

# Atypical Postcesarean Epithelioid Trophoblastic Lesion with Cyst Formation: A Rare Case Report with Review of Literature

## Abstract

We report an extremely rare case of atypical epithelioid trophoblastic lesion arising from cesarean section scar in a 27-year-old woman with a history of undergoing cesarean delivery 2 years back. The patient presented with amenorrhea and increased frequency of micturition and negative urine pregnancy test. MRI was suggestive of a thin-walled exophytic hemorrhagic cyst arising from the anterior wall of lower uterine segment, communicating with the endometrial cavity. Cyst was excised and histology indicated a lesion consisting of epithelioid trophoblastic cells with an intermediate pattern between a classical placental site nodule and an epithelioid trophoblastic tumor. Immunohistochemistry revealed positivity for CK18, PLAP, and p63. Beta HCG was negative and Ki-67 index was 8%–10%.

**Keywords:** Cyst formation, epithelioid, intermediate trophoblastic cells, postcesarean delivery, uterus

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## Introduction

Gestational trophoblastic diseases arising from the previous cesarean scars are very rare. The entire spectrum of gestational trophoblastic diseases which includes ectopic pregnancy,<sup>[1]</sup> hydatidiform moles,<sup>[2]</sup> placental site nodule (PSN),<sup>[3]</sup> epithelioid trophoblastic tumors (ETT),<sup>[3]</sup> placental site trophoblastic tumors (PSTTs),<sup>[3]</sup> and choriocarcinoma<sup>[4]</sup> arising in the cesarean scar site has been reported. However, exceptionally rare cases of atypical postcesarean epithelioid trophoblastic lesion (APETL) with cyst formation have been reported in cesarean scar.<sup>[5-8]</sup> Atypical ETT was first described by Zhou *et al.*<sup>[7]</sup> in 2012 as a cystic lesion arising from cesarean scar. These lesions typically presented as a cystic mass arising from the serosal surface of the lower uterine segment from the cesarean scar and histologically revealed findings with an intermediate pattern between a classical PSN and an ETT. Nothing much has been described about this entity as only 6 cases have been reported so far. We report one such rare occurrence in a 27-year-old female who presented with amenorrhea. We also reviewed all the previously reported cases.

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Awareness regarding this entity is important to avoid misdiagnosis as malignant trophoblastic tumor.

## Case Report

A 27-year-old female presented with amenorrhea and increased frequency of micturition for the past 3 months. She had already done urine pregnancy test which was negative. She gave a history of undergoing lower segment cesarean section 2 years back. On USG pelvis, there was dehiscence of cesarean scar with hemorrhagic collection (10.3 cm × 7.6 cm × 4.6 cm) anterior to uterus and posterior to urinary bladder, communicating with endometrial cavity. MRI was suggestive of a thin-walled exophytic hemorrhagic cyst (10 cm × 6 cm × 4 cm) arising from the anterior wall of lower uterine segment, communicating with the endometrial cavity [Figure 1]. A preliminary diagnosis of cesarean scar defect (hematoma/dehiscence) was made, and the patient underwent exploratory laparotomy procedure and perioperatively, there was a smooth-walled cyst arising from the cesarean scar in the lower uterine segment communicating with the endometrial cavity and filled with chocolate-colored fluid. The cyst was excised and the defect in the lower uterine segment was closed in layers.

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The excised cyst was then sent for histopathological examination. On gross examination, the cyst measured 3 cm in diameter. The outer surface of the cyst was smooth, gray-brown. On cut opening, the cyst wall showed variably thickness (0.2–0.5 cm). The inner surface was smooth with focal tan-brown areas. Microscopic examination of sections from cyst wall showed implantation site trophoblast arranged in nests, cords, and isolated cells, infiltrating the fibromuscular wall of the cyst [Figure 2]. The cells were round to polygonal, moderate to markedly pleomorphic, with round/ovoid/multilobated nuclei, fine nuclear chromatin, one to multiple small nucleoli, frequent nuclear grooves/clefts, occasional intranuclear cytoplasmic inclusions, abundant light eosinophilic cytoplasm with distinct cytoplasmic borders [Figure 3]. The trophoblastic cells embedded in fibrin and occasional trophoblasts in the cyst wall had elongated/irregular hyperchromatic nuclei, inconspicuous nucleoli, and scanty to moderate amounts of eosinophilic cytoplasm. Focal areas of dystrophic calcification and lymphoid aggregates were also seen. Mitosis was absent and areas of necrosis/hemorrhage were not seen. There was no invasion of the surrounding endometrium and myometrium. Immunohistochemistry revealed positivity for CK18, PLAP [Figure 4], and p63. Beta HCG was negative and Ki-67 index was 8%–10%. Keeping in view the clinical, radiological, histological, and IHC findings, the lesion was diagnosed as APETL. The patient was advised a close careful follow-up along with serial serum hCG monitoring.

## Discussion

Four distinctive lesions can arise from intermediate trophoblast which includes exaggerated placental site, PSN, PSTT, and ETT. All these lesions can arise from previous cesarean scar.<sup>[3–8]</sup>

A morphologically distinctive lesion arising from intermediate trophoblasts known as “Atypical ETT” was

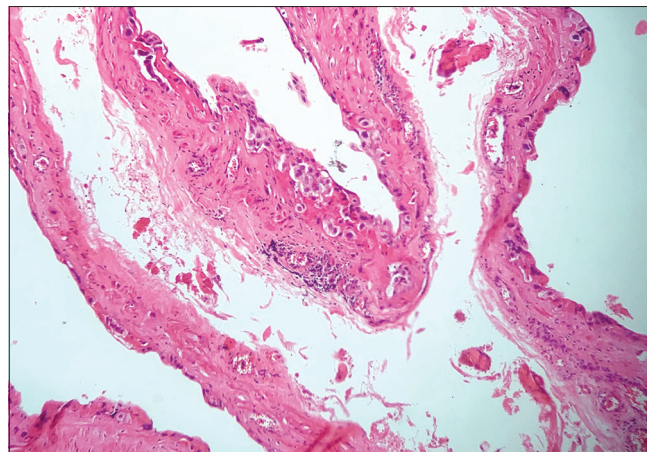
first described by Zhou *et al.*<sup>[7]</sup> in 2012 as a cystic lesion arising from cesarean scar. They described 2 cases both of which showed cystic lesions arising from cesarean scar. Microscopically, these cysts were lined with multiple layers of bland intermediate trophoblastic cells. These cells were not penetrating into the surrounding myometrium, endometrium, or blood vessels. However, there were occasional trophoblastic cells with large, hyperchromatic nuclei. Immunohistochemically, these trophoblastic cells were positive for p63 and negative for human placental lactogen. The Ki-67 indexes were 12.7% and 8.6%, respectively. They proposed to call them as atypical epithelioid trophoblastic lesions with cyst and fistula formation after a cesarean section.

After the initial description of 2 cases by Liang *et al.*, Zhou *et al.*<sup>[5]</sup> described an additional case 2015, in a 41-year-old Chinese women. They described it as a cystic lesion consisting of epithelioid trophoblastic cells with an intermediate pattern between classical PSN and an ETT. They also felt it appropriate to use the term “APETL with cyst formation” to describe this lesion.

In 2019, again Zhou *et al.*<sup>[6]</sup> reported a short series of 4 cases in which the age of the 4 patients ranged from 32 to 41 years, with a mean age of 36.5 years. Three of these patients underwent cystectomy and one underwent subtotal hysterectomy. All the lesions were well circumscribed and consisted of uniform cells of medium size, irregularly enlarged with hyperchromatic nuclei and 1–2 inconspicuous nucleoli embedded in abundant hyalinized matrix with fibrinoid material in the center. Immunohistochemically, these cells exhibited features of chorionic-type intermediate trophoblastic cells with positivity for CK18 and p63. On follow-up of 1–40 months, all of them were alive without recurrence. They concluded that atypical epithelioid trophoblastic lesion with cyst and fistula formation after cesarean section has unique histological features. However, their biological behavior and prognosis are still unclear.



**Figure 1:** MRI revealing thin-walled hemorrhagic cyst arising from the anterior wall of lower uterine segment



**Figure 2:** Cyst wall lined by and infiltrated by intermediate implantation site trophoblasts (H and E, ×10)

Clinicopathological features of all the 6 cases reported so far have been summarized in Table 1.

Our patient is the first patient among the reported cases to present with amenorrhea. Otherwise, this case had all the typical features of atypical ETT, i.e., history of previous cesarean section, cyst arising in lower uterine segment from cesarean scar, lining of cyst by epithelioid trophoblastic cells, and positivity for CK18, PLAP, and p63. In spite of amenorrhea, urine pregnancy test was negative, and serum beta HCG levels were low in our patient. Similar findings were noted in case reported by Zhou *et al.*<sup>[5]</sup>

PSN, PSTT, ETT, and choriocarcinoma should be excluded before making the diagnosis of AETL. PSNs are small lesions, vary in size from 1 to 14 mm, and usually appear as yellow, white, and necrotic appearing nodule in the endometrium or superficial myometrium and typically shows "immature (epithelioid) extravillous" type (p63+, CD146-) trophoblast usually distributed in the outer portion of nodule around a central hyalinized extracellular matrix with absent or rare mitotic figures. Although PSTT comprises tumor cells of similar morphology, they are

differentiated from APETL by large areas of necrosis, myometrial invasion, higher mitotic index, and diffuse positivity for hPL, MUC4, HSD3B1, CD146 (Mel-CAM), HLA-G. APETL is differentiated from ETT, by lack of extensive geographic necrosis, calcification, and myometrial invasion. Ki-67 index is also higher in ETT (>10%). Cyclin E is expressed in ETT and absent in APETL. Similarly, choriocarcinoma was also ruled out by lack of extensive area of hemorrhage/necrosis, biphasic pattern of cyto and syncytiotrophoblasts, and high mitotic index. Zhou *et al.*<sup>[8]</sup> suggest that as in atypical PSN, serum hCG monitoring after treatment is necessary. Our patient was advised careful follow-up with periodic serum HCG monitoring. The patient is showing normal serum HCG levels for 1 year after surgery, and the tumor has not shown recurrence till date.

In conclusion, atypical epithelioid trophoblastic lesion with cyst and fistula formation after cesarean section is unique trophoblastic lesion with distinct gross and histological features. Due to its rarity, only 6 cases have been reported so far. Its biological behavior and prognosis are still unclear and need more cases to be documented and followed.

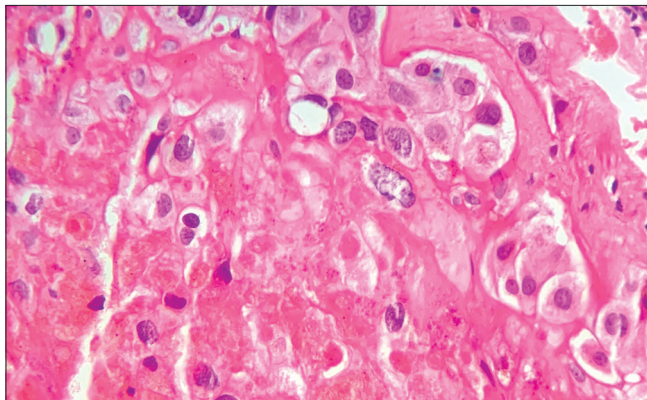


Figure 3: Higher magnification of intermediate implantation site trophoblasts embedded in fibrin (H and E, ×40)

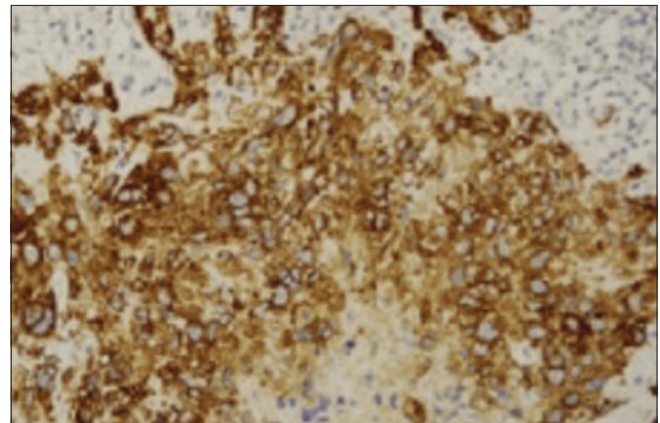


Figure 4: Tumor cells showing PLAP positivity (IHC, ×40)

**Table 1: Clinicopathological features of reported cases of Atypical postcesarean epithelioid trophoblastic lesion**

Case number	Year	Author	Age of patient	Presenting symptom	H/O previous cesarean section	Gross	Histopathology	IHC	Treatment
1	2012	Liang Y <i>et al.</i>	32	Vaginal bleeding	Present	Cyst and fistula	Atypical epithelioid trophoblastic lesion	p63 + hPL -ve	Cystectomy
2	2012	Liang Y <i>et al.</i>	41	Pelvic mass	Present	Cyst and fistula	Atypical epithelioid trophoblastic lesion	Not known	Cystectomy
3	2015	Zhou F <i>et al.</i>	41	Lower abdominal pain	Present	Cyst	Atypical epithelioid trophoblastic lesion	CK18+, p63+	Cystectomy
4	2018	Zhou F <i>et al.</i>	25	37-week gestation	Present	Solid	Atypical epithelioid trophoblastic lesion	CK18+, p63+	Cystectomy
5	2019	Zhou F <i>et al.</i>	32	Not known	Present	Cyst and fistula	Atypical epithelioid trophoblastic lesion	CK18+, p63+	Cystectomy
6	2019	Zhou F <i>et al.</i>	37	Not known	Present	Cyst and fistula	Atypical epithelioid trophoblastic lesion	CK18+, p63+	Subtotal hysterectomy
7	2020	Present case	20	Amenorrhea	Present	Cyst and fistula	Atypical epithelioid trophoblastic lesion	CK18+, p63+	Cystectomy

H/O: History of



### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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