Sonographic characteristics of placental site trophoblastic tumor

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ABSTRACT

Objective To investigate clinical features and ultrasound findings in cases of placental site trophoblastic tumor (PSTT).

Methods Fourteen cases of PSTT treated at our institution between May 2004 and October 2010 were identified and the clinical features and findings on transvaginal sonography (TVS) were investigated. Pathological confirmation of PSTT was obtained in all cases.

Results The most frequent symptoms associated with PSTT were abnormal vaginal bleeding, which was present in 11 cases, and amenorrhea, which was present in five cases. The interval from antecedent pregnancy to diagnosis was 4–36 (median, 12.5) months. Blood serum was positive for beta-human chorionic gonadotropin (β-hCG) at the time of ultrasound examination, although the level was generally low, with a median of 166.2 IU/L (range, 4.5–3480.2). Sonographic presentation of PSTT was classified into one of three types according to the characteristics observed on TVS: Type I, heterogeneous solid mass in the uterine cavity (four cases), with minimal to a moderate degree of vascularization on color Doppler imaging; Type II, heterogeneous solid mass in the myometrium (six cases), with minimal to a high degree of vascularization (only one case was highly vascularized); and Type III, cystic lesions in the myometrium (four cases) with a high degree of vascularization (lacunar-type lesions).

Conclusions Combined with clinical features, characteristics demonstrated by TVS provide evidence for the suspicion of PSTT and could contribute to clinical decision making. Copyright © 2012 ISUOG. Published by John Wiley & Sons Ltd.

INTRODUCTION

Placental site trophoblastic tumor (PSTT) is a rare form of gestational trophoblastic disease, accounting for approximately 1–2% of all trophoblastic tumors. Scully and Young coined the name ‘placental site trophoblastic tumor’ to describe the malignant potential of this tumor1. Since then, fewer than 200 cases have been described in the English language literature2.

Pathologically, PSTT derives from intermediate (placental site) trophoblast tissue. It is typically a slow-growing malignant tumor which usually forms a nodule in the endometrium and myometrium3,4. The gross appearance is gray or yellow with a circumscribed border and hemorrhagic areas.

PSTT may occur after normal or abnormal pregnancy and thus affects women of reproductive age. Symptoms may present weeks to years after the preceding pregnancy. The clinical diagnosis of PSTT can be difficult because signs and symptoms are often non-specific. The most common presenting symptoms are abnormal vaginal bleeding or amenorrhea5–7. Most patients are initially diagnosed by endometrial curettage. The tumor is usually confined to the uterine corpus but may metastasize to the lungs, liver, lymph nodes, brain or other organs. Metastasis can occur years after the initial diagnosis of PSTT.

Ultrasound examination, including Doppler imaging, is helpful in the diagnosis of gestational trophoblastic disease (GTD)8–12. Real-time grayscale sonography can be used to evaluate the presence of a mass within the uterine cavity or the myometrium, which is characterized as solid or cystic, and color Doppler imaging allows in-vivo assessment of tumor blood flow, which in turn reflects tumor angiogenesis13.

Little is known about the characteristic ultrasound findings in cases of PSTT14–21. The aim of this study was to
describe the clinical history of and the ultrasound findings in women with PSTT, and to determine whether there are specific sonographic criteria that could be used prospectively to accurately distinguish PSTT from other lesions.

METHODS

We identified 14 patients with a pathological diagnosis of PSTT with available documentation of ultrasound examination between May 2004 and October 2010 at our institution. Pathology was reviewed to confirm the diagnosis of PSTT in each case. Medical and ultrasound examination records of each patient were reviewed retrospectively. Of the 14 patients included in this study, 10 who were also treated in our institution have been previously described by Chen et al. in a study on clinical features, treatment and outcomes of PSTT. The availability of ultrasound findings was not required for inclusion in the Chen et al. study.

All patients were assessed by transvaginal sonography (TVS) prior to surgery or biopsy using a Logic 7 (GE Healthcare, Asahigaoka, Japan), a Voluson 730 (GE Medical Systems, Zipf, Austria), a Philips HD-11XE (Philips Medical Systems, Bothell, WA, USA), a Technos MPX (Esaote SpA, Genoa, Italy) or a SonoAce 8000 live (Medison, Seoul, South Korea) ultrasound machine. All machines were equipped with a 5.0–9.0-MHz transvaginal probe. The pulse repetition frequency was set at 0.3–1.0 KHz. Presence of a mass within the uterine cavity or the myometrium was evaluated and characterized as solid or cystic tissue. Color Doppler examination was performed to evaluate blood flow within the mass and the degree of vascularization was subjectively classified as: minimal (<5 points of Doppler flow signals detected); moderate (≥5 points of Doppler flow signals or single branching vessel detected); high (multiple focal vessels detected). Intratumoral flow was assessed by spectral Doppler, with the peak systolic velocity (PSV) and resistance index (RI) measured in all cases.

Clinical data collected included age, gravidity, parity, presenting symptoms, type of antecedent pregnancy, interval from antecedent pregnancy to diagnosis and serum beta-human chorionic gonadotropin (β-hCG) level at ultrasound examination. Electrochemiluminescence immunoassay was used to quantify serum β-hCG and the third international reference point was used. It should be noted that, in the paper by Chen et al., β-hCG levels are reported at time of diagnosis rather than at ultrasound examination. Because of the small number of patients, no statistical analysis was performed.

RESULTS

Median age of women in the study was 30 years (range, 25–41). Median gravidity and parity were 2 (range, 1–7) and 1 (range, 1–2), respectively. Antecedent pregnancy was a term delivery in 12 cases (86%) and termination of pregnancy in two cases (14%). Median interval from antecedent pregnancy to diagnosis was 12.5 (range, 4–36) months. Only two cases were diagnosed more than 24 months after the antecedent pregnancy. The most common clinical symptoms were irregular vaginal bleeding and amenorrhea. Eight patients (57%) presented with irregular vaginal bleeding, two (14%) presented with amenorrhea and three (22%) initially presented with amenorrhea and subsequently developed vaginal bleeding. One patient (7%) was asymptomatic.

Positive serum β-hCG levels were observed in all cases at ultrasound examination. The median β-hCG level was 166.2 (range, 4.5–3480.2) IU/L. Although the β-hCG level was generally low, one patient with lung metastases had a high level (3480.2 IU/L).

On TVS, the lesions were of varying sizes with poorly defined borders within the uterus. Maximum diameter of the masses was 2–6 cm, with a mean mass diameter of 3 cm. On color Doppler imaging, the degree of vascularization varied between minimal and high, with blood flow observed in the center or at the border of tumors. Doppler waveform analysis of vessels within the PSTT typically demonstrated high velocity flow and low impedance. The mean RI was 0.36 (range, 0.21–0.46) and mean PSV was 27.2 (range, 11.0–59.4) cm/s.

Sonographic presentation of PSTT was classified into one of three types according to location and characteristics of the lesion. In four cases a heterogeneous solid mass was located primarily in the uterine cavity and these were classified as Type I. In all of these cases there was invasion of the myometrium by the mass to a depth of greater than half of its thickness. Color Doppler imaging showed minimal (n = 1) to moderate (n = 3) vascularization (Figures 1 and 2). In six cases a heterogeneous solid mass was located within the myometrium and these were classified as Type II. In two of these cases, the mass protruded into the uterine cavity. Color Doppler imaging showed a minimal (n = 3), moderate (n = 2) or high degree (n = 1) of vascularization (Figures 3 and 4). In four cases there were cystic lesions within the myometrium and these were classified as Type III. Color Doppler imaging revealed the vascular pattern of a lacunar-type lesion with a marked increase in uterine vascularity, indicating an arteriovenous shunt (Figure 5). Sonographic findings and clinical characteristics of all 14 patients are summarized in Table 1.

DISCUSSION

We believe that a better understanding of the sonographic appearance of PSTT would contribute to the diagnosis of this rare disease. Although TVS did not ultimately lead to a diagnosis in the patients in this study, uterine lesions were detected in all cases. We classified the sonographic presentation of PSTT into one of three types according to location and characteristics of the lesion. Type I lesions were located in the uterine cavity and Type II and III lesions within the myometrium. It is interesting to note that the interval from previous pregnancy to presentation was, on average, lower in cases of Type I than in cases of Type II and III lesions, although the small sample size for each group prevented statistical analysis.
Table 1 Summary of sonographic findings and clinical characteristics in 14 cases of placental site trophoblastic tumor

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years)</th>
<th>Gravidity</th>
<th>Parity</th>
<th>Antecedent pregnancy</th>
<th>Interval to diagnosis (months)</th>
<th>Amenorrhea</th>
<th>Vaginal bleeding</th>
<th>β-hCG (IU/L)</th>
<th>Lesion type</th>
<th>Vascularity</th>
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<td>31</td>
<td>1</td>
<td>2</td>
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<td>–</td>
<td>+</td>
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<td>Type I</td>
<td>Moderate</td>
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<td>2</td>
<td>1</td>
<td>Term delivery</td>
<td>4</td>
<td>–</td>
<td>+</td>
<td>157.2</td>
<td>Type I</td>
<td>Minimal</td>
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<td>27</td>
<td>4</td>
<td>1</td>
<td>Term delivery</td>
<td>6</td>
<td>–</td>
<td>+</td>
<td>175.2</td>
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</tr>
<tr>
<td>4</td>
<td>28</td>
<td>2</td>
<td>1</td>
<td>Term delivery</td>
<td>13</td>
<td>–</td>
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<td>Term delivery</td>
<td>10</td>
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<td>+</td>
<td>204.3</td>
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<td>Term delivery</td>
<td>8</td>
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<td>–</td>
<td>175.9</td>
<td>Type II</td>
<td>Minimal</td>
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<tr>
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<td>+</td>
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<td>2</td>
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<td>+</td>
<td>208.9</td>
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<td>Lacunar-type lesions</td>
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<td>1</td>
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<td>+</td>
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<td>–</td>
<td>45.7</td>
<td>Type III</td>
<td>Lacunar-type lesions</td>
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</table>

TOP, termination of pregnancy.

With regard to sonographic characteristics of the lesions, Types I and II were solid masses and Type III were cystic lesions. Associated cystic spaces and prominent blood vessels have been described in most reports on PSTT\textsuperscript{19–21}. However, Abulafia \textit{et al.}\textsuperscript{18} described one case of PSTT as a well circumscribed solid mass within the myometrium without prominent vascularity. In this study, although a few cases presented cystic lesions with markedly increased vascularization on color Doppler imaging, in most cases there were poorly defined solid lesions with minimal to moderate vascularization, with a high degree of vascularization in one case.
Transvaginal ultrasound images in a Type II placental site trophoblastic tumor: (a) demonstrating a heterogeneous echogenic mass at the fundus of the uterus, displacing the endometrium, and (b) showing moderate blood flow within the mass on color Doppler imaging.

The differential diagnosis of PSTT includes other forms of gestational trophoblastic neoplasia (GTN), retained products of conception (RPC) and uterine arteriovenous malformation (AVM). Because PSTT is composed of neoplastic intermediate trophoblast cells, which produce only a small amount of hCG, serum levels of β-hCG are much lower in PSTT than in invasive mole or choriocarcinoma. In most cases of PSTT in this study there were solid intrauterine lesions without a high degree of vascularization, suggesting that PSTT should be suspected in patients with this finding who present with amenorrhea or vaginal bleeding and a low serum β-hCG level. This is in contrast to the common findings of cystic lesions with prominent blood flow and high β-hCG levels in cases of invasive mole. The sonographic features of choriocarcinoma are variable. They have been reported to resemble invasive mole but also heterogeneous masses associated with areas of necrosis and hemorrhage. The latter may resemble the Type I and II PSTT lesions described in this study, although choriocarcinoma is always markedly hypervascular on color Doppler imaging. We therefore consider that hypervascular PSTT lesions are particularly difficult to distinguish from other forms of GTN.

 RPC often resemble GTN (including PSTT) on ultrasound examination, and the general opinion is that they cannot be distinguished by sonographic characteristics alone. Another confounding factor is that β-hCG levels are usually only mildly elevated in cases of both PSTT and RPC. Therefore, RPC is the main
with normal surrounding myometrial perfusion. The sonographic appearance of Type III lesions in our series could be identical to that of an AVM, with the only distinguishing feature being an elevated β-hCG level in PSTT.

Unlike other types of GTN, PSTT is relatively unresponsive to chemotherapy, and therefore surgery remains the cornerstone of treatment. When prominent tumor vascularity is detected by color Doppler imaging, hysteroscopic biopsy for histological diagnosis rather than dilatation and curettage should be considered, because the latter may cause uncontrollable hemorrhage. On the other hand, conservative uterine surgery may be possible in patients with localized, hypovascular lesions.

In conclusion, we classified the sonographic presentation in cases of PSTT according to location and characteristics of the lesion; however, the generalizability of our results may be limited by the small sample size. In combination with clinical features, the findings described on sonographic examination could be helpful in raising the suspicion of PSTT and therefore contribute to clinical decision making.

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