Case Report

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Epithelioid Trophoblastic Tumour Masquerading as Ectopic Pregnancy in Uterine Caesarean Scar: A Case Report

Pathology Section

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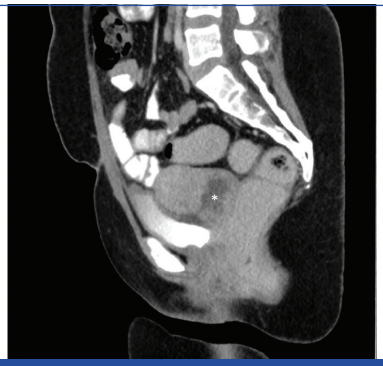
ABSTRACT

Gestational trophoblastic disease includes a spectrum of proliferative disorders ranging from non-neoplastic hydatidiform moles to malignant neoplastic conditions, each with phenotypic features of the different trophoblastic cells in the placenta. Epithelioid Trophoblastic Tumours (ETTs) are exceedingly rare, accounting for only 1-2% of all gestational trophoblastic neoplasms. Workup of persistent gestational trophoblastic disease requires serial measurement of Beta-human chorionic gonadotropin (β-hCG) along with imaging studies and monitoring of response to standard chemotherapy. Cases with atypical clinical features or chemoresistance should undergo tissue evaluation to exclude the rarer types of intermediate trophoblastic neoplasms. Diagnosis of ETT is challenging owing to the rarity of these tumours, long latency from antecedent gestation and significant histologic overlap with other more common gynaecological tumours. Awareness of these rare tumours with a high index of suspicion is crucial for accurate diagnosis. ETT needs to be distinguished from its mimics, including cervical squamous cell carcinoma and choriocarcinoma, as this has significant clinical and therapeutic implications. We present the case of a 37-year-old female with a prior history of caesarean delivery who presented with amenorrhoea and a positive urine pregnancy test. She was diagnosed as a case of caesarean scar ectopic pregnancy based on clinical and imaging findings. Later, excision of the scar ectopic was done, however β-hCG remained elevated. Medical management with methotrexate and standard chemotherapy for persistent gestational trophoblastic disease was unsuccessful, and the patient subsequently underwent hysterectomy due to persistent elevation of β-hCG and Contrast-Enhanced Computed Tomography (CECT) finding of a lower uterine segment mass lesion. Histopathological examination revealed an epithelioid trophoblastic tumour.

Keywords: Beta hCG, Caesarean section scar, Chemoresistance, Intermediate trophoblast, Lower uterine segment

CASE REPORT

A 37-year-old woman with a history of LSCS 12 years ago presented with a positive urine pregnancy test 10 days after a missed period. MRI was reported as an irregular gestational sac in the lower uterine segment with no viable foetal parts, suggestive of an ectopic pregnancy. Her β-hCG at diagnosis was 204 IU/mL (Normal: Less than 5 IU/mL in non-pregnant women). She was treated with two doses of systemic methotrexate followed by excision of the scar ectopic. Because of persistent elevation of β-hCG values (varying from 44-90 IU/mL), she was referred to the Gynaecologic Oncology department of our institution. With a clinical diagnosis of persistent gestational trophoblastic disease- WHO risk score 3, low risk, she was started on chemotherapy with three cycles of Actinomycin D followed by three cycles of Etoposide, Methotrexate, Actinomycin D, Cyclophosphamide and Vincristine (EMACO) regimen. However, β-hCG continued to be high (259 IU/mL). CECT showed a 3.5×2.1 cm endometrial mass lesion with myometrial invasion and severe thinning of the myometrium [Table/Fig-1]. She underwent a total abdominal hysterectomy and bilateral salpingectomy.

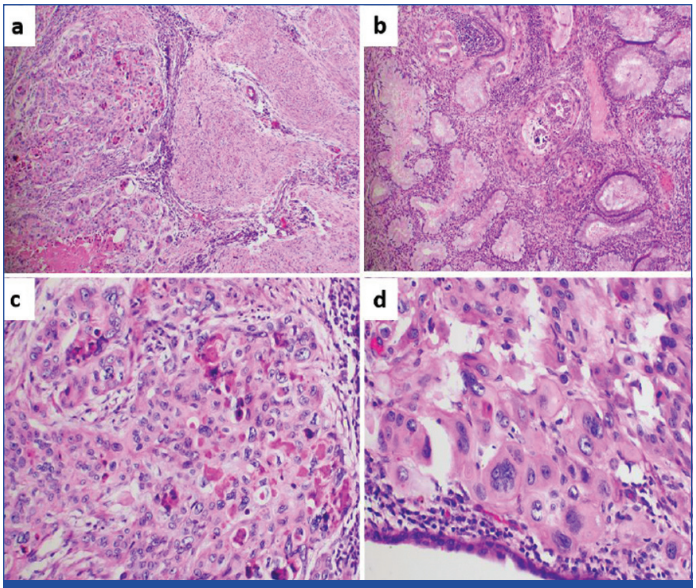


[Table/Fig-1]: CECT abdomen and pelvis axial image showing mass lesion in the lower uterine segment (asterix).

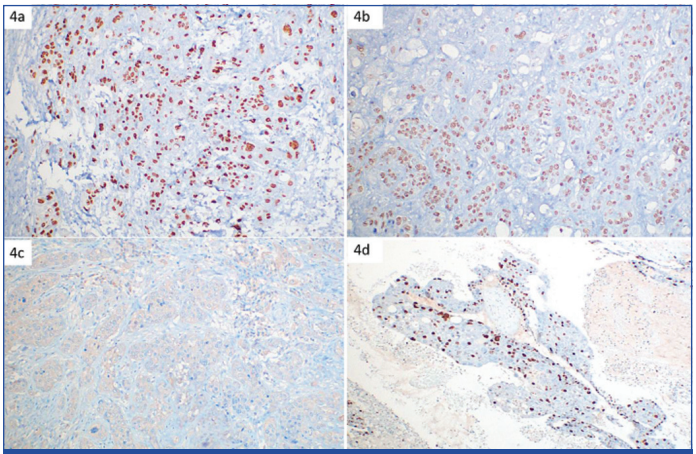
Grossly, the uterus showed a surface rent in the lower uterine segment and a 2.8×2.5×1.8 cm tan growth involving the lower uterine segment and cervix [Table/Fig-2].

[Table/Fig-2]: Gross image showing the homogenous solid tan mass (asterix) and the rent in the lower uterine segment.

Microscopy showed nodular proliferation of atypical epithelioid cells infiltrating the uterine myometrium with cells arranged as nests and cords. Cells were round to polygonal with moderate to abundant pale eosinophilic cytoplasm, moderate nuclear atypia, vesicular chromatin and a conspicuous nucleolus. Areas of necrosis, hyalinisation and extracellular keratin-like hyaline material were seen. The tumour was seen colonising the endocervical glandular epithelium in areas [Table/Fig-3]. On immunohistochemistry, the atypical cells were positive for GATA3 and p63 and negative for CK5/6. Ki-67 labelling index was 15 to 18% [Table/Fig-4]. A diagnosis of epithelioid trophoblastic tumour involving the caesarean scar was made. The slides of the initial biopsy reported outside as Aria Stella reaction, on review was consistent with epithelioid trophoblastic tumour.

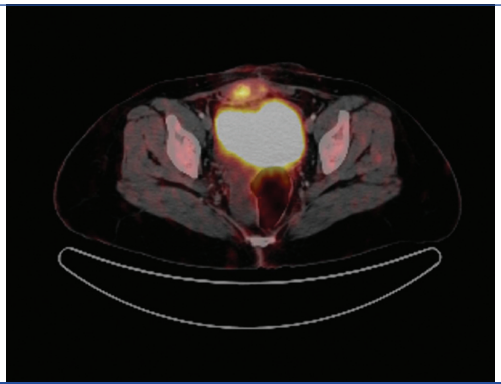


[Table/Fig-3]: (a) Nodules of atypical epithelioid cells infiltrating the myometrium (asterix) (H&E, 10x). (b) Tumour cells colonising endocervical glands mimicking a high-grade squamous intraepithelial lesion (H&E, 10x). (c) Squamoid appearance of the cells with extracellular eosinophilic hyaline-like material simulating keratin (H&E, 20x). (d) Mononuclear epithelioid cells with mild to moderate nuclear atypia and a few multinucleated tumour cells (H&E, 40x).



[Table/Fig 4]: (a,b) Tumour cells showing diffuse strong nuclear positivity with GATA3 and diffuse moderate nuclear positivity with p63, respectively (20x). (c) Tumour cells negative for CK5/6 (20x). (d) Ki-67 labelling index 16-18% (10x).

PET CT done 8 months after the surgery showed metabolically active deposits within the right rectus abdominis muscle [Table/Fig-5], external iliac lymph node and left upper lung. She received 5 cycles of TP/TE (Paclitaxel, Cisplatin/Paclitaxel, Etoposide). Post-chemotherapy cytoreductive surgery confirmed persistent ETT deposits in the bladder on histopathology and chemotherapy was continued with 6 cycles of EMA/EP (Etoposide, Methotrexate, Actinomycin D/Etoposide, Cisplatin) regimen. She has completed her chemotherapy and is currently under close follow-up with beta-hCG level monitoring. Her last beta-hCG was 2 IU/mL.



[Table/Fig-5]: PET CT showing FDG avid deposits in the rectus abdominis muscle (asterix).

DISCUSSION

First described by Shih and Kurman in 1998 as a gestational trophoblastic tumour distinct from Choriocarcinoma (CC) and Placental Site Trophoblastic Tumour (PSTT) simulating a carcinoma, ETTs are the rarest form of gestational trophoblastic tumours derived from neoplastic chorionic type intermediate trophoblast [1]. Most of the patients are women of reproductive age, but ETT can occur in post-menopausal women as well [2]. The most common symptom is vaginal bleeding, with only a few patients presenting with amenorrhoea as in the present case [3]. Serum β-hCG level is usually less than 2,500 IU/L and only rarely rises to more than 10,000 IU/L. The lower uterine segment is involved in approximately 40% of ETT cases [4]. However, the occurrence of ETT specifically within a prior caesarean scar is exceedingly rare, with only one case documented in the literature by Black KA et al., which reports ETT in a caesarean scar defect in a 36-year-old with three prior caesarean sections and a diagnosis of ETT made 4 months after a spontaneous abortion with retained products of conception [5].

The main histological differential diagnosis includes other gestational trophoblastic proliferations and neoplasms like Placental Site Nodule (PSN), Atypical Placental Site Nodule (APSN), PSTT, CC and cervical Squamous Cell Carcinoma (SCC). PSN is a microscopic, paucicellular and hyalinised lesion which represents nodular persistence of chorionic type intermediate trophoblasts with degenerative features [3]. APSN is a proposed precursor lesion for ETT with features intermediate between PSN and ETT. The current criteria for diagnosis are poorly defined and include larger nodule size (5-10 mm), increased cellularity, marked nuclear atypia, increased mitotic activity, and a Ki-67 proliferation index of 5-10%. Patients with APSN morphology on small biopsies should undergo imaging studies to rule out an underlying mass lesion and require clinical follow-up [6].

PSTT is another differential that shares similar clinical features with ETT. However, the neoplastic cells are larger, more pleomorphic, have characteristic vascular invasion and non-destructive splitting of individual myometrial fibres, unlike ETT, which has a pushing invasive front. Immunohistochemistry also assists in distinguishing the two. ETT is diffusely positive for p63, while PSTT is negative. hPL and MelCam is diffusely positive in PSTT, while the staining is patchy and weaker in ETT [2]. CC presents with a persistent marked elevation in serum and urine beta hCG, haemorrhagic and necrotic uterine mass and has a biphasic growth pattern with mononucleated and multinucleated trophoblastic cells exhibiting diffuse staining with SALL4 and β-hCG [7].

ETT is notorious for being misdiagnosed as cervical squamous cell carcinoma. Both tumours share epithelioid morphology, keratin-like hyaline material and p63 positivity. ETT can colonise the endocervical glands and mimic HSIL, adding to the diagnostic dilemma. The presence of keratin pearls, intercellular bridges, CK5/6 positivity and diffuse p16 positivity are useful features that favour SCC over ETT [8]. Short Tandem Repeat (STR) DNA genotyping to look for the presence of paternal allele is useful to confirm the gestational nature of the tumour in difficult cases, particularly those mimicking a poorly differentiated carcinoma at unusual sites [9]. Distinguishing ETT from its mimics has clinical and therapeutic implications. ETTs are chemo-resistant tumours, with surgery being the primary modality of treatment. Limited evidence on fertility conserving treatment of epithelioid trophoblastic tumours does not seem favourable [5]. Cervical squamous cell carcinoma is managed by hysterectomy or radiotherapy in early-stage disease and chemoradiation in advanced stages. The first-line treatment for choriocarcinoma is chemotherapy alone, which is sufficient to cure the majority of patients.

Metastasis occurs in 25-30% of cases and is usually haematogenous, the common sites being lung, liver, brain, ovary, vagina, spine, etc.

and patients die of disease in 10-24% of cases. ETT also has a higher propensity to spread to pelvic lymph nodes compared to other trophoblastic tumours. High mitotic count and an interval of > 4 years since antecedent pregnancy may portend a worse prognosis [10].

The cystic and gestational sac-like morphology of ETT on imaging, especially in the location of the LSCS scar, can closely mimic ectopic pregnancy, retained products of conception or haematoma, often leading to delay in diagnosis and patient management, as happened in our case. Doppler and MRI may help in challenging cases by assessing the accurate epicentre, margins, vascularity and depth of invasion of the lesion [11]. Histopathological examination remains the gold standard for diagnosis and distinguishing ETT from its mimics.

CONCLUSION

In our case, the clinical and initial imaging findings were suggestive of an ectopic pregnancy. However, the lesion's resistance to chemotherapy, coupled with persistently elevated β-hCG levels and a uterine mass lesion, prompted surgical intervention and histologic confirmation of ETT. This case report adds to the limited literature on ETT and highlights the importance of considering this tumour in the differential diagnosis of lower uterine segment masses in women with prior caesarean delivery.

Declaration: This case report was presented as a poster at the British Association of Gynecologic Pathologists (BAGP) 2024 Annual Meeting e-poster competition.

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