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Case Report

Characteristics of Epithelioid Trophoblastic Tumor: Endoscopic and Magnetic Resonance Imaging Findings

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Abstract

Introduction: Epithelioid endothelial tumor (ETT) is an extremely rare tumor that typically occurs in women of reproductive age. The diagnosis tends to be delayed because it often necessitates a total hysterectomy. Therefore, it is important to understand ETT macroscopic and imaging findings. Here, we report a case of ETT with detailed macroscopic and imaging findings. ***Case Presentation:*** A 39-year-old woman with positive pregnancy test results was admitted to a nearby hospital. No gestational sac was found in the uterus, and magnetic resonance imaging (MRI) revealed a cystic mass of approximately 7 cm that extended continuously from the anterior wall of the lower uterine segment into the pelvic cavity. She underwent laparoscopic and hysteroscopic surgeries for a ruptured cervical pregnancy. Pathology of the specimens obtained from this surgery did not allow for the diagnosis of ETT. Two months after the surgery, as the serum human chorionic gonadotropin β subunit (β-HCG) level did not decrease, she was diagnosed with low-grade gestational trophoblastic neoplasia, leading to the administration of chemotherapy. After three regimens of chemotherapy over 9 months, her β-HCG level decreased but did not reach normal levels. Ultimately, a total hysterectomy was performed. The pathological diagnosis was mixed ETT and choriocarcinoma. A literature review revealed several cases similar to ours. ***Conclusion:*** ETT in the lower uterus often perforates the myometrium and forms cystic lesions in the retroperitoneal space or subserosa. The MRI and laparoscopic/hysteroscopic findings in this case may have contributed to the early diagnosis of ETT.

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Introduction

Epithelioid endothelial tumor (ETT) was first proposed as a new disease concept by Shih and Kurman in 1998 [1]. The definitive diagnosis and treatment of ETT usually require a total hysterectomy. However, ETT often occurs in women of childbearing age who often desire uterine preservation. Subsequently, the diagnosis and treatment of ETT are prone to be delayed [1–4]. Therefore, macroscopic and imaging findings of ETT are important for early diagnosis. However, given the rarity of ETT, constituting only 1–2% of trophoblastic diseases, there is limited reporting on endoscopic and imaging findings for ETT [5]. We report a case of ETT that required 9 months for diagnosis and discuss the endoscopic and magnetic resonance imaging (MRI) findings useful for the early diagnosis of this disease.

Case Report

A 39-year-old woman, gravida one, para one, consulted a local doctor, reporting a positive pregnancy test result. Her child had been born via normal vaginal delivery 7 years earlier. An ectopic pregnancy was suspected because no gestational sac was found in the uterus, and a cystic mass was present in the extrauterine space on transvaginal ultrasonography, leading to a closer investigation (shown in online suppl. Fig. 1; for all online suppl. material, see https://doi.org/10.1159/000539428). Serum human chorionic gonadotropin β subunit (β-HCG) level at the initial visit was 142.4 mIU/mL. MRI revealed a cystic mass measuring approximately 7 cm that extended continuously from the anterior wall of the lower uterine segment into the pelvic cavity. The mass showed subacute hemorrhagic contents, demonstrating high signal intensity on both T2-weighted images (T2WI) and T1-weighted images (T1WI) (shown in Fig. 1a–c). A provisional diagnosis of ruptured cervical pregnancy was made. Hysteroscopic and laparoscopic surgeries were performed to investigate and remove hemorrhagic masses. Intraoperative examination revealed a cystic mass containing old hemorrhagic material in the left paracervical retroperitoneal space (shown in Fig. 2a–c). Hysteroscopy revealed a fistula extending from the lower uterine cavity into the cystic mass (shown in Fig. 2d and online suppl. Fig. 2a, b). There were no abnormal findings in the bilateral adnexa except for a right para-tubal cyst. Suture closure of the fistula following removal of the cystic mass and para-tubal cyst was performed laparoscopically. Unfortunately, because the pathological tissue sample mainly contained necrotic tissue, hemorrhagic material, and decidua, an accurate pathological diagnosis could not be provided. Therefore, she was diagnosed with a ruptured cervical pregnancy which had occurred several days previously. On the 21st postoperative day (POD), the serum β-HCG level was 304.6 mIU/mL; the persistent gestational trophoblastic neoplasia (GTN) diagnosis was established. A single dose of methotrexate (80 mg intramuscularly once a week) was administrated for 8 weeks (shown in online suppl. Fig. 3). However, on 88th POD, the serum β-HCG was still as high as 119.8 mIU/mL. The patient then presented to our institution. At that time, MRI confirmed a 21 × 12 × 10 mm mass in the left myometrial portion of the lower uterus. On T2WI, the mass appeared as a slightly hyperintense lesion compared with the surrounding normal uterine myometrium (shown in online suppl. Fig. 4a). Contrast-enhanced computed tomography revealed no metastatic lesions. In measurements at our facility, her serum β-HCG level was 132.9 mIU/mL. According to The International Federation of Gynecology and Obstetrics (FIGO) scoring system, she was diagnosed with low-risk GTN. As the patient desired fertility-sparing treatment, chemotherapy with a single dose of actinomycin D was administered. Following chemotherapy, the serum β-HCG level decreased to 6.7 mIU/mL, but it re-elevated to 21.7 mIU/mL. Therefore, in accordance with treatment for high-risk GTN, a methotrexate-etoposide-actinomycin D (MEA)

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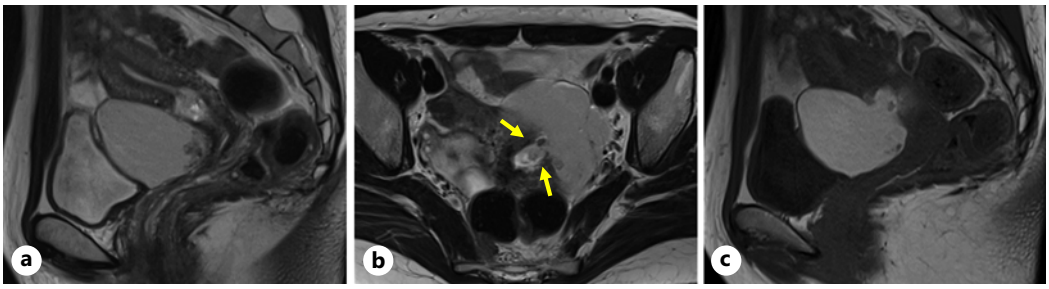

Fig. 1. MRI findings. **a**, **b** T2-weighted images. **c** T1-weighted images. The cystic mass, measuring approximately 7 cm, extended continuously from the anterior wall of the lower uterine segment into the pelvic cavity (yellow arrows).

regimen was administered [6]. After three courses of the MEA regimen, the β-HCG level decreased to 4.9 mIU/mL but remained outside the normal range (normal, <0.5 mIU/mL). In addition, MRI showed a residual mass with a hematoma on the left side of the lower uterus (shown in online suppl. Fig. 4b). Finally, the patient agreed to undergo uterus removal, and a total hysterectomy with left parametrial excision and bilateral salpingectomy was performed. Intraoperative findings included a mass containing a hematoma contiguous with the lower uterine myometrium. The postoperative course was uneventful, and the patient was discharged on the 12th POD.

Pathologically, dark red, mottled lesions involving the entire thickness of the myometrium were observed in the lower uterine segment, in continuity with cystic lesions protruding from the uterine serosa (shown in Fig. 3a). In this lesion, medium-sized tumor cells with distinct nucleoli and round nuclei proliferated and formed sheets and nests with geographical necrosis. Immunohistochemically, the tumor cells were negative for β-HCG, MUC4, and placental alkaline phosphatase, and positive for cytokeratin AE1/AE3, p40, and p63. A diagnosis of ETT was made based on these findings (shown in Fig. 3b, c). In contrast, HCG-positive multinucleated large cells were sporadically intermingled with ETT cells, and the Ki67 labeling index of the tumor cells was as high as 70%. These findings suggest the coexistence of choriocarcinoma. The final pathological diagnosis was mixed ETT and choriocarcinoma. The choriocarcinoma portion was negligible, with ETT accounting for most of the tumor. The patient's postoperative serum β-HCG level was 0.3 mIU/mL. She then received three courses of chemotherapy with the MEA regimen. Thereafter, the serum β-HCG level has been maintained within the normal range for 23 months after surgery, and there was no clinical evidence of recurrence until now. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material.

Discussion

The following two points are important for the early diagnosis of ETT. First, an ETT located in the lower uterus (lower uterine segment/uterine cervix) often perforates the myometrium and forms a cystic lesion in the retroperitoneal space or subserosa; laparoscopy with hysteroscopy is a useful examination to confirm these findings. Second, because the contents are necrotic tissue and subacute hemorrhagic material, the cystic lesion exhibits a high signal both in the T2WI and T1WI on MRI.

Unlike other trophoblastic tumors that typically grow in the uterine corpus, ETT is commonly found in the lower uterus. More than 30% and approximately half of ETTs are reported to occur in the uterine cervix and lower uterus, respectively [7]. However, only a few

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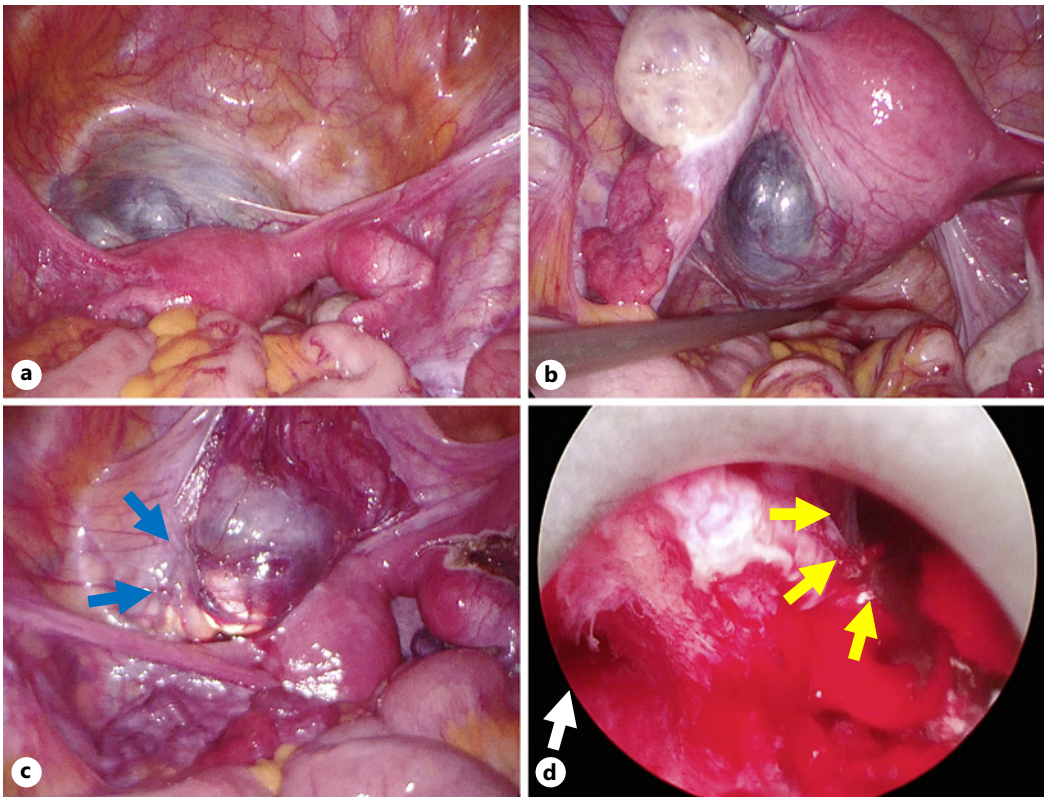

Fig. 2. Laparoscopic (**a–c**) and hysteroscopic (**d**) findings. Cystic mass containing old hemorrhagic material was observed growing in the left paracervical retroperitoneal space. The light from the hysteroscope could be observed from the abdominal cavity (blue arrow). Cervical cavity (white arrow). A fistula from the cervical cavity into a cystic mass (yellow arrows).

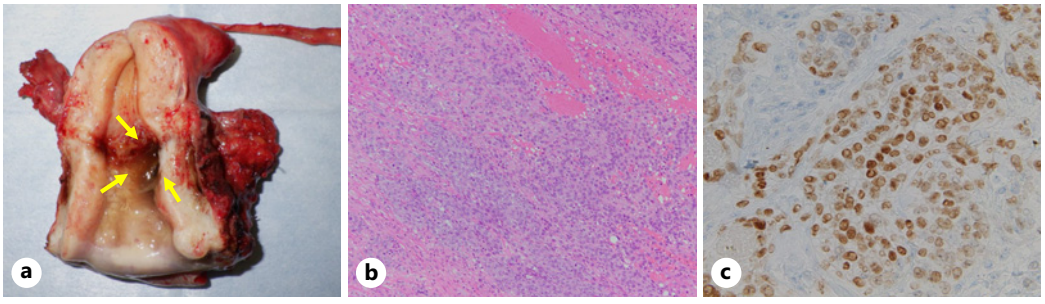

Fig. 3. a Macroscopic findings of the resected specimen. Dark red mottled lesions involving the entire thickness of the myometrium and fistula to a cystic mass were observed (yellow arrows). **b** Hematoxylin and eosin staining showed medium-sized tumor cells with distinct nucleoli and round nuclei proliferated, forming sheets, and nests with geographic necrosis. **c** Immunohistochemical staining for p63. The tumor cells were positive for p63.

studies have included detailed imaging findings. As far as ETT in the lower uterus is concerned, only three clinical reports have provided detailed imaging findings [8–10]. In two of the three cases, the ETT displayed an intramural lower uterine mass with a cystic lesion expanding to the retroperitoneal space or subserosa. The two cases reported by Kageyama

et al. [8] and Noh et al. had findings similar to those of the present case [7, 8]. Interestingly, there have been no reports of ETTs in the uterine corpus penetrating the uterine myometrium and expanding into the subserosa.

This case report provides detailed hysteroscopic and laparoscopic findings. Hysteroscopy revealed trafficking from the lower uterine cavity to the retroperitoneal space and necrotic tissue around the passage. This finding reflects that the ETT contains a large amount of necrotic tissue. On the other hand, the ETT was observed as a cystic lesion containing hemorrhage in the subserosa on the laparoscopic view of the abdominal cavity. This finding may reflect the natural history of the ETT, characterized by a gradual increase accompanied by necrosis and hemorrhage. As there are few reports of detailed hysteroscopic and laparoscopic findings of ETT, these findings would be valuable to aid in diagnosis. Penetration through the myometrium and extension into the subserosa or retroperitoneal space may be typical findings of an ETT in the lower uterus.

MRI findings of ETT located in the lower uterus are also important. In the present case, T2-weighted MRI images showed an infiltrative cystic mass with higher signal intensity than the surrounding normal muscle layer in the lower uterus. These MRI findings are consistent in that the ETT consists of two parts: a substantial tumor within the uterine muscle layer and a cystic lesion extending to the subserosa. The former is hypovascular and has a slightly higher signal intensity than the surrounding muscle layer on T2WI. The cystic lesion demonstrating high signal intensity in both the T2WI and T1WI indicated hemorrhage in the acute phase. The slightly solid components found dorsally within the cystic lesion appeared to be a mixture of necrotic tissue and old hemorrhagic material. These MRI findings resemble blood clots on the wall of an ovarian endometrial cyst. However, the presence of a slightly higher signal on T2WI of the solid part in the present case may reflect the characteristic findings of ETT, in which necrosis is concomitant. These MRI findings are similar to the two cases reported by Kageyama et al. and Noh et al. [8, 9]. In contrast, in a case of an ETT located in the lower uterus reported by Kara et al. [10], MRI showed no invasive masses or cystic lesions. Therefore, detecting ETT on MRI was challenging. This may be because, in this case, the fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography scan revealed early ETT. However, similar findings in 3 of the 4 cases may be interpreted as characteristic MRI findings of ETT in the lower uterus. This case contained a choriocarcinoma component; however, most of the lesion was ETT. Therefore, this case is considered to have shown imaging features of ETT.

In this case, an initial diagnosis of low-grade GTN arising from a ruptured cervical pregnancy was made. Indeed, GTN can arise from any pregnancy event [11]; however, it typically occurs after a molar pregnancy. The initial pathology did not show chorionic villi or a hydatidiform mole; therefore, a differential diagnosis of ETT should have been considered at this point. However, ETT was only identified on the final pathology post-hysterectomy. The imaging and laparoscopic findings presented in this article could aid in the early diagnosis of similar cases.

In conclusion, ETT is an extremely rare disease that is difficult to diagnose before a total hysterectomy. However, ETT in the lower uterus often forms cystic lesions containing necrotic tissue and hemorrhage in the retroperitoneal space or subserosa with an intramural mass. The MRI, hysteroscopy, and laparoscopy findings in the present case may contribute to the early diagnosis of ETT.

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Statement of Ethics

This study has been granted an exemption from requiring ethics approval by the Shiga University of Medical Science Research Ethics Committee. This retrospective review of patient data did not require ethical approval in accordance with national guidelines. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

D.I. and T.A. contributed to the design and drafting of this work. H.T. and S.T. contributed to the acquisition of data for this work. M.U. and T.M. reviewed important intellectual content.

Data Availability Statement

All data generated or analyzed during this study are included in the article and its online supplementary material files. Further inquiries can be directed to the corresponding author.

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