metastatic workup (which revealed no metastasis), the patient was categorized as having FIGO (the International Federation of Gynecology & Obstetrics) stage I disease with a WHO prognostic score of 9, indicating a high-risk profile. Considering the tumor's FIGO stage and the absence of metastasis, adjuvant chemotherapy was not administered. Post-surgery, her βhCG levels decreased to < 1mIU/mL, and she remained symptom-free during follow-up visits until 2023 (Fig. 1).

Discussion

Gestational choriocarcinoma is a rare and malignant trophoblastic neoplasm, which can develop following any type of pregnancy (mostly hydatidiform mole) [4]. It presents a distinctive histological pattern of cytotrophoblast and syncytiotrophoblastic hyperplasia, often accompanied by necrosis and hemorrhage, in the absence of chorionic villi [4]. Due to its strong vascular affinity, it frequently disseminates hematogenously, leading to an elevated

risk of early distant metastasis and concurrent necrosis and hemorrhage in adjacent tissues [4]. While gestational choriocarcinomas predominantly originate within the uterine cavity, there have been occasional reports of their occurrence at cesarean scar sites [2]. Patients with CSC commonly present clinical symptoms resembling those of ectopic pregnancy, including amenorrhea, abnormal vaginal bleeding (e.g., spotting), and elevated serum βhCG levels [2]. Consequently, CSC without distant metastasis may be prone to misdiagnosis as a cesarean scar ectopic pregnancy.

Previous research underscores the significance of dynamically tracking serum βhCG levels in suspected CSC cases, as they commonly experience a rapid βhCG surge upon the onset of amenorrhea [2], mirroring our case. Given the rarity of CSC, established treatment protocols are lacking. Prior studies recommended that for cases suspected of CSC, an initial treatment approach involving MTX injection and surgical resection of the lesion through hysteroscopy or laparoscopy should be considered [2]. This approach is justified due to the elevated risk of metastasis and the potentially life-threatening bleeding associated with CSC [2]. Furthermore, the diagnostic surgery offers distinct advantages in managing suspected CSC cases, as it allows for histopathological examination of the lesion and the selection of the most suitable treatment strategy [2].

To date, there have been seven documented cases of CSC, all falling under FIGO stage I [2, 5-9]. Among these cases, four exhibited resistance to the initial single-agent chemotherapy treatment, characterized by sustained high levels of βhCG or the recurrence of symptoms [5, 7, 8]. In a case presented by Lin et al. in 2021, a patient with CSC showed sustained elevated βhCG levels following dilation and curettage and MTX treatment [7]. However, complete symptom remission and the normalization of βhCG levels were achieved after the administration of the EMA-CO regimen, which includes etoposide, MTX, actinomycine D, cyclophosphamide, and vincristine [7]. Similarly, in a case reported by Bakir et al. in 2021, a CSC patient had persistently high βhCG levels after dilation and curettage and MTX. After receiving eight cycles of EMA-CO, undergoing a hysterectomy, and two additional adjuvant EMA-CO cycles, the patient attained normal βhCG levels and maintained symptom remission for up to three months [5]. Additionally, Nasiri et al. presented a case of CSC in 2018 that demonstrated resistance to MTX monotherapy, leading to a hysterectomy, which significantly reduced the patient's βhCG levels [8]. However, the patient's βhCG levels remained elevated (30mIU/mL), and subsequently, a single-agent chemotherapy with actinomycine D was administered, resulting in the normalization of βhCG levels [8].

Nasiri et al. [2018] also detailed another case of chemoresistant CSC that received a treatment protocol similar to our case [8]. In this case, following the diagnosis of non-metastatic (FIGO stage I) CSC, the patient received four courses of actinomycin D, leading to normalized βhCG plasma levels [8]. Nonetheless, two weeks later, the patient experienced severe vaginal bleeding and underwent a hysterectomy, ultimately resolving her symptoms, with βhCG plasma levels remaining negative for pregnancy during follow-up visits extending up to eight months [8]. It is noteworthy that our presented case closely resembles the latter case from the Nasiri et al. [2018] study in which a hysterectomy was performed on a chemoresistant FIGO stage I CSC patient without the prescription of adjuvant chemotherapy, with monitoring primarily based on βhCG plasma level assessments. Over two subsequent years, βhCG levels remained below 1mIU/mL, with no signs of metastasis. This highlights the potential effectiveness of a hysterectomy followed by vigilant monitoring for the treatment of patients with FIGO stage I CSC and without further fertility desires.

The guidelines for the treatment of choriocarcinoma predominantly recommend a specific approach for patients based on their disease stage and grade [10]. Patients with non-metastatic lesions (FIGO stage I) or those with metastatic (FIGO stage II-III) low-grade lesions (WHO score < 7) are typically advised to undergo a single-agent sequential chemotherapy regimen, which includes the use of MTX followed by actinomycin D [7, 10, 11]. Furthermore, in instances where resistance to a single-agent chemotherapy regimen is encountered, the preferred treatment approach involves multi-agent therapy with EMA-CO [10]. Nevertheless, for patients with a FIGO stage I CSC and no fertility preservation desires, a hysterectomy may be considered as an option to reduce exposure to multiple courses of chemotherapeutic agents [10]. Moreover, there have been some cases with a chemoresistant non-metastatic high-risk (WHO score ≥ 7) choriocarcinoma that did not receive any adjuvant chemotherapy and displayed symptom-free status and normal βhCG levels following the hysterectomy [12, 13].

Considering this body of evidence and taking into account the patient's lack of desire for future pregnancy, in our case of chemoresistant CSC, we opted for a hysterectomy without the prescription of any adjuvant chemotherapy agents. This management

approach resulted in the normalization of the patient's βhCG levels, which remained stable throughout a 2-year follow-up period. These findings suggest that a hysterectomy may serve as a viable treatment option for patients with chemoresistant FIGO stage I CSC. However, in patients with more advanced FIGO stages (with the presence of genitourinary organ invasion or distant metastasis) or in patients with fertility desires, adjuvant multi-agent chemotherapy, especially EMA-CO, should be strongly considered.

Conclusion

Our findings suggest that surgical resection, in conjunction with thorough monitoring, may offer potential as a treatment approach for FIGO Stage I CSC. However, the necessity for more extensive studies persists to evaluate the suitability of diverse treatment methods for CSC across different FIGO stages.

Acknowledgements

None.

Ethical Considerations

Conflict of Interest Statement

The authors declare no conflict of interest.

Ethical Approval

We strictly adhered to the principles of the Declaration of Helsinki throughout the entire study process. Additionally, this study received approval from the Research and Ethics Committee of Tehran University of Medical Sciences.

Consent

Written and official consent for the publication of this case report was secured from both the patient and her family.

Data Availability Statement

Data sharing is not applicable to this article, as no datasets were generated or analyzed during the course of the study.

Role of Funding

None.

Submission Declaration

We confirm that this paper has not been published previously and is not under consideration for publication elsewhere, and if accepted, it will not be published elsewhere in the same form, in English or in any other language, including electronically without the written consent of the copyright-holder. Also, all of the authors have read the paper and approved the manuscript for the publication.

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