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Case Report

Tru-cut placental site trophoblastic tumor biopsy: A novel way for diagnosis. Case report

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Abstract

Background: A Placental Site Trophoblastic Tumor (PSTT) is a rare form of gestational trophoblastic disease and usually manifests itself with abnormal uterine bleeding and elevated β -hCG serum levels even months or years after any antecedent pregnancy event. Typically, tumors are confined into the uterus and secrete lower levels of β -hCG compared with other Gestational Trophoblastic Neoplasia (GTN). They can be detected sonographically like heterogeneous solid mass in the uterine cavity with minimal to high vascularization, but sometimes they develop into myometrium without endometrial involvement. To the best of our knowledge, uterine biopsy is the only way to make a reliable diagnosis, but for these reasons sometimes Dilation and Curettage (D&C) or hysteroscopy are not exhaustive. Their final diagnosis is histopathological and often very difficult due to their rarity, thus many times they directly present metastasis symptoms (mainly pulmonary) or paraneoplastic syndromes.

Case presentation: A 37-year-old woman with the purpose of a second pregnancy, after seven weeks of amenorrhea, complained irregular bleeding and metrorrhagia. The patient underwent transvaginal ultrasound (US) and a lesion of 50 mm was found in myometrium, its echostructure was inhomogeneous and richly vascularised (CS4) with rear acoustic reinforcement. It was associated with slightly elevated serum levels of β -hCG. The patient performed a hysteroscopy with simultaneous tru-cut biopsy of the lesion under US guidance and a placental site trophoblastic tumor was diagnosed by histological examination.

Conclusion: In this paper we suggest a novel method to perform the PSTT diagnosis. A tru-cut core biopsy allows a deep and precise biopsy with less invasivity and low risk of bleeding or uterine damage. Our case study shows that the employment of this novel technique can help in the diagnosis through a targeted sampling of the myometrium even in those cases in which the endometrial cavity is not involved.

Introduction

Placental Site Trophoblastic Tumor (PSTT) is a rare form of gestational trophoblastic disease accounting for about 1% - 2% of all trophoblastic tumors [1].

PSTT most common presentation in reproductive age women is abnormal uterine bleeding associated with elevated β -hCG serum levels after any former gestational event but it can also present with metastasis or paraneoplastic syndrome.

In PSTT serum levels of β -hCG are typically in the range

of thousands of IU/L, which is much lower than in case of choriocarcinoma [1].

Imaging is essential for staging PSTT: Zhou, et al. [2] identified three sonographic PSTT patterns: it looks like a vascularized heterogeneous solid mass in uterine cavity (type 1), in the myometrium (type 2) or a lacunar like lesion with cystic areas within the myometrium with high vascularization (type 3).

Given both its rarity and its wide variety of presentation, it is easy to understand why PSTT may be misdiagnosed in nearly one third of patients [1].

Dilation and Curettage (D&C) or hysteroscopic biopsy are considered gold standard for histological diagnosis, even if in several times they are not adequate. D&C are at risk of uterine perforation, copious blood loss and they don't allow a targeted and satisfactory biopsy. Hysteroscopy is useful to see the uterine cavity but unless the tumor has a polypoid appearance, the endometrium may look like secretive endometrium while the mass has developed inside myometrium.

For these reasons, tru-cut biopsy should be indicated as an alternative or at least as an ancillary technique to help the diagnosis.

Case report

The patient was a 37-year-old woman with no significant previous medical history, menarche at fifteen years old and subsequent regular menstrual cycles.

Concerning her familiar history, her mother was diagnosed with breast cancer at age 57 and her father had prostatic cancer at 65 years old.

Her first pregnancy, complicated by late pre-eclampsia, ended at 37 weeks of gestation with a spontaneous labour followed by vaginal delivery on February 2021. Normal menstrual periods started again after few weeks.

On November 2021 she underwent a preconceptional gynaecological visit with the purpose of a second pregnancy. The visit showed a good health status and normal pelvic scan.

On February 2022, after seven weeks of amenorrhea, she complained irregular bleeding and metrorrhagia. A value of 120 - 130 IU/ml β -hCG serum level was found, followed by a lower value of 61.8 IU/ml. Then, four days after, a spontaneous miscarriage was suspected and the patient performed transvaginal Ultrasound (US) (Figure 1a,1b).

A detailed exam of the pelvis' US by the expert operator using Voluson E6 (General Electric Healthcare GE, Zipf, Austria) with broadband from 5 - 9 MHz endocavitary transducer was performed with a Color Doppler examination. It showed a retroverted uterus and regular morphology of the external profile measuring 84 mm LL x 55 mm AP x 70 mm TD. Cavity length was 50 mm while cervical length was 22 mm. The right laterofundic portion of myometrium was occupied by a lesion measuring 50 x 44 x 48 mm with an inhomogeneous echostructure of the grey scale. Color Doppler shows that the lesion was richly vascularized (CS4) with rear acoustic reinforcement (Figure 2a,2b). The endometrial line was 9 mm, with homogeneous hyperechogenicity and regular mio-endometrial junction. Ovaries were bilaterally regular, measuring 29 x 15 mm on the right and 31 x 17 mm with corpus luteum on the left. Free fluid in Douglas was absent.

β -hCG dosage decreased but never below 59 IU/ml: for this reason, a trophoblastic disease was suspected.

Since most of the neof ormation developed within the myometrium, with the intent to biopsy the affected part

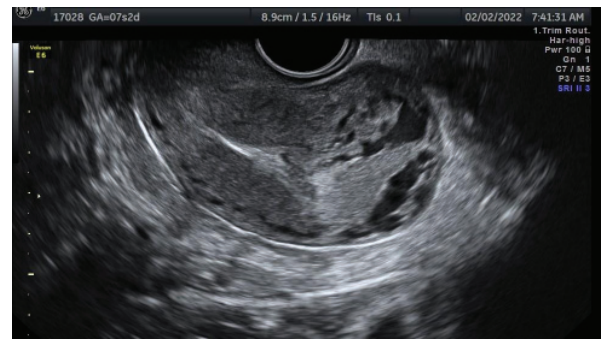


Figure 1a: Transvaginal ultrasound of the uterus affected by placental site trophoblastic tumor at the time of diagnosis. 1a: Longitudinal section.



Figure 1b: Transvaginal ultrasound of the uterus affected by placental site trophoblastic tumor at the time of diagnosis. 1b: Transversal section.



Figure 2a: Transvaginal ultrasound of the uterus affected by placental site trophoblastic tumor at the time of diagnosis with Color Doppler examination. 2a: Longitudinal section.

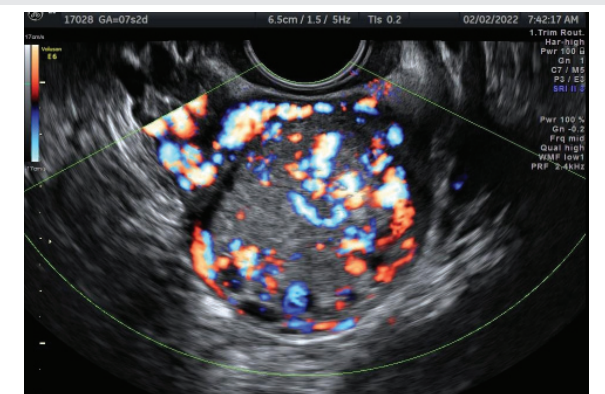


Figure 2b: Transvaginal ultrasound of the uterus affected by placental site trophoblastic tumor at the time of diagnosis with Color Doppler examination. 2b: Transversal section.

and reach a diagnosis as soon as possible, it was decided to perform a tru-cut biopsy of the lesion under US guidance with a simultaneous hysteroscopy.

A detailed exam of the pelvis' US by the expert operator using *Voluson E6* (General Electric Healthcare GE, Zipf, Austria) with broadband from 5 - 9 MHz endocavitary transducer was performed with a Color Doppler examination. *Tru-cut Bard Max Core* instrument has 22 mm penetration depth, two firing buttons, and color coding promotes accurate needle gauge identification. One-handed cocking and lightweight ergonomic design improve both handling and control, therefore efficiency and accuracy.

The transvaginal procedure was performed in the lithotomy position, with a needle guide attached to the vaginal US probe, with an empty bladder after the vagina and anus disinfection with 10% povidone-iodine. The procedure was performed under US needle tip guidance, paying close attention to the surrounding anatomical structures, avoiding necrotic tissue or the most vascularize parts. After the administration of local anesthetic, the needle was passed through the posterior vaginal fornix and posterior uterine wall until reaching the target lesion. The cut penetration depth was controlled by setting the stopper at 22 mm and during the procedure 3 samples were collected from the target lesion. Thanks to the characteristics of tru-cut needle it was possible to perform a deeper, less invasive, targeted biopsy with a reduced risk of bleeding and uterine perforation (Figure 3).

Hysteroscopy showed a regular cavity with secretive endometrium and a small endometrial polyp, consequently removed with endoscopic scissors. Both tubal ostia were visualized.

After the procedure, the patient was checked for bleeding from the biopsy site, observed for a couple of hours and sent home with a regular postoperative course.

On the histological report highly vascularized myometrial tissue full of large pleomorphic atypical cells showing vascular tropism with likely trophoblastic origin was found. Within the Regional Program for the Centralization of trophoblastic disease the case was referred to Diagnostic Gynecopathology and Foetus-Perinatal Pathology of Scientific Institute for Research, Hospitalization and Healthcare "Giannina Gaslini" that confirmed a trophoblastic neoplasm. Specifically, a trophoblastic tumor of implantation site was diagnosed.

Microscopic observation (Figures 4a-c) showed myometrium fragments with leiomyuscular fascicles intertwined and intercalated with richly represented arterial and venous vascular structures of small and medium caliber. Medium grade of inflammatory reaction with proliferation of large polymorphic atypical elements, with big irregular nucleus and pseudo syncytial aspects. Even without karyokinetic figures, they had elevated Ki67. Test for CD146 and PLAP were positive while p63 negative, with no endothelial infiltration.

A TC scan confirmed the mass presence, showing a hypodense neoformation 50 x 42 x 50 mm located in the

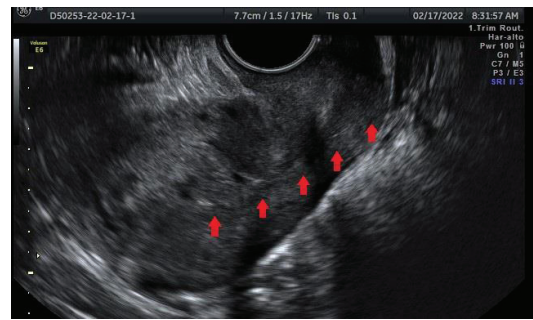


Figure 3: Tru-cut biopsy under transvaginal ultrasound guide: it is possible to see the uterus affected by placental site trophoblastic tumor and the echogenicity of the tru-cut during the procedure.

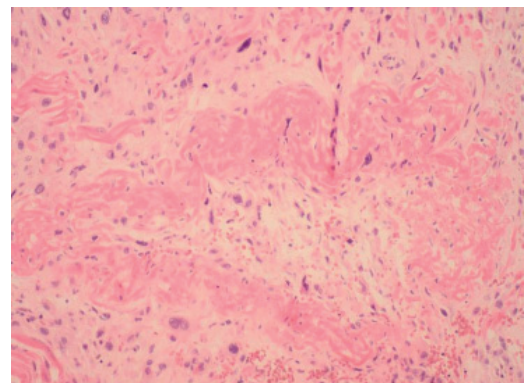


Figure 4a: Hematoxylin eosin 10x: Atypical extravillar intermediate trophoblast elements mixed with fascicles of leiomyuscular tissue.

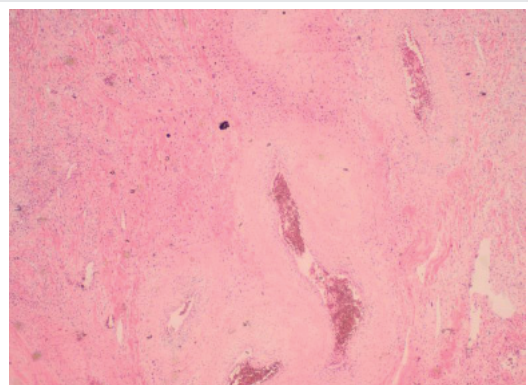


Figure 4b: Hematoxylin eosin 2x: Atypical extravillar intermediate trophoblast elements attached to vascular walls.

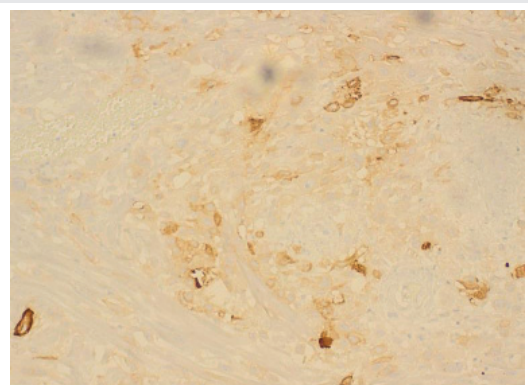


Figure 4c: Hematoxylin eosin 10x: Atypical extravillous intermediate trophoblast elements positive on immunohistochemical staining for placental alkaline phosphatase (PLAP).



uterine fundus (the same site of placenta during the first pregnancy), highly vascularized, with nodular varicosities, seemingly regular margins, not passing the uterine surface. No other locations were indicated.

On April the patient was treated with hysterectomy plus bilateral salpingectomy and sentinel lymph node mapping. Right external iliac lymph node and left internal iliac lymph node were identified after injection of 4cc of indocyanine green into the cervix, and removed.

The definitive histological report confirmed placental site trophoblastic tumour without lymph nodes involvement.

The patient's postoperative course was uneventful and she received regular follow-up at our clinic. Currently, the patient is alive, without evidence of disease recurrence after 12 months.

Discussion

Dilation and curettage are considered the first choice to treat uterine abnormal bleeding after an abortion or a mola, but they are invalidated by the inability to perform a targeted biopsy and by the risk of uterine perforation and copious blood loss.

On the other hand, hysteroscopy allows to see the uterine cavity and is the gold standard in case of abnormal uterine bleeding due to intracavitary disease like polyps, leiomyomas, or malignancies; but it becomes less useful in the event of a lesion confined to the myometrium (similar to type 2 and 3 sonographic patterns of PSTT).

In (Table 1) some cases of inefficacy of dilation and curettage or hysteroscopy are reported. On several occasions, these methods were performed twice due to failure at the first attempt. In some cases, a wrong diagnosis led to a significant diagnostic delay.

Specifically, Alexander, et al. [3] and Chang, et al. [4] reported a case series and they found that the percentage of successful curettage for diagnosis of PSTT was 62% and 54%, respectively. Zhang, et al. [5] reported that they directly performed a laparoscopy with an intraoperative frozen section,

thus obtaining a proper diagnosis in the case of PSTT but with a high invasivity compared to the other diagnostic techniques.

Considering its needle-based shaping, tru-cut has a high penetration depth which enhances its efficiency, minimally-invasive and accuracy, in particular under an ultrasound guidance. Tru-cut reduces the after-exam risk of bleeding and it is useful to penetrate into myometrium where PSTT usually grows. It is a safe diagnostic method in the management of advanced, recurrent or atypical abnorminopelvic tumors and thank to the preservation of tissue architecture it offers a high accuracy for grading and typing in case of pelvic tumors.

However, a deep pelvic lesion is a diagnostic challenge too because the risk of injury to space-occupying organs, such as bowel and urinary bladder. Also the route of approach may be limited because of the presence of vessels, nerves and bony structures covering the pelvic cavity. Obesity is considered as an obstacle for the proper performance of trucut biopsy as it reduces the accuracy of ultrasound. Other limits of tru-cut are sampling errors, especially in large tumors, resulting only in necrosis, hemorrhage ore degenerated tissue bits. In case of mixed tumors one component can be missed and hard tumors can result in inadequate reporting.

In our case, both the histological exam of tru-cut sample and of the hysteroscopic removed polyp were satisfactory and concordant. For this reason, the innovative approach with tru-cut should be suggested as an ancillary technique or as a safe alternative for PSTT diagnosis. Indeed, it provides a reliable, minimally-invasive and targeted sampling of the myometrium even in those cases in which the endometrial cavity is not involved by the disease and its use can help avoiding unnecessary, expensive and invasive diagnostic procedures.

Conclusion

To the best of our knowledge this is the first time that such a technique, widely employed in other tumor diagnosis (e.g., breast, thyroid and prostate cancers), has been applied to this type of tumor.

As future directions, the use of tru-cut biopsy, at least as ancillary technique, should not be limited to PSTT diagnosis.

Table 1: Case studies taken from the literature in which biopsy by dilation and curettage or hysteroscopic technique failed.

Author	D & C	Efficacy	Hysteroscopy	Efficacy	Surgery	Efficacy	Others	Efficacy
Alexander, et al. [3]	curettage	PSTT 8/13 (62%)	/	/	hysterectomy	PSTT 4/13 (31%)	ultrasound	1/13 (8%)
Chang, et al. [4]	curettage	Yes (two cases)	/	/	hysterectomy	PSTT	/	/
	curettage	no	/	/	hysterectomy	PSTT	/	/
Zhang, et al. [5]	curettage	48/88 (54%)	/	/	Hysterectomy	PSTT	/	/
	curettage	74/88 (84%)	/	/	Hysterectomy	PSTT	/	/
De Nola, et al. [6]	/	/	/	/	hysterectomy	PSTT	cryostato leiomyoma	PSTT
	curettage	no (mola)	/	/	hysterectomy	PSTT	/	/
Nagamine, et al. [7]	/	/	hysteroscopy	PSTT	Hysterectomy	PSTT+ PSN	/	/
	curettage	twice	/	/	hysterectomy	PSTT	/	/
Ba, et al. [8]	curettage	no, suspicious	hysteroscopy	No: uterine perforation hemoperitoneum	hysterectomy	PSTT	/	/
Sato, et al. [9]	/	/	hysteroscopy	no	hysterectomy	PSTT	/	/
Behnamfar, et al. [10]	curettage	No: hemorrhage	/	/	hysterectomy	PSTT	/	/



It could be applied to the other diagnosis and play a crucial role when patients with suspected oncology conditions are involved.

Author contributions

RS, DP and VR are involved in care of the patient, surgery, conception, manuscript editing. DP, EG, GS involved in data collection, analysis and interpretation. EG, DP, VR in conception and manuscript writing.

Compliance with ethical standards

Institutional Review Board (IRB) approval is not required. Clinical management described it as part of normal clinical practice. We obtained written informed consent from the patient for surgical procedures, as required by normal clinical practice, and also for the publication of this case report and related photographs and it is retained by us.

Précis and accurate

Tru-cut biopsy can help in the diagnosis of placental site trophoblastic tumors through a targeted sampling of the myometrium, especially when the endometrial cavity is not involved.

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