Case Report: Placental site trophoblastic tumor revealed by a clinical pelvic abscess [version 3; peer review: 1 approved, 2 approved with reservations, 1 not approved]

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Abstract
We report an uncommon clinical presentation of a placental site trophoblastic tumor. The patient presented initially with abdominal pain with, fever, bleeding and pelvic mass on ultrasonography leading to the wrong diagnosis of a pelvic abscess. Dilation and curettage were performed and pathological examination confirmed the diagnosis of placental site trophoblastic tumor. Therefore, she underwent abdominal hysterectomy. Four years after surgery, the patient is still disease free. Gestational trophoblastic diseases should be considered in every patient presenting abnormal uterine bleeding after delivery or pregnancy loss despite the associated symptoms being very unusual.

Keywords
Gestational Trophoblastic Disease, Placenta Diseases, Trophoblastic Tumor, Placental Site, pathology.

This article is included in the Oncology gateway.
Introduction
Placental site trophoblastic tumor (PSTT) is a rare tumor, representing 1% of gestational trophoblastic diseases.\(^1\)\(^,\)\(^2\) It mainly affects women of childbearing age after delivery or pregnancy loss.\(^1\)\(^,\)\(^3\) In this paper, we report a case of placental site trophoblastic tumor diagnosed by an array of pelvic abscess associated with bleeding occurring two months after delivery. The evolution, after surgical treatment by hysterectomy, was favorable.

Case report
We report the case of an unemployed 32-year-old Arabic woman, gravida 1 and para 1, without medical history, gave birth naturally and without complications to a full-term healthy newborn. Two months after her delivery, she consulted our department with persisting metrorrhagia associated with fever of 39°C. The patient’s examination revealed that the bleeding has been noted since the delivery day and it had increased two days earlier.

A physical examination revealed a fever of 39.5°C and abdominal tenderness. The blood pressure was 110/70 mm Hg and the heart rate was 82 beats/mn. Furthermore, there was no specific digestive or urinary symptom. Per speculum examination, the cervix was enlarged with purulent vaginal discharge. On digital pelvic examination, the uterus was increased in size accessed at 12 week gestation and its mobilization was painful. Blood tests showed an inflammatory syndrome with a C-reactive protein at 200 mg/l \(\leq\) 6mg/l and white blood cells at 17000/mm\(^3\) \(\leq\) 4000-10000/mm\(^3\). The beta-human chorionic gonadotropin (β-HCG) rate was positive at 674 U/l \(<\) 5U/l. The transvaginal sonography showed a large sized uterus containing an echogenic heterogeneous endometrial mass, vascularized on Doppler examination. This mass seemed to partially invade the myometrium, which suggests hyper vascularized trophoblastic retention. In addition, ultrasound showed an average effusion in the Douglas' pouch (Figure 1) with a left adnexal echogenic mass, suggesting in this context a post-partum pelvic abscess.

Laparoscopic adnexal drainage and endometrial curettage were performed. The infectious episode resolved promptly with antibiotics; gentamicin 160 mg per day for 5 days metronidazole 500 mg three times a day for 15 days and cefotaxim 1g three times a day for 15 days. Pathological examination of the endometrial curettage specimen reported a proliferation of large tumor cell with eosinophilic cytoplasm and nuclear atypia, infiltrating the myometrium. These cells were positive for pro inflammatory cytokine (IL6) in the immunohistochemistry studies and the final diagnosis was a placental site trophoblastic tumor. A thoracoabdominopelvic CT scan was performed, and it did not reveal any secondary locations.

A laparoscopic endometrial curettage with preservation of ovaries was performed. On gross examination there was a mass of 6 cm localized to the myometrium of bluish appearance with areas of hemorrhage and necrosis. The tumors had ill-defined borders and invaded into the myometrium (Figure 2). Pathological examination was similar to that described in the curettage specimen, showing a proliferation of monomorphic intermediate trophoblasts (Figure 3A). The tumor cells demonstrated nuclear atypia, eosinophilic cytoplasm (Figure 3D) and myometrial invasion (Figure 3B,C). Extensive necrosis, hemorrhage and vascular invasion are observed (Figure 3E). We carefully considered and excluded exaggerated placental site response (EPSR), epithelioid trophoblastic tumor (ETT), and gestational choriocarcinoma (GCC) based on specific pathological features observed in this case. EPSR is a benign condition characterized by a lack of nuclear atypia and invasive behavior, features that were not present in this case. Instead, the tumor demonstrated nuclear atypia, eosinophilic cytoplasm, and myometrial invasion, as seen in Figure 3B-D, which are consistent with placental site trophoblastic tumor (PSTT) rather than EPSR. Furthermore, the extensive necrosis, hemorrhage, and vascular invasion observed in the specimen (Figure 3E) are not typical of EPSR. ETT was excluded based on the tumor's cellular morphology and growth pattern. ETT typically exhibits more epithelioid cells with less eosinophilic cytoplasm and a nested growth pattern, which contrasts with the monomorphic intermediate trophoblasts and diffuse growth pattern seen in our case. Immunohistochemical staining could further support this distinction, but the morphological differences were sufficiently clear. GCC was ruled out due to the lack of a biphasic population of trophoblasts, which is characteristic of
Figure 1. **Sonographic appearance of the tumor of the placental site tumor.** (A) Echogenic tumor occupying the uterine cavity (arrow) with infiltration of the myometrium; (B) appearance vascularized tumor at color Doppler.

Figure 2. **Macroscopic appearance of the placental site tumor.** (A) Peri operative view showing increased uterine size, yellowish area seat (arrow); (B) appearance of the tumor to cut, yellowish tumor occupying the uterine cavity and infiltrating the myometrium.
choriocarcinoma. GCC typically shows a mixture of cytotrophoblasts, syncytiotrophoblasts, and intermediate trophoblasts, often with significantly elevated serum beta-HCG. In contrast, our case showed only monomorphic intermediate trophoblasts with no such biphasic arrangement. Therefore, based on the tumor’s morphological features—nuclear atypia, myometrial invasion, and necrosis—and the absence of patterns typical of EPSR, ETT, and GCC, we confirmed the diagnosis of PSTT in this case.

Figure 3. Histological appearance of the placental site tumor. (A) Monomorphic cell proliferation of intermediate trophoblast; (B, C) tumor cells infiltrate the myometrium form of clusters, dissociating smooth muscle bundles (B: low magnification, C: magnification); (D) proliferation of large cells with eosinophilic cytoplasm and lobulated nucleus; (E) home of tumor cells with the presence of vascular emboli.
The postoperative course was favorable. The patient had a regular follow-up every month for the first year combining a clinical examination and a serum level of β-HCG. She had a clinical check-up and pelvic ultrasound every year for two years, no sign of recurrence was noted. Four years after surgery, the patient is still disease free.

Discussion

In 1895, Marchand first described PSTT and named it atypical chorioepithelioma. In 1981, Scully and Young described the morphological details and recognized it as a neoplastic process, and named it PSTT. PSTTs are a rare subtype of gestational trophoblastic disease, accounting for less than 1% of all cases. It mainly affects women of childbearing age and it is seen in patients between 19-62 years, with an average age of 30 years. PSTT can occur after a normal pregnancy, abortion, term delivery, ectopic pregnancy or molar pregnancy. When there is extension beyond the uterus, surgical treatment should be associated to chemotherapy. Fertility sparing surgery, particularly less responding to chemotherapy than hydatiform mole, invasive mole and choriocarcinoma. When there is extension beyond the uterus, surgical treatment should be associated to chemotherapy. Fertility sparing surgery, particularly less responding to chemotherapy than hydatiform mole, invasive mole and choriocarcinoma.

In 1981, Scully and Young described the morphological details and recognized it as a neoplastic process, and named it PSTT. PSTTs are a rare subtype of gestational trophoblastic disease, accounting for less than 1% of all cases. It mainly affects women of childbearing age and it is seen in patients between 19-62 years, with an average age of 30 years. PSTT can occur after a normal pregnancy, abortion, term delivery, ectopic pregnancy or molar pregnancy. Here we reported a case of PSTT occurring after a normal pregnancy. This pathology may occur months to years after pregnancy with the average interval between the antecedent pregnancy and diagnosis being 16 to 18 months. Diagnosis of PSTT can be difficult due to the nonspecific clinical signs. Abnormal uterine bleeding is the most common presenting feature. Metrorrhagia can also be associated with amenorrhea. In addition to PSTT, other gestational trophoblastic diseases should be discussed in the face of abnormal uterine bleeding in postpartum such as intraplacental choriocarcinoma (IC).

Diagnosing IC is often delayed because of the lack of specific symptoms. While not always routinely performed, histological examination of the placenta is crucial when clinical warning signs or concerning ultrasound findings are present. Indicators such as sudden fetal distress, fetal or neonatal anemia, perinatal death, and unusual postpartum vaginal bleeding could signify IC associated with foeto-maternal hemorrhage and warrant thorough investigation, including placental histology. Thus, it would be wise to preserve the placenta for 24-48 hours after each birth.

On gross examination, the tumors are located primarily in the Endometrium, presenting as polypoid or nodular masses, with a variable diameter up to 10 cm. The sectioned surfaces of the tumors are solid, often fleshy, and usually yellow with necrosis, and hemorrhage. The tumor may extend into the cervix or infiltrate the serous, the adnexa or the round ligaments. In our case, the tumor invaded the myometrium without reaching the serous. The diagnosis of PSTT is based on pathological examination.

On microscopic examination, we typically find a proliferation of intermediate trophoblastic cells without chorionic villi, which infiltrate muscle fibers. Vascular invasion, necrosis and hemorrhage are also often observed.

The tumor is composed of a relatively monotonous population of polygonal cells with nuclear atypia and moderately abundant cytoplasm that can be amphophilic, eosinophilic or clear. The distinctive pattern of vascular invasion and deposition of fibrinoid material are the key diagnostic features. Usually, PSTTs have an unpredictable malignant potential and between 10 and 20% of patients have metastatic disease at the time of presentation. Metastasis site include peritoneum, vagina, lung, liver and brain.

Hysterectomy without bilateral oophorectomy is the gold standard in PSTT management. In fact, this entity is particularly less responding to chemotherapy than hydatiform mole, invasive mole and choriocarcinoma. When there is extension beyond the uterus, surgical treatment should be associated to chemotherapy. Fertility sparing surgery, such as hysteroscopic resection or transperitoneal local uterine excision, may be offered to young patients with nonmetastatic disease who desiring to preserve their fertility.

In addition to the FIGO anatomical staging system, which remains a key prognostic factor for placental site trophoblastic tumor (PSTT) survival, recent studies have identified the interval between the last pregnancy and the initiation of treatment as another crucial prognostic indicator. Specifically, a time interval of more than 48 months between the preceding pregnancy and the onset of treatment has been associated with poorer outcomes. This extended interval is linked to an increased risk of metastasis and a more aggressive disease course, emphasizing the need for early diagnosis and timely treatment in cases of suspected PSTT. Therefore, both FIGO staging and the pregnancy-to-treatment interval should be considered when assessing prognosis and planning management strategies for patients with PSTT.
After surgical treatment, patients should be followed up during years to optimize the chance of detecting a relapse or metastasis. There is no consensus regarding the frequency and modalities of follow-up for patients treated for PSTT. However, follow-up must necessarily include a detailed clinical examination and quantitative serum hCG measurement to detect recurrences. Additional radiological examinations may be requested based on clinical symptomatology.

**Perspectives**

On future studies related to placental site trophoblastic tumor (PSTT), researchers should focus on several key areas:

- Genetic Markers: Understanding these markers could aid in early diagnosis, prognosis, and tailored treatment approaches.

- Rare Forms with High hCG levels: Investigation into rare PSTT cases presenting with elevated hCG levels is essential to comprehend their unique pathogenesis and optimize treatment strategies for these atypical cases.

- New Chemotherapeutic Agents: Developing secondary chemotherapeutic agents is crucial for patients with primary chemoresistant PSTT, offering potential alternative treatment options for this challenging group.

Further research into these areas may lead to significant advancements in the understanding and management of PSTT.

**Strengths and limitations**

This case report is interesting since it is the first reporting PSTT simulating a pelvic abscess. However, PTTT are rare which prevents researchers from realizing large scale studies in order to develop valid management protocols.

**Conclusion**

Although PSTTs are extremely rare worldwide, the diagnosis should be considered during the post-partum and post-abortion periods if there is persistent metrorrhagia. After surgical treatment, the follow up is needed to be accurate, to help recognize a relapse or metastasis.

**Data availability**

All data underlying the results are available as part of the article and no additional source data are required.

**Consent**

Written informed consent for publication of clinical details and clinical images was obtained from the patient.

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Open Peer Review

Current Peer Review Status:  ❓  ❌  ✓  ❓

Version 3

Reviewer Report 23 October 2024
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✅ Guglielmo Stabile

Department of Medical and Surgical Sciences, Institute of Obstetrics and Gynecology, University of Foggia Departments of Medicine (Ringgold ID: 507873), Foggia, Foggia, Italy

The manuscript has been improved. The manuscript is suitable for indexing.

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Expert in Placental Pathology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 23 October 2024
https://doi.org/10.5256/f1000research.173598.r333452

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❓ Seetu Palo

All India Institute of Medical Sciences, Hyderabad, India

Although the authors have added a note on differential diagnoses, further refinement and correction is needed in this section. For example, the authors have mentioned that exaggerated placental site response (EPSR) is characterized by lack of nuclear atypia and invasive behavior, which is in contrast to existing literature. EPSR can exhibit certain degree of nuclear atypia and it is known to invade the superficial myometrium as well (Ref 1, Ref 2).
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Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Pathology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Version 2

Reviewer Report 25 September 2024

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Seetu Palo
All India Institute of Medical Sciences, Hyderabad, India

This is a well-documented case report on a rare condition, providing valuable insights into the diagnosis and management of placental site trophoblastic tumor (PSTT). Strengthening the discussion around the unique presentation and refinement in structure and depth of discussion, particularly around clinical implications and differential diagnosis, would improve the manuscript. The description of imaging findings is well-executed, and the figures provide useful visual aids. However, there are some issues with figure referencing and clarity. Figure 1 is briefly mentioned in the text, but the explanation could be expanded to better connect the ultrasound findings to the case narrative. Similarly, the histopathological micro-photographs, which forms the basis of diagnosis, need to be of better resolution with appropriate annotations for better understanding of the readers. The authors should discuss about microscopic differential diagnoses, such as, exaggerated placental site response, epithelioid trophoblastic tumor and gestational choriocarcinoma, and state how were these differentials excluded in this particular case. The description of the surgical management (hysterectomy) is clear, and the follow-up section is well done, providing a clear timeline of surveillance for recurrence, which is crucial in managing PSTT. However, additional information regarding β-HCG levels over time would further strengthen the post-treatment monitoring discussion. A brief note on emerging treatment options or potential prognostic factors could further enrich the discussion.
Is the background of the case's history and progression described in sufficient detail?
Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
Partly

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
Yes

Is the case presented with sufficient detail to be useful for other practitioners?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Pathology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 16 Oct 2024
chaouki mbarki

Dear Reviewer,
Thank you for reviewing our article. I truly appreciate all your remarks and comments. I have made the necessary revisions, which you can find in the revised manuscript (version 3). I hope the updated version meets your approval.
Thank you once again.

Competing Interests: None

Reviewer Report 24 September 2024
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Guglielmo Stabile
Department of Medical and Surgical Sciences, Institute of Obstetrics and Gynecology, University of Foggia Departments of Medicine (Ringgold ID: 507873), Foggia, Foggia, Italy
Dear Authors and Editor, thank you for allowing me to review this interesting case report. In my opinion, the subject is very interesting, and the report is useful for the diagnosis and management of such rare clinical events.

In my opinion, an important point to be discussed is the possibility to preserve the placenta for 24-48 hours after each birth, to perform histological examination even in the case in which the birth was physiological but particular symptoms appeared in the hours immediately after birth (also in this case, after an in-depth medical history, the bleeding was already abundant after birth. This procedure could lead to a better and faster diagnosis of this as well as other even rarer placental pathologies [ref 1]. A few more histological tests would improve the outcomes in terms of survival and fertility sparing of the patients.

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Is the background of the case’s history and progression described in sufficient detail?
Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
No

Is the case presented with sufficient detail to be useful for other practitioners?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Expert in Placental Pathology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 16 Oct 2024
chaouki mbarki

Dear Reviewer,
Thank you for reviewing our article. I truly appreciate all your remarks and comments. I have made the necessary revisions, which you can find in the revised manuscript (version 3). I hope the updated version meets your approval.
Thank you once again.
Competing Interests: No competing interests were disclosed.

Version 1

Reviewer Report 19 January 2023

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Maria-Gabriela Aniţei
University of Medicine and Pharmacy, Iasi, Romania

I was pleased to review the article Case Report: Placental site trophoblastic tumor revealed by a clinical pelvic abscess.

The methodology used by the authors is appropriate for the purpose of the study and conclusions are narrowly linked to available evidence. The title expresses clearly the content of the manuscript and highlights the importance of the study. As the authors note in Strengths and limitations, this case report is interesting since it is the first reporting of PSTT simulating a pelvic abscess. There was rapid evolution of tumor development, only 2 months after natural birth, apparently without a risk factor from her medical history. There are interesting images intraoperative and microscopy.

The article respects the presentation algorithm that is required for a case report type article, but there is a number of medical details are missing, such as no detailed investigations (CT-scan, for example) to exclude metastases, both at the time of diagnosis and follow-up.

In the same direction, to improve the methodology of this study, the introduction section must be improved. It is too short, and I suggest that some information regarding diagnosis and prognosis of PSTT should be included. Likewise, Immunohistochemistry data and the FIGO score are missing from the anatomopathological presentation, this information would increase the value of the article.

Likewise, to be more convincing, the authors could image the patient at a distance through a CT-scan exam to confirm, through this high-performance investigation, the absence of local or distant disease. These tests would help to exclude metastases, both at the time of diagnosis and follow-up, especially as the anatomical-pathological examination shows a vascular invasion.

The conclusion of the article could be strengthened. Although PSTTs are extremely rare worldwide, the diagnosis should be considered during the post-partum and postabortion periods if there is persistent metrorrhagia - this means that, in front of a patient with
metrorrhagia and febrile syndrome that appeared early after delivery, this differential diagnosis (PSTT) must also be taken into account.

Other points:

1. It doesn't seem representative to me that pathology should be a Keywords
2. immunohistochemistry data and the FIGO score are missing from the anatomopathological presentation
3. Usually, ‘PSTTs are benign tumors’ – I am not agree with this affirmation
4. In figure 3- the microscopy details must be specified - is it an image of HE? , how many times is it amplified ( which objective was used?) . As the area of interest is identified in image D, I recommend that the same thing be done for the other images (Figure 3- A, B, C, E)

Is the background of the case's history and progression described in sufficient detail?
Partly

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
Partly

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
Yes

Is the case presented with sufficient detail to be useful for other practitioners?
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: oncological gynecology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Reviewer Report 07 March 2022

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Antonio Braga
Rio de Janeiro Trophoblastic Disease Center, Antonio Pedro University Hospital, Maternity School
Dear Authors and Editors,

I would like to thank you for the opportunity to review the paper entitled: “Case Report: Placental site trophoblastic tumor revealed by a clinical pelvic abscess”, submitted to the F1000. Similarly, I would like to congratulate the authors for their interest in the topic.

In this case report, the authors presented a description of a PSTT presenting as abdominal abscess, reviewing the literature of this subject.

I would like to highlight some aspects that deserve attention.

1. The authors must describe in the case report the screening for metastatic disease, to justify the decision for TAH.
2. PSTT is always cancer, not a benign tumor as described.
3. Nowadays we have, besides FIGO anatomical staging system as prognostic factor for PSTT surviving, the interval of last pregnancy and the initiating of treatment of 48 months.\textsuperscript{1}
4. In the section ‘Strengths and Limitations’ there is a PTTT that should be corrected.

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Partly

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
Partly

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
Yes

Is the case presented with sufficient detail to be useful for other practitioners?
Yes

\textbf{Competing Interests:} No competing interests were disclosed.

\textbf{Reviewer Expertise:} Gestational trophoblastic disease

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.
Author Response 20 Oct 2023

chaouki mbarki

Dear reviewer,

Thank you for taking the time to review our article and for your valuable feedback. I will address your comments as follows:

Regarding your first comment, the patient had undergone a total abdominal hysterectomy after a thoracoabdominopelvic CT scan revealed no metastatic lesions.

We have also addressed all the other issues as per your request, which you can verify in the revised version.

We would greatly appreciate it if you could approve this paper now that we have made the necessary amendments.

Thank you for your assistance.

**Competing Interests:** No competing interests were disclosed.

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