Case Report
Placental site trophoblastic tumor presented with vaginal metastasis

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Abstract: Placental site trophoblastic tumor (PSTT) is a rare type of gestational trophoblastic neoplasia (GTN). It is rising from the abnormal proliferation of intermediate trophoblastic cells with occasional multinuclear giant cells, with the potential for local invasion and metastasis. For its untypical and changeable clinical characteristics, the diagnosis and management are still poorly understood. Here we documented a case of PSTT with vaginal lesion as her unique presentation. After surgery and adjuvant chemotherapy, the patient was cured.

Keywords: Placental site trophoblastic tumor, gestational trophoblastic neoplasia, diagnosis, metastasis

Introduction

PSTT was first described as an exaggerated expression of the invasive nature of normal trophoblastic tissue and named as trophoblastic pseudotumor in 1976 [1]. Until to 1981, it was reported that two of 14 cases of trophoblastic pseudotumor died from metastatic disease, which revealed its malignant potential [2]. PSTT occurs rarely with less than 300 cases as documented [3]. It derives from intermediate trophoblastic cells which infiltrate both myometrium and blood vessels [4]. 70% patients localized to the uterus, while 30% of patients had metastatic lesions at first presentation [5]. As a result, the symptoms of PSTT are variable, including amenorrhea, irregular bleeding, abdominal pain, uterine rupture and galactorrhea. We report the case of a patient with vaginal lesion as her unique presentation and analysis the documented reports for the different strategies in diagnosis and treatment of PSTT.

History

A 40-year-old woman, gravida 3, para 1 (vaginal production), presented to her gynecologist complaining of vaginal tumor prolapsed two month ago. Her past medical history was complicated. The patient had a regular history of menstrual cycle, the menarche age of 16, 7/30 days, and no dysmenorrhea. In 2011, the patient had the abortion at the 57th days of menopause, with the pathologic examination proved hydatidiform mole with trophoblastic cells hyperplasia moderately. During follow-up, with the elevated serum Human Chorionic Gonadotrophin (HCG) level and new focus occurred in the lungs, she was diagnosed as gestational trophoblastic neoplasia (stage III: 6). Then she experienced 7 courses chemotherapy of 5-Fu+KSM project. Up to today, she still had a normal serum HCG level and no focus in lungs. In 2012, due to contacted hemorrhages after sex, cervical biopsy revealed an unexpected cervical squamous cell carcinoma in situ. Then she was taken a cervical LEEP (Loop Electrosurgical Excision Procedure) surgery and regular follow-up. Two month ago, she suffered with vaginal tumor prolapsed with irregular bleeding, and had a biopsy in her hometown hospital. The pathological report implied she had epithelioid trophoblastic tumors (ETTs) [7]. She was therefore referred to out hospital, a specific gynecologic oncologic hospital. Physical and gynecological examination, pelvic ultrasononic and PET-CT identified suspicious a 2.0 cm mass limited to the vaginal vault without parametrial extension (Figure 1).
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The patient underwent resection of the vaginal lesion. The macroscopic examination of the vaginal tumor revealed an ill-defined nodular growth measuring 1.5 × 2.0 × 0.8 cm. On microscopic examination, the tumor consisted of a population of polygonal intermediate trophoblast cells with amphophilic to clear cytoplasm. These cells have often a single irregular

Figure 1. PET-CT identified suspicious a 2.0 cm mass limited to the vaginal vault without parametrial extension.

Figure 2. Immunohistochemical staining of CKAE1/AE3 and Ki-67 in vaginal lesion. A. HE staining showed intermediate trophoblast cells. B. Staining of CKAE1/AE3. C. Staining of Ki-67.
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from the trophoblast layer, including hydatidiform mole (complete or partial), invasive moles, choriocarcinoma and placental trophoblastic tumor. PSTT is a tumor of intermediate trophoblast, and accounts for 1-2% gestational trophoblastic neoplasia [1]. Sometimes, it is difficult to distinguish PSTT from other forms of GTN or non-trophoblastic tumors just as the referring hospital on the base of morphological and clinical data.

The symptoms of gestational trophoblastic disease usually occur after delivery or abortion. According to the epidemiological retrospective survey, gestational trophoblastic neoplasia, 60% was secondary to hydatidiform mole, 30% to abortion, and 10% secondary to full term pregnancy or ectopic pregnancy. However, PSTT may complicate or follow any type of normal or abnormal gestations (hydatiform mole) and its interval may vary from weeks to years after the preceding pregnancy. Comparing with the high level in other types of GTN, the serum-hCG in PSTT may be mild elevated or just at normal level, which has no help for the diagnosis preoperatively. Over 30% of patients have metastatic lesions at first presentation, such as the peritoneum, the lung, the liver and the brain. The symptoms of PSTT are variable, including amenorrhea, irregular bleeding, abdominal pain, uterine rupture and galactorrhea.

However, identification of the GTN subtypes and differentiating them from other tumors is important clinically because the therapeutic approaches towards these diseases are difference. In contrast to other forms of GTDs, because of its low chemosensitivity, surgery and polychemotherapy are the main treatments depend on different stages [6]. Immunochemistry is a useful diagnostic method. The diagnosis should therefore rely on intense hPL-positivity as well as the ultrastructural image of the tumor.

In the present case, the patient was presented with symptoms of GTN that was diagnosed to

typical nucleus with focally prominent nucleoli, but some are multinucleate, resembling to syncytiotrophoblastic giant cells (Figure 2). The immunohistochemical pattern is ambiguous. The staining of hPL and P53 is only focally positive while the staining of placental alkaline phosphatase (PLAP) is more diffuse. The staining of CKAE1/AE3 and EMA is positive and the staining of hCG, P16 and P63 is negative. Finally, Ki-67 is expressed in 5% of the tumor cells. The pathological diagnosis of PSTT is proposed and confirmed by the expert panel of pathologists of our hospital. Meantime, the pathology slides of the abortion performed in the year of 2011 previously were reviewed and showed no sign of PSTT. The serum hCG concentration dropped and be kept to normal from the 5th course chemotherapy till now as showed in Figure 3. Serum hPL level was not measured. An extended radiological work-up did not show evidence of metastasis. Treatment options including observation versus adjuvant chemotherapy were discussed. Although PSTT tends to be resistant to chemotherapy, considering that the patient had a fertility persevered surgery, two courses of EMA-EP adjuvant chemotherapy had been elected. After a follow-up of 6 months, the patient is still remission in clinical, biological (β-hCG) and radiological (pelvic MRI) examinations.

Discussion

Gestational trophoblastic disease describes a number of gynecological tumors that originate

![Figure 3. Changes in β-hCG levels (mIU/mL) during the treatment period.](image-url)

![chart](chart-url)
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be molar pregnancy by ultrasonic three years ago. Her serum-hCG level was high at that time. The patient underwent suction evacuation but the serum-hCG level was still high and she presented to hospital two months later with vaginal bleeding and respiration symptoms. CT scan of lungs showed invasive mole metastasis of the lungs. The patient was started on chemotherapy with 5-Fu+KSM project according FIGO 2000 score system. After 7 courses of chemotherapy, the lungs were clear and the serum-hCG level was persisted at normal level until now. Despite of serious adverse reaction of chemotherapy, the patient was still refusing total abdominal hysterectomy. We reviewed the pathological sides of her suction previously, no proof was found to support the diagnosis of PSTT.

Three year later, the patient presented again with vaginal tumor prolapsed with irregular bleeding as the unique symptom. Pathological examination of the biopsy tissue, the referring hospital diagnosed as ETT. However, pathological report of our hospital was suggestive of PSTT depending on immuno-histological staining.

We presumed the case might be the recurrence of an ignored PSTT three years ago. Patients with PSTT often have persistent low levels of serum HCG. However, higher serum HCG titers have been reported in patients with placental site trophoblastic tumors [8]. Initial curettage is often equivocal and the diagnosis of PSTT can be missed if tissues showing muscle invasion by intermediate trophoblast cells can’t be found [9].

In addition, confronted with vaginal mass without other abnormal features in this case, gynecologists should consider both primary and secondary vaginal tumors. It is reported that about 90% of vaginal tumors are metastases and derive not only from gynecologic malignancies including GTN but also from other organs such as kidney, bladder and colorectal carcinoma [10]. Information about optimal management strategy is restricted for its low occurrence. Considering patient’s request and no lesion in uterus, we only had vaginal mass excised and two courses of EMA-EP chemotherapy followed. More information is needed for further following.

Conclusions

In summary, PSTT stands for a diagnostic challenge and treatment dilemma to both pathologist and gynecologists. It is a great and important job to make the specific diagnosis as it is distinct from other GTNs. More efforts are needed to establish a diagnosis and management algorithm for PSTT.

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Disclosure of conflict of interest

None.

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