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Cesarean section scar choriocarcinoma, an unusual entity with ultrasound, MRI and pathologic correlation

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1. Introduction

Cesarean scar pregnancy (CSP) is an uncommon form of ectopic pregnancy, which is embedded in the myometrium of a prior cesarean scar. In this paper, the authors describe and examine a rare case of cesarean scar choriocarcinoma in a 52-year-old premenopausal female who presented to ER with heavy vaginal bleeding with blood clots. The patient's transvaginal ultrasound initially demonstrated a classic “snow storm” appearance within a cesarean section scar, suspicious for molar pregnancy and/or gestational trophoblastic disease (GTD). CT scan of the chest, abdomen and pelvis excluded any evidence of metastatic disease. MRI demonstrated a T2 heterogeneous mass at the level of the cesarean section scar, and post-contrast images showed a peripherally enhancing mass at the lower uterine segment wall at the level of the cesarean section scar, suspicious for “scar” molar pregnancy. The patient underwent laparoscopic hysterectomy and bilateral salpingectomy, and final pathology was consistent with uterine choriocarcinoma. This case is unique because it is one of the first reported cases of choriocarcinoma found within a cesarean section scar and the second overall case of cesarean scar GTD to be imaged by magnetic resonance imaging. By illustrating the imaging and pathologic confirmation of this rare entity, the authors hope to emphasize the importance of recognizing the range of differential diagnoses for extrauterine masses as well as when it is appropriate to suspect GTD in a cesarean section scar.

2. Clinical and laboratory assessment

A 52-year-old premenopausal female presented to the Emergency Department with complaint of vaginal bleeding for a total of twelve months. She had been experiencing heavy vaginal bleeding with passage of large blood clots associated with nausea and fatigue, which had progressed over the one month prior to her ER presentation. The patient's last menstrual period was 8 days prior to her ER visit. Past surgical history revealed a cesarean section 10 years prior and dilation and curettage following a failed intrauterine pregnancy 8 years prior. Social history revealed that the patient was married and a non-smoker. Physical examination demonstrated a 3 cm blue-purple bulge in the right lateral vaginal wall. A 20 cc dark red clot was evacuated from the vagina on speculum exam. On bimanual exam, the cervix was closed with an approximately 9-week-size, anteverted uterus. Laboratory assessment was significant for a positive urine β-hCG, with a quantitative β-hCG level of 453,839 mIU/mL.

3. Imaging assessment

Transabdominal and endovaginal ultrasounds were performed and demonstrated a heterogeneous mass with a classic “snow storm” appearance at the region of the patient's cesarean section scar, measuring 4.6 × 4.2 × 4.5 cm. The mass contained internal cystic areas with mild peripheral vascularity on Doppler imaging (Fig. 1a,b). Spectral Doppler investigation demonstrated low resistance arterial waveform (Fig. 2). These sonographic features suggested a mass that was highly suspicious for a molar pregnancy and/or gestational trophoblastic disease within the cesarean section scar. A “snow storm” appearance, which may also be referred to as “Swiss cheese” appearance on sonographic imaging or as “bunch of grapes” appearance on pathology, suggests the visualization of many large villi forming transparent vesicles of variable sizes. This was the primary suspected diagnosis given that there was no discernible intrauterine gestational sac or fetal parts found within the endometrial cavity or cervix. With a normal intrauterine pregnancy, β-hCG may be unusually elevated if there are multiple gestations.

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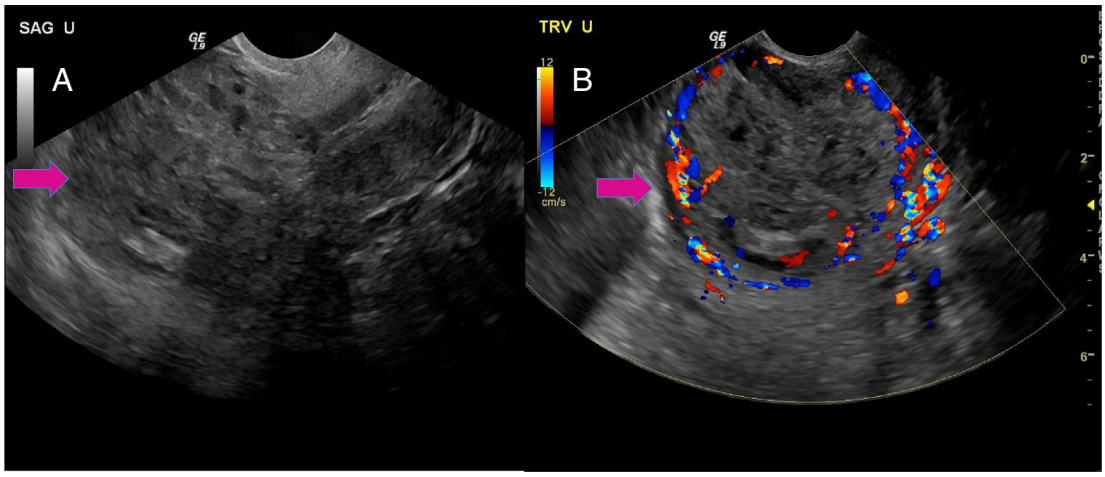

Fig. 1. Echogenic mass: Echogenic mass on transvaginal images demonstrates "snow storm" appearance suggestive of molar pregnancy at level of C-section scar of the uterus with peripheral vascularity on transvaginal gray scale in sagittal (A) and transvaginal transverse color images (B) (pink arrows). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

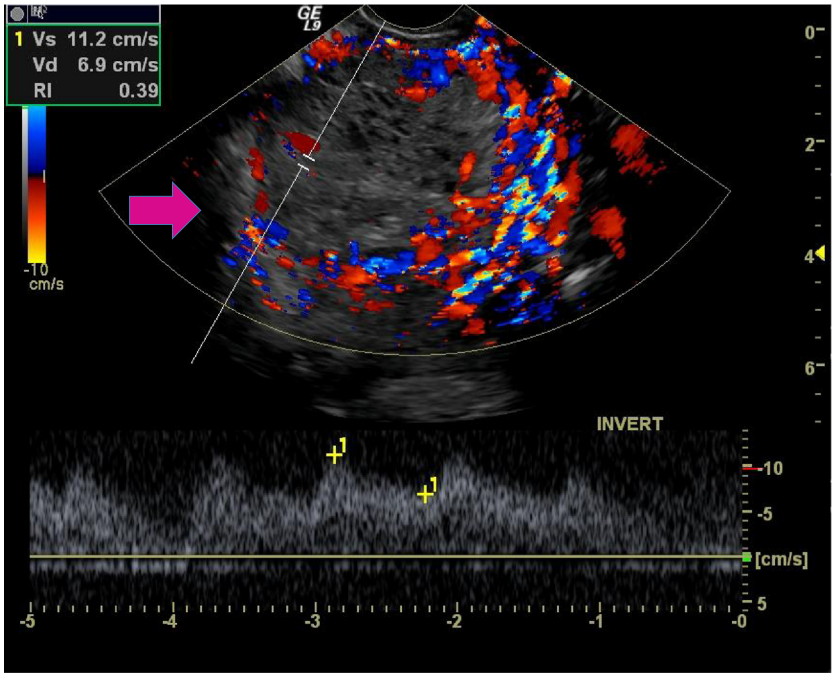

Fig. 2. Low resistance arterial wave form: Spectral Doppler image demonstrates low resistance arterial wave form at the level of the mass, which extends from the C-section scar to the endometrial stripe, demonstrating peripheral vascularity (pink arrow). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

However, normal pregnancies typically present with amenorrhea and an intrauterine gestational sac, yolk sac(s) and/or fetal pole(s) with cardiac activity readily identified on transvaginal ultrasound.

CT of the chest, abdomen and pelvis was performed with acquisition of sequential images from the chest to the pubic symphysis in order to evaluate for metastatic gestational trophoblastic neoplasm. Intravenous injection of 95 mL of Isovue 300 was administered for the examination. 30 mL of Omnipaque 300 was mixed with 1000 mL of water and administered orally. Tube current modulation, weight based voltage adjustment, and/or interactive reconstruction dose reduction techniques were employed. A 5.6 × 4.6 cm hypoenhancing mass was identified within the anterior lower uterine wall with heterogenenous peripheral enhancement, suspicious for molar pregnancy and/or gestational trophoblastic disease. There was no evidence of metastatic disease to the chest or abdomen. MRI was recommended for further characterization of the mass.

MRI of the abdomen/pelvis was completed in order to evaluate for myometrial invasion on a 1.5 Tesla GE magnet utilizing a two-channel torso phased array coil. The female pelvis MR imaging protocol consisted of axial respiratory triggered diffusion weighted images, axial and coronal T2 single shot images of the abdomen (with and without fat saturation), axial T1 in and out of phase images, axial and coronal T1 gradient echo images before and after intravenous administration of 7 mL of Gadobutrol (Gadavist, Bayer Healthineers) acquired in the portal venous and delayed phases, and axial and coronal subtraction images.

Single shot fat spin echo MR sequences demonstrated a T2 heterogeneous mass at the level of the cesarean section scar corresponding to the uterine mass seen on ultrasound and CT (Fig. 3a,b,c). T2 fat saturation revealed internal T2 hyperintensity within the mass (Fig. 4a,b). Post-contrast images demonstrated a normal uterus and endometrial stripe with a peripherally enhancing mass inferiorly at the lower uterine segment wall (Fig. 5a,b) measuring 5.0 × 5.0 × 5.0 cm at the level of the C-section scar, suspicious for "scar" molar pregnancy. Malignancy of trophoblastic origin could not be excluded based on imaging features.

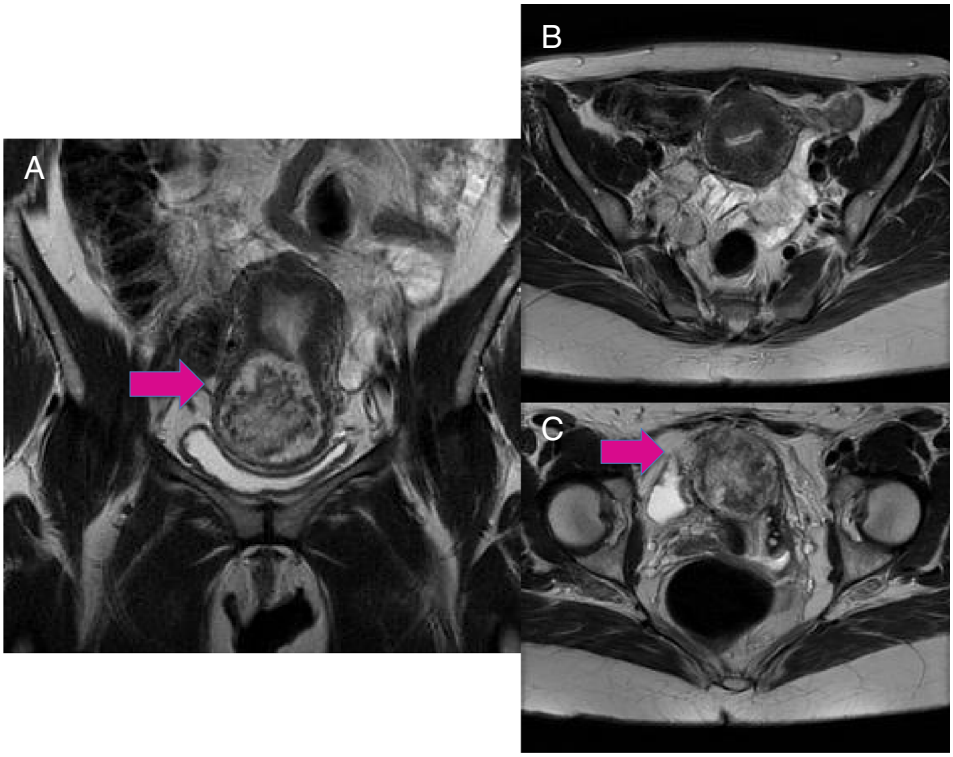

Fig. 3. Heterogeneous mass: SSFSE Coronal (A) and Axial images (B,C) demonstrate T2 heterogeneous mass at level of C-section scar (pink arrows). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

4. Pathologic assessment

3 days following diagnostic workup, the patient underwent uncomplicated laparoscopic hysterectomy and bilateral prophylactic salpingectomy performed by gynecologic oncology (Fig. 6a,b). Gross sectioning of the surgical specimen demonstrated a tan-red to yellow hemorrhagic lesion occupying the body of the uterine cavity measuring 4.5 cm in greatest dimension. The tumor was noted to abut but not penetrate the serosal surface, most prominent at the lower segment. Lymphovascular invasion was present with 90% myometrial invasion of a 1 cm. thick myometrium (Fig. 7a,b,c,d). The final pathology report was consistent with uterine choriocarcinoma with extensive hemorrhage and necrosis (Fig. 8a,b).

5. Discussion

Cesarean scar pregnancy (CSP) is an uncommon form of ectopic pregnancy, which is embedded in the myometrium of a prior cesarean scar. The incidence of CSP is approximately 1 in 2000 pregnancies and constitutes up to 6% of ectopic pregnancies among patients who have had a previous cesarean delivery [1–3]. The reported incidence of CSP is increasing recently though, due to the rising rates of cesarean delivery and increased awareness of the condition [4–6]. Gestational trophoblastic disease (GTD) within a cesarean scar, however, remains an exceedingly rare entity in clinical practice. To date, only 7 cases of cesarean scar GTD have been published in the literature [7–12].

GTD comprises 5 interrelated diseases that arise from placental

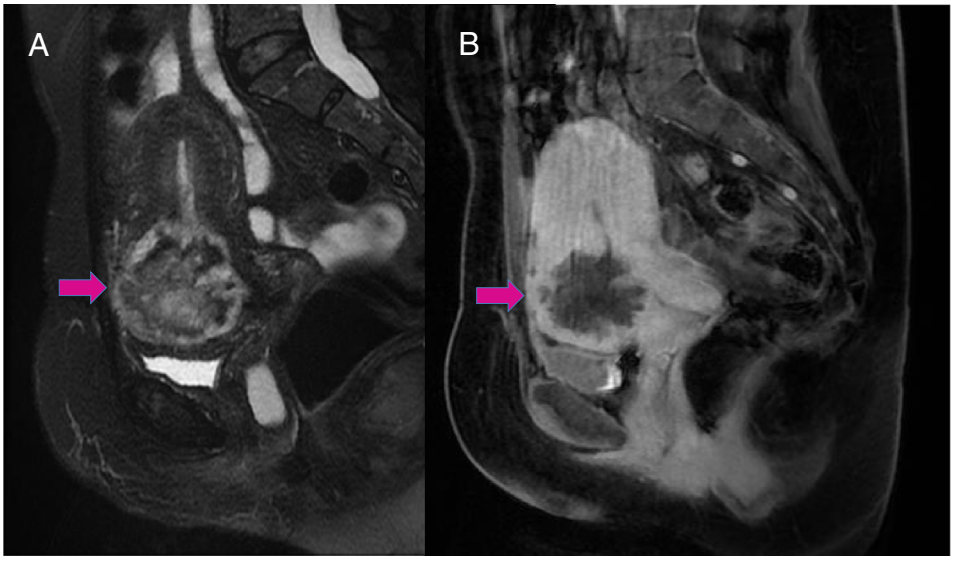

Fig. 4. Heterogeneous mass: T2 FS Sagittal sequence (A) demonstrates heterogenous mass at lower uterine segment with internal T2 hyperintensity at level of C-section scar (pink arrow). Corresponding Sagittal post contrast sequence (B) demonstrates peripherally enhancing centrally mass (pink arrow). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

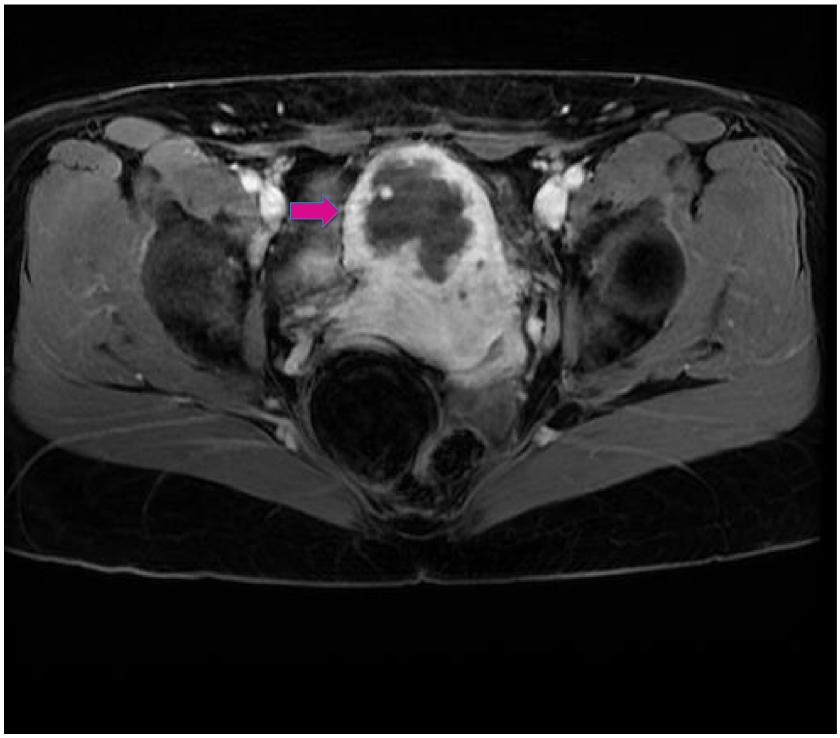

Fig. 5. Peripherally enhancing mass: Axial post contrast images demonstrate peripherally enhancing mass inferiorly at lower uterine segment (pink arrow). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

tissue with varying degrees of local tissue invasion and tendency to metastasize [13,14]. The first of these entities is a hydatidiform mole, which is further divided into complete hydatidiform mole and partial hydatidiform mole and vary in clinical presentation, prognosis, chromosomal pattern, and histopathology [15–17]. A hydatidiform mole is considered benign but, in all actuality, is premalignant to the other forms of GTD, which include invasive mole, choriocarcinoma, placental site trophoblastic tumor, and epithelioid trophoblastic tumor [18]. These later 4 categories of GTD comprise a group of pathologies that together are referred to as gestational trophoblastic neoplasia (GTN) and differ based on histology.

Choriocarcinoma is the most aggressive form of GTN, characteristically invading the myometrium and spreading hematogenously to the brain, lung, liver, spleen, kidneys, intestines, pelvis, and vagina [19]. Clinical presentation is usually secondary to bleeding from a metastatic site. The current case was unique in that the patient presented prior to metastasis. Choriocarcinoma can arise from any form of trophoblastic tissue, including intrauterine pregnancy, ectopic (extrauterine) pregnancy, failed intrauterine pregnancy or hydatidiform mole [20,21]. Extrauterine choriocarcinoma is exceedingly rare, especially within a cesarean section scar. Additionally, only 2–3% of molar pregnancies progress to choriocarcinoma [22].

Upon literature review, the previously reported cases of cesarean scar choriocarcinoma presented with findings and lab values not too dissimilar from the current patient's presentation, including lack of metastases [9,12]. Since choriocarcinoma is such a rare entity and usually presents due to symptoms from the sites of distant metastases, the diagnosis of choriocarcinoma was ultimately made at histological examination during all 3 cases.

The clinical presentation of GTD has changed significantly over the last several decades. GTD was previously diagnosed with late complications, such as excessive uterine size, hyperthyroidism, theca lutein cysts, preeclampsia, and anemia in molar pregnancy [23,24]. With increased availability of diagnostic measures, such as transvaginal ultrasound and β-hCG assays, the clinical presentation for GTD now often overlaps with that of early pregnancy. In addition to having an elevated

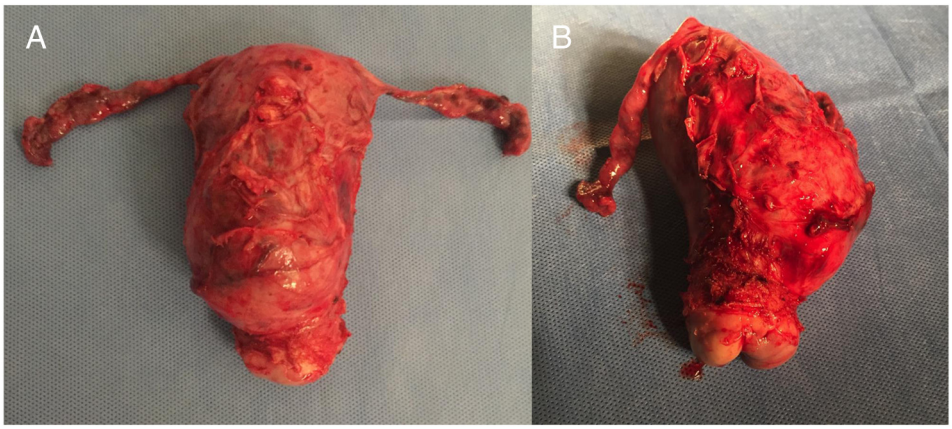

Fig. 6. TAH with BSO: Total abdominal hysterectomy and bilateral saplingo-oophorectomy specimen (A,B).

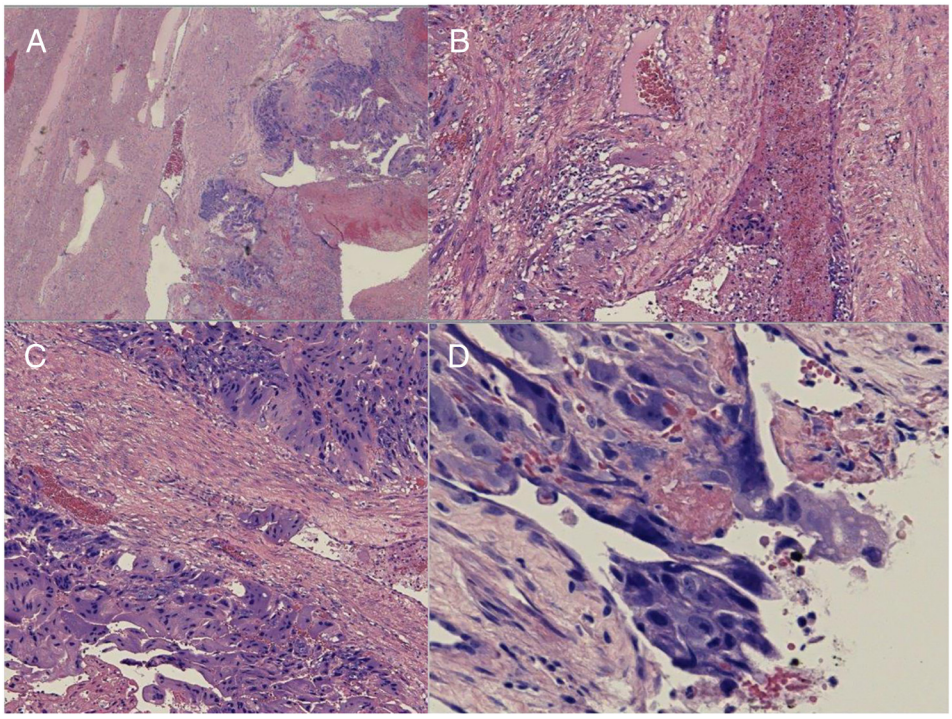

Fig. 7. Atypical trophoblasts and stromal and lymphovascular invasion.
(A) Low power view with scattered atypical trimorphic trophoblasts and associated stromal and lymphovascular invasion, fibrinoid necrosis and hemorrhage.
(B) High power view with fibrinoid necrosis and atypical trophoblasts invading the vessel and the stroma.
(C) High power view showing tumor thrombus with intravascular trophoblasts expressing marked cytological atypia.
(D) Very high power view showing lymphovascular invasion with trophoblast tumor thrombus showing cellular atypia.

β-hCG, women present with more common symptoms, including vaginal bleeding, pelvic pain, an enlarged uterus and hyperemesis gravidarum [10]. The patient in the current case presented with irregular vaginal bleeding, nausea, fatigue and an enlarged uterus. Most molar pregnancies are initially clinically diagnosed as a failed intrauterine pregnancy until pathologic evaluation is available [25].

Diagnostic workup in cases of suspected GTD includes a serum β-hCG, thyroid function test, liver function tests and a transvaginal ultrasound [26]. Chest imaging should also be performed to evaluate for lung metastases. Women with GTD typically present with elevated quantitative β-hCG, which varies in degree based on the form of GTD. A level > 100,000 m-international units/mL is particularly more common in invasive mole and choriocarcinoma. On transvaginal ultrasound, CSP typically presents with an empty uterus, empty cervical canal, a gestational sac in the anterior part of the uterus with a diminished myometrial layer between the bladder and the sac, and a discontinuity in the anterior wall of the uterus [27]. Additionally, on transvaginal ultrasound, GTD presents as a mass that enlarges the uterus with hypervascularity on color Doppler and a heterogenous appearance, which is likely secondary to areas of hemorrhage and necrosis. Tumor extension into the parametrium of the cervix may be seen as well. The patient's ultrasound revealed a heterogeneous mass with classic “snow storm” appearance in the region of the patient's cesarean section scar containing internal cystic areas with mild peripheral vascularity on Doppler imaging. Spectral Doppler demonstrated a low resistance arterial waveform. There was no discernible gestational sac or fetal parts found within the endometrial cavity or cervix.

GTD is distinguished by other conditions that also present with elevated β-hCG, including normal pregnancy, spontaneous abortion, ectopic pregnancy, and hCG-producing germ cell tumor base on several factors including its characteristic sonographic imaging appearance and histology. Of course, in order to suspect a CSP, a good obstetric history must be obtained to elicit the fact that the patient has undergone prior cesarean section. At pathology, trophoblastic cells help distinguish between GTD and nonmolar disease. In a spontaneous abortion, the chorionic villi degenerate and can form hydropic villi, however villi surrounded by trophoblast are characteristic for molar pregnancies. The hydropic villi appear as vesicles on ultrasound which may be a large fluid collection or part of a heterogeneous mass. The combination of vaginal bleeding, abnormally high β-hCG, and ultrasound showing an echogenic heterogeneous structure, with or without anechoic spaces, leads to a high clinical suspicion of a molar pregnancy. Moreover,

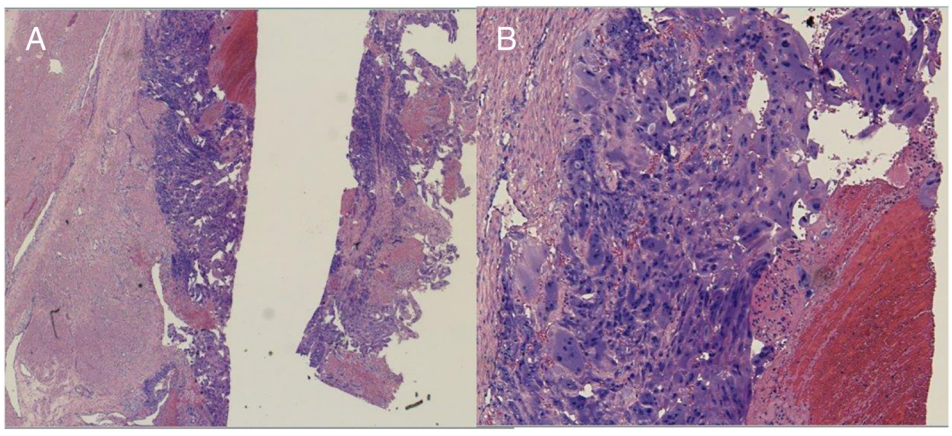

Fig. 8. Infiltrative tumor and cellular atypia.
A) Low-power photomicrograph shows diffusely infiltrative tumor with cohesive sheets of trimorphic trophoblasts and a zone of hemorrhage and necrosis. Tumor cells are invading the adjoining myometrial stroma.
(B) High power view showing the area of hemorrhage and necrosis surrounded by a few cytotrophoblasts with clear cytoplasm and multinucleated syncytio-trophoblasts with abundant eosinophilic cytoplasm and smudged nuclei. There is marked cellular atypia and numerous mitotic figures.

radiologists should routinely include GTD in the differential diagnosis for extrauterine masses, given the fact that this patient presented with choriocarcinoma 10 years after a cesarean section and 8 years after a failed pregnancy, much longer after the time one would expect GTD to present. Additional risk factors present in this case included increased maternal age > 35 years, an obstetric history of a prior cesarean section and failed pregnancy with D&C. There have been rare case reports of primary gestational choriocarcinoma in women who were postmenopausal at the time of the diagnosis. [30] Therefore, choriocarcinoma should be included in the differential in postmenopausal women with an elevated serum β-hCG. The diagnosis of the type of GTD is made by histologic evaluation of the trophoblastic tissue.

Traditionally the decision on whether to treat someone with gestational trophoblastic disease with chemotherapy following surgical resection is based primarily on a score calculated using the World Health Organization (WHO) Prognostic Scoring System. This system takes into account eight risk factors that have been shown to predict the potential for the development of resistance to single-agent chemotherapy. These factors include age, antecedent pregnancy, interval from last pregnancy, β-hCG level, tumor size, site of metastases, number of metastases, as well as prior exposure to chemotherapy. While it is accepted that women with metastatic or high-risk GTN (score ≥ 7) should be universally treated with multiagent chemotherapy, there is still debate regarding the most efficient approach to treatment of women with low-risk GTN (score < 7).

Though histologic diagnosis of choriocarcinoma is not included as a risk factor in the WHO scoring system, several studies have reported that a clinicopathologic diagnosis of choriocarcinoma alone is associated with increased resistance to first-line single-agent chemotherapy in patients with low-risk GTN and considered by many a poor prognostic factor [28,29]. At the same time, other studies suggest that there is a subset of patients with gestational choriocarcinoma who may avoid the toxicity of chemotherapy without compromising disease outcomes. One of the largest studies addressing this question used the data from five international trophoblastic disease centers. 36 patients were identified that had undergone complete excision of their histologically diagnosed choriocarcinoma, had normalized β-hCG without chemotherapy, and had > 6 months of follow-up. In this series, there were no relapses and no deaths attributable to disease. The authors of the study concluded that surveillance without chemotherapy may be a reasonable option in this highly selected subset of women diagnosed with gestational choriocarcinoma [31,32].

The patient opted for observation with serum β-hCG surveillance, witch normalized 11 weeks after the procedure.

6. Conclusion

Our rare case adds to the increasing awareness of the unique imaging features that lead to suspected CSP/GTD. This rare case of choriocarcinoma found within a cesarean section scar exemplifies the importance of understanding the spectrum of differential diagnoses for extrauterine masses and when to suspect GTD based on characteristic imaging features. Ultrasound is the initial diagnostic imaging test of choice. MRI provides additional tissue characterization, appropriate anatomic localization and helps determine the presence of myometrial invasion. Prompt surgical removal and confirmation by histology are instrumental in the appropriate management of these complicated cases.

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