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Case Report

A Case of Placental Implantation with Exaggerated Placental Site

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Abstract

Objective: This study aims to investigate the clinical symptoms, diagnosis, differential diagnosis, and prognosis of exaggerated placental site (EPS), in order to reduce misdiagnosis and missed diagnosis of EPS, avoid the occurrence of serious complications such as massive hemorrhage, and provide some references for clinical doctors. Methods: Retrospective analysis of the medical history and treatment of a patient with placental implantation with exaggerated placental site. A 23-year-old female presented with persistent vaginal bleeding after medical abortion. She was diagnosed with retained products of conception and underwent hysteroscopic surgery. The preliminary postoperative pathological results indicate the possibility of EPS and placental site trophoblastic tumor (PSTT). Further immunohistochemical testing was performed, and the results suggested EPS. Results: The patient recovered well after surgery and did not require further treatment. Her serum human chorionic gonadotropin levels and transvaginal ultrasound findings were normal. Conclusion: EPS is a benign disease, and symptoms will disappear after lesion clearance, requiring no special treatment or follow-up, with a good prognosis. Due to the low incidence rate, atypical clinical symptoms, and insufficient recognition by clinical doctors, EPS are prone to misdiagnosis and missed diagnosis, leading to serious consequences such as massive hemorrhage and hysterectomy. EPS should be considered as a possible diagnosis in any woman who has irregular bleeding following medical abortion.

Keywords

Exaggerated Placental Site, Placental Implantation, Placental Site Trophoblastic Tumor

1. Introduction

Exaggerated Placental Site (EPS) is a benign lesion characterized by excessive proliferation of intermediate trophoblastic cells in the implantation site of the placenta associated with pregnancy. It can occur after normal delivery or miscarriage, with the main clinical manifestation being irregular vaginal bleeding. Due to its low incidence and atypical clinical symptoms, clinicians have insufficient awareness of EPS, which can easily lead to misdiagnosis. There have been no reported cases of placental implantation with exaggerated placental site reaction domestically or internationally. Here we report a case of placental implantation with exaggerated placental site reaction in a patient treated at the First Affiliated Hospital of Jinan University, aiming to increase awareness of this condition among clinicians.

2. Case Reports

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A 23-year-old female patient presented to our hospital on October 30, 2023, with continued vaginal bleeding for 21 days following a medication-induced abortion. She had a history of 2 pregnancies, with one surgical abortion and one medication-induced abortion. She had no past medical history, no additional past surgical history and no family history of malignancy.

The patient underwent medication-induced abortion with mifepristone combined with misoprostol at the Third Affiliated Hospital of Southern Medical University on October 9, 2023, due to "7 weeks of intrauterine pregnancy and voluntary request for abortion." Following the abortion, the patient experienced continued slight vaginal bleeding without fever, abdominal pain, nausea, vomiting, urinary frequency, urgency, or dysuria. Despite treatment with oral Drospirenone and Ethinylestradiol Tablets (II), the bleeding did not stop. A transvaginal ultrasound on October 25, 2023, revealed an irregular echogenic area measuring 32×17mm within the uterine cavity, with unclear boundaries and multiple color Doppler signals. An electrocardiogram and chest X-ray showed no abnormalities. The diagnosis of retained products of conception was considered. Consequently, a hysteroscopic surgery was performed on October 30, 2023, revealing remnants of pregnancy tissue and partial placental implantation on the anterior wall and fundus of the uterus, with remnants measuring approximately 3×4cm. Pathological examination post-surgery showed a small amount of proliferative endometrium, decidualized endometrium, degenerated necrotic decidual tissue, and chorionic villi, as well as small pieces of smooth muscle tissue with scattered infiltrates of nourishing cells, rich cytoplasm, nuclear atypia, rare mitotic figures, and suspected excessive placental site reaction (EPS) and placental site trophoblastic tumor (PSTT), warranting immunohistochemical testing. An additional immunohistochemical report on November 10, 2023, showed P-CK (+), P63 (-), a-inhibin (partially +), HCG (scattered +), Ki67 approximately 2% (+), and SMA (smooth muscle +), leading to the diagnosis of Exaggerated Placental Site (ESP). The patient was discharged on the first day post-surgery, followed up regularly with no discomfort, and a repeat transvaginal ultrasound showed no abnormalities, with serum human chorionic gonadotropin (HCG) levels within normal range.

3. Discussion

Gestational trophoblastic disease (GTD) covers a spectrum of disorders, which includes hydatidiform molar pregnancies, and neoplastic and neoplastic tumor like lesions arising from trophoblasts [1]. Gestational trophoblastic neoplasia (GTN) includes three well-defined pathological entities: choriocarcinoma, placental site trophoblastic tumor (PSTT) and epithelioid placental site nodule (ETT) [2]. Exaggerated Placental Site (EPS) is a benign lesion characterized by non-neoplastic proliferation of intermediate trophoblastic cells in the implantation site of the placenta associated with pregnancy, which occur approximately 1.6% of abortions [3]. During normal pregnancy, intermediate trophoblastic cells derived from chorionic villi come into contact with the endometrium, invade the decidua basalis and superficial myometrium, and replace the walls of the uterine spiral arteries at the implantation site, establishing maternal-fetal blood circulation. EPS, on the other hand, is characterized by excessive proliferation of intermediate trophoblastic cells in the placental implantation site, infiltrating the myometrium, as an exaggerated response to physiological processes [4]. However, the distinction between a normal placental site and EPS is subjective, as there is no reliable data to quantify the extent of trophoblastic cell infiltration at different stages of normal pregnancy [5, 6]. EPS can occur in both normal pregnancies and after miscarriages, presenting clinically as irregular vaginal bleeding or even severe hemorrhage post-miscarriage or postpartum. Diagnosis of EPS is based on pathological and immunohistochemical testing.

The pathogenesis of Exaggerated Placental Site (EPS) remains unclear. Some researchers believe that the occurrence of EPS may be related to the formation of abnormal decidua caused by repeated uterine curettage during pregnancy, as well as the infiltration of a large number of intermediate trophoblastic cells into the muscle layer [7]. Cesarean section surgery can lead to thinning or loss of the decidua basalis in the lower uterine segment scar area, poor incision healing forming tiny cracks, and excessive reaction and proliferation of intermediate trophoblastic cells at the implantation site during this pregnancy when the fertilized egg implants in the scar area [8]. Some researchers believe that the direct invasion of trophoblastic cells into the uterine muscle layer may increase the risk of trophoblastic cell tumor during pregnancy [9, 10], but this requires further research for verification.

EPS is mainly observed in women during the reproductive period. Its clinical manifestations lack specificity, mainly presenting as miscarriage or recurrent vaginal bleeding after childbirth, which is unexplained, persistent, and severe, often accompanied by abdominal pain [11]. These symptoms resemble those of postpartum hemorrhage caused by retained products of conception, placental adhesion, or placental implantation, posing challenges to clinical diagnosis. According to a meta-analysis of 127 cases of EPS, approximately 58% of EPS cases manifest as postpartum hemorrhage. The uterine bleeding may be attributed to the increased number of intermediate trophoblast cells in the placental bed, infiltrating the uterine smooth muscle and vascular walls, leading to separation of muscle fibers, increased infiltration of lymphocytes, deposition of fibrin-like material in the vessel walls, and most of the diseased vessel walls being in a dilated state. This affects the contraction of postpartum uterine smooth muscle and the restoration of blood vessels. Alternatively, intermediate trophoblast cells infiltrating the decidua and muscle layers may secrete certain substances that hinder the contraction of the uterine muscle layer, leading to increased miscarriage or postpartum bleeding [12]. Although EPS is defined as an

exaggerated response to physiological processes rather than a true pathology, postpartum hemorrhage caused by it requires attention from clinical obstetricians and gynecologists.

In EPS, the intermediate trophoblastic cells are often distributed in a cord-like pattern, usually not forming distinct masses. Microscopic examination reveals extensive infiltration of intermediate trophoblastic cells within the endometrium and muscle layer of the implantation site, but the structure of the endometrium and muscle layer remains intact, maintaining the original characteristics of the placental site. Some cells may exhibit nuclear atypia, but nuclear division figures or mitotic figures are rare. Immunohistochemically, the diseased cells show diffuse positivity for Mel-CAM and hPL, while hCG and PLAP exhibit focal positivity, with a Ki-67 index generally less than 1% [13]. The clinical manifestations of EPS are atypical, and both B-ultrasound and pelvic MRI lack specificity, therefore its differentiation from other diseases relies on pathological and immunohistochemical detection. EPS needs to be distinguished from placental site trophoblastic tumor (PSTT), as both originate from intermediate trophoblastic cells at the placental implantation site, with similar immunohistochemical staining patterns. However, PSTT is a neoplastic lesion, with a wider range of infiltration by proliferating intermediate trophoblastic cells, tumor cells often exhibiting clustered distribution, potentially disrupting the muscle layer, and showing mitotic figures, with a Ki-67 index often exceeding 10% [14].

Currently, most researchers believe that EPS is a benign disease, and symptoms will disappear after lesion clearance. EPS unrelated to hydatidiform mole does not increase the risk of persistent gestational trophoblastic disease, requiring no special treatment or follow-up, with a good prognosis [3]. If the diagnosis is unclear, serum β-hCG levels should be monitored. Persistent elevation of serum β-hCG levels indicates the presence of residual trophoblastic cells, requiring further evaluation. Due to the difficulty of preoperative diagnosis of EPS, the misdiagnosis and missed diagnosis rates are extremely high [15]. Many doctors choose to perform hysterectomy surgery to save lives or prevent the progression of gestational trophoblastic tumors due to massive bleeding. Although this effectively treats the disease, the degree of surgical trauma varies, which may lead to a larger surgical scope and increased incidence of complications. If the condition allows, tissue should be removed as soon as possible through hysteroscopy or curettage for pathological examination to confirm the diagnosis, reduce the misdiagnosis rate, and treat the disease through hysteroscopy exploration and electrocoagulation to avoid hysterectomy, preserve fertility, and reduce patient trauma.

4. Conclusion

EPS is difficult to diagnose without histopathological examination of hysterectomy specimens. An awareness of EPS and recognition of various types of trophoblastic diseases in women are very important for preventing misdiagnosis and guiding patient management, especially in reproductive-age women who desire further pregnancies.

Abbreviations

EPS: Exaggerated Placental Site
ETT: Epithelioid Placental Site Nodule
GTD: Gestational Trophoblastic Disease
GTN: Gestational Trophoblastic Neoplasia
HCG: Human Chorionic Gonadotropin
hPL: human Placental Lactogen
PSTT: Placental Site Trophoblastic Tumor
PLAP: Placental Alkaline Phosphatase

Conflicts of Interest

The authors declare no conflicts of interest.

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