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Case report

Epithelioid trophoblastic tumor presenting as a Caesarean scar defect: A case report

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ABSTRACT

Background: Epithelioid trophoblastic tumor is a rare form of gestational trophoblastic neoplasia. We present the first known case of this rare malignancy presenting as a Caesarean scar defect.
Case: A patient with 3 prior Caesarean sections presented with vaginal bleeding 2 months following management of retained products of conception. Her hCG was negative. She underwent surgical repair of a Caesarean scar defect, and pathology was consistent with epithelioid trophoblastic tumor.
Conclusion: This case highlights the possibility of malignancy presenting to the general gynecologist as a Caesarean scar defect. The diagnosis of gestational trophoblastic neoplasia should always be considered in the differential diagnosis of a patient with postpartum vaginal bleeding. Limited evidence on fertility conserving treatment of epithelioid trophoblastic tumors does not seem favorable.

1. Introduction

Caesarean section is one of the most common surgeries performed worldwide, with rates ranging from 6% to 27% (Betran et al., 2016). Caesarean scar defect has been recognized as a potential complication of Caesarean section, which involves a myometrial discontinuity at the lower uterine segment or a wedge-shaped anechoic area on ultrasound (Tulandi and Cohen, 2016; Kremer et al., 2019). The prevalence has been reported as high as 24% to 70% on ultrasound in women with one or more prior Caesarean deliveries (Tulandi and Cohen, 2016). Most Caesarean scar defects are asymptomatic, but they can present with abnormal uterine bleeding, pelvic pain, and secondary infertility and are associated with obstetrical complications including placenta accreta, uterine rupture and Caesarean scar ectopic pregnancy (Kremer et al., 2019). Management options include medical and surgical management with hysteroscopic, laparoscopic, and abdominal approaches (Setubal et al., 2018).

Epithelioid trophoblastic tumor (ETT) is a rare form of gestational trophoblastic neoplasia (GTN). Since its first description in 1998, there have been approximately 110 reported cases (Frijstein et al., 2019). ETT arises from the intermediate trophoblasts, and most commonly presents in reproductive-aged women following pregnancy (Frijstein et al., 2019). The most common presenting symptom of ETT is abnormal uterine bleeding, however patients can also present with amenorrhea or symptoms from extra-uterine disease (Frijstein et al., 2019; Gadducci et al., 2019). We present a unique case of a patient with a Caesarean scar defect who was diagnosed with ETT, discuss the diagnostic challenges and review considerations for patients desiring future fertility.

2. Case

The patient is a 36 year old G5P3A2 with 3 prior Caesarean sections who had been followed for a spontaneous abortion with retained products of conception. Ultrasound demonstrated an intrauterine gestational sac in the lower uterine segment with an absent fetal pole. Follow up ultrasounds at 3 and 4 months continued to demonstrate a fluid collection in the uterus, and a beta human chorionic gonadotropin (hCG) was still mildly elevated at 10 IU/L. She underwent a suction dilation and curettage; the pathology of this specimen was consistent with retained products of conception with degenerative placental tissue.

Abbreviations: ETT, epithelioid trophoblastic tumor; GTN, gestational trophoblastic neoplasia; hCG, human chorionic gonadotropin; PSTT, placental site trophoblastic tumor.

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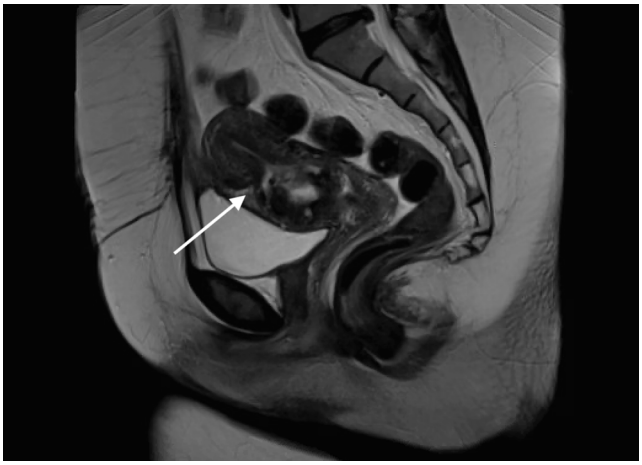

Fig. 1. MRI demonstrating 3.9 cm defect in myometrium with underlying heterogenous soft tissue mass (arrow).

The patient presented to the emergency department two months later with significant vaginal bleeding requiring transfusion. Ultrasound demonstrated a heterogenous mass in the endometrial canal and her hCG was < 5 IU/L. This was followed with an MRI which confirmed a heterogenous mass measuring 4.0 × 4.4 × 3.1 cm located within a 3.9 cm defect in the myometrium at the location of the Caesarean scar (Fig. 1).

The patient wished to pursue fertility conserving options. Her initial surgery was delayed by logistic factors and patient request. She underwent resection of the defect and re-approximation of the uterine wall 15 months after initial presentation. The pathology of this specimen was consistent with ETT with focal invasion into the smooth muscle (Fig. 2). Imaging was negative for signs of metastatic disease, and tumor markers including hCG were negative. She was referred to Gynecologic Oncology and underwent total abdominal hysterectomy and bilateral salpingectomy. Intra-operatively, the area of uterine scar appeared friable (Fig. 3A), and there was no metastatic disease seen outside the uterus. Pathology of the specimen was consistent with ETT FIGO stage II arising from the Caesarean scar (Fig. 3B). At 5 months, the patient has no evidence of disease and a negative hCG.

3. Discussion

To our knowledge, this represents the first reported case of an ETT presenting with a Caesarean scar defect. GTN has been described at the Caesarean scar, with case reports of choriocarcinoma and placental site trophoblastic tumor (PSTT) (Qian and Zhu, 2014; Nesiri, 2017). A retrospective review of patients with GTN found that 3.3% had GTN located in the Caesarean scar, most commonly invasive mole or choriocarcinoma (Wang et al., 2018). There was a high rate of misdiagnosis at initial presentation with 35% initially diagnosed as Caesarean ectopic pregnancy, incomplete abortion or retained products of conception (Wang et al., 2018). Additional case reports describe patients who presented after Caesarean section with cystic lesion on ultrasound; however, the authors of these reports describe a benign pathologic entity distinct from ETT (Zhou et al., 2015).

The diagnosis of ETT can be challenging, and the majority of patients have an interval of greater than 12 months from the antecedent pregnancy to the time of diagnosis (Frijstein et al., 2019). The type of pregnancy is most commonly a term gestation, followed by molar pregnancy and spontaneous abortion (Frijstein et al., 2019; Gadducci et al., 2019). hCG elevation is common, however it is often only mildly elevated and in some patients is normal, which can hinder diagnosis (Zhang et al., 2013). Significantly elevated hCG is more commonly seen with mixed ETT and other GTN, usually choriocarcinoma. For our patient, her initial hCG was greater than 144,000 IU/L but spontaneously decreased, consistent with pregnancy failure. Her hCG had been negative for more than a year prior to the diagnosis of ETT, which decreased suspicion of any concerning pathology. Imaging features have been described specific to ETT that can aid in diagnosis; on ultrasound ETT appears as a well-circumscribed mass with a hypoechoic halo (Gadducci et al., 2019). On pathology examination, ETT is described as monomorphic cells with a nodular well-circumscribed growth pattern. Immunohistochemistry of Cyclin E and p63 are useful to differentiate ETT from placental site trophoblastic tumor. Another common diagnostic challenge is differentiating ETT from squamous cell carcinoma of the cervix as ETT can frequently involve the cervix. However, ETT will be negative for p16, which should be positive in cervical cancer (Mao et al., 2006).

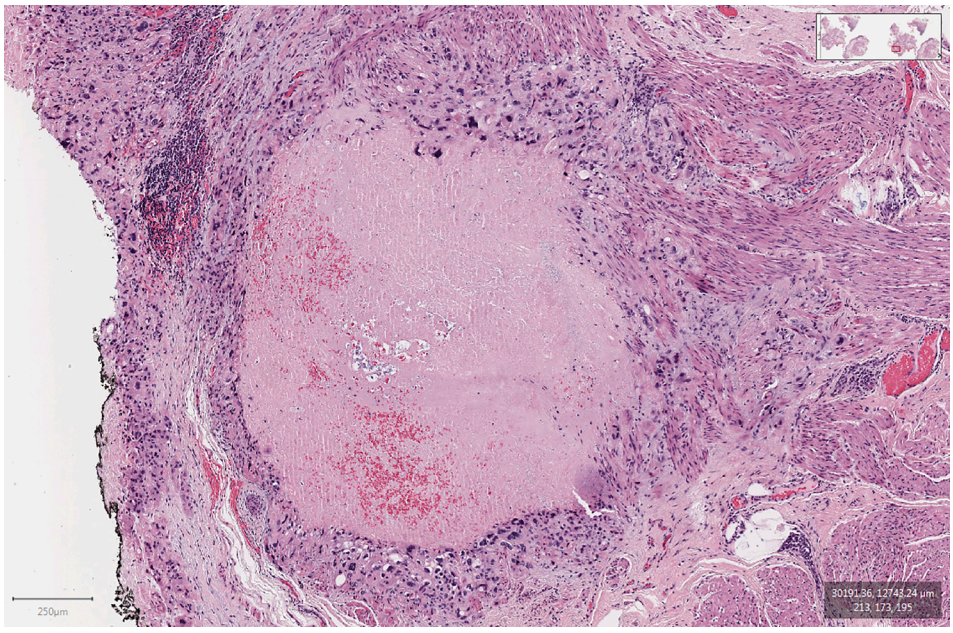

Fig. 2. Histology from Caesarean scar resection demonstrating atypical epithelioid cells, which are chorionic-type intermediate trophoblasts, palisading around fibrillar necrotic debris. Image from Dr. Adrian Sim.

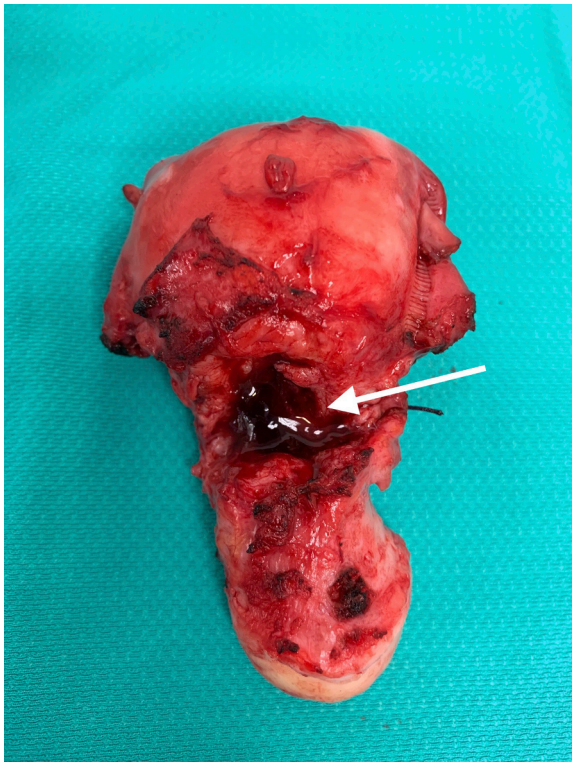

Fig. 3A. Hysterectomy gross specimen with defect in the lower uterine segment (arrow).

Since ETT is relatively nonresponsive to chemotherapy, surgery forms the mainstay of treatment, typically hysterectomy and excision of any extra-uterine disease (Frijstein et al., 2019). There is a wide variation of reported regimens for patients who do receive chemotherapy (Gadducci et al., 2019; Zhang et al., 2013). Poor prognostic factors include an interval of greater than 48 months since the antecedent pregnancy and FIGO stage II or greater. Adjuvant chemotherapy should be considered for patients with advanced stage or with incomplete surgical resection, however the optimal chemotherapy regimen or treatment duration remains unknown (Frijstein et al., 2019). There is limited available evidence to guide management of patients with ETT interested in fertility sparing treatment. Two case reports describe patients treated with fertility-sparing techniques, one with surgical resection of a posterior uterine mass (Tse et al., 2018), and one who had local resection with adjuvant chemotherapy of a mixed ETT and choriocarcinoma (Imamura et al., 2015). Conversely, Davis *et al.*, describe two patients who were treated with uterine-sparing techniques and developed disease recurrence or progression (Davis et al., 2015). Patients with ETT considering fertility conservation should be counselled that the published success rates are less than 50%, and this should not be considered standard of care.

4. Conclusion

This case adds to the literature on ETT and highlights the possibility of a patient with malignancy presenting to the general gynecologist for management of a Caesarean scar defect. Diagnosis of ETT can be difficult and GTN should always be considered in the differential diagnosis of a patient presenting with bleeding and an elevated hCG, especially following pregnancy. There is a paucity of literature on fertility conserving treatment of ETT, and available evidence does not seem favorable.

Consent statement

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

CRediT authorship contribution statement

Kristin A. Black: Conceptualization, Writing - original draft, Writing - review & editing. **Kristen Simone:** Conceptualization, Writing - original draft, Writing - review & editing. **Cassandra Hirt-Walsh:** Writing - original draft, Writing - review & editing. **Jeanelle Sabourin:** Supervision, Writing - original draft, Writing - review & editing.

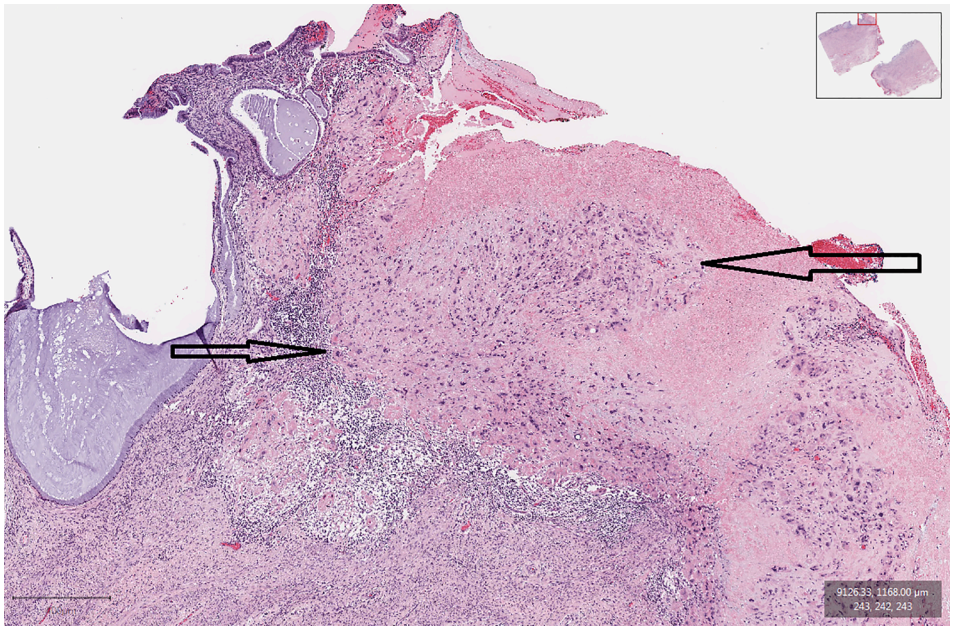

Fig. 3B. Histology of specimen demonstrating chorionic type intermediate trophoblasts (arrows) palisading around fibrillar necrotic debris, with adjacent endometrium. Image from Dr. Adrian Sim.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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