

Placental site trophoblastic tumour: the value of transvaginal colour and pulsed Doppler sonography (TV-CDS) in its diagnosis: case report

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Summary

The clinical, transvaginal sonography and colour flow mapping of one patient with placental site trophoblastic tumour is presented. Colour Doppler documented a marked increase in uterine vascularity, characterised by low diastolic flow suggestive of low resistance blood flow, without regression after completion of apparently successful chemotherapy, when negative β -hCG plasma levels were obtained.

Surgical treatment was based upon our experience with colour Doppler assessment of gestational trophoblastic tumours and a review of the literature.

This case suggests that TV-CDS, performed serially, is very useful in monitoring patients during chemotherapy and in detecting residual tumour, and should greatly increase the accuracy of diagnosis of PSTT.

Key words: Placental Site Trophoblastic Tumour; Transvaginal colour and pulsed Doppler sonography.

Introduction

Placental Site Trophoblastic Tumour (PSTT) is the most recently recognised and rarest form of gestational trophoblastic tumour. Approximately 100 cases have been reported in the English literature [1], most of them individual case reports and in limited series [1-5]. Like choriocarcinoma, it can follow any type of normal or abnormal pregnancy, and its natural history and risk factors are not well-understood; its clinical course is variable, ranging from a condition that can be cured to persistent or metastatic diseases resistant to chemotherapy, which can be fatal. Because of this tumor's poor response to chemotherapy, early diagnosis, followed by hysterectomy, is believed to be the best treatment.

The use of vaginal sonography with colour flow Doppler, enabling detailed non-invasive assessment of morphology and tumour blood supply, has recently been used for the evaluation of malignant trophoblastic tumours [6, 7, 8]. From our experience, transvaginal and colour pulsed-Doppler Sonography (TV-CDS) is useful in monitoring the effectiveness of treatment because vascular areas tend to regress, disappearing completely with successful chemotherapy [9]. The clue to a correct diagnosis of PSTT is the detection of persistent blood flow with β -subunit of human chorionic gonadotrophine (β -hCG) plasma levels lower than those seen in choriocarcinoma, reflecting the histology of PSTT, which is composed mainly of extravillous intermediate trophoblast and a small amount of syncytiotrophoblast cells.

The following case illustrates the value of TV-CDS in the diagnosis and management of placental site trophoblastic tumour.

Case Report

MASM, a 42-year-old woman, who was gesta III, para I, was admitted to the local hospital in April 1993, because of a six week pregnancy with heavy irregular vaginal bleeding. She underwent dilatation and curettage. The pathologic report demonstrated a complete hydatiform mole.

After she was discharged to the outpatient department, weekly serum β -hCG levels were done. Because of persistent postevacuation β -hCG serum levels, she was treated with single-agent chemotherapy for nonmetastatic gestational trophoblastic neoplasia. The β -hCG level prior to the therapy was 8,174 UI/L and after eight courses of methotrexate (50 mg a day), β -hCG was still present at 72.2 UI/L.

In November 1993, the patient was sent to the Gynaecology Department at the University Hospital with the diagnosis of persistent gestational trophoblastic disease failing to respond to methotrexate.

Examination on admission disclosed an enlarged uterus, with bilateral ovarian cysts confirmed by pelvic sonogram. The haematological and biochemical indices, the chest x-ray, the hepatic sonogram and brain computed tomography scan were normal. The β -hCG serum levels were 264 UI/L and one week later were 327 UI/L.

Before multiagent regimen was performed, the patient was enrolled in our study for assessment of persistent gestational trophoblastic tumours by transvaginal colour and pulsed Doppler sonography. The purpose of this study was to evaluate prospectively the blood flow characteristics of the intratumoral vascularisation at initial diagnosis, during chemotherapy, and when negative β -hCG levels were obtained. The equipment used was a colour Doppler ultrasound unit, Toshiba sonolayer SS140 with a 6 MHz transvaginal probe. The high pass filter was set at 50 Hz to eliminate low frequency signals caused by vessel motion.

On each examination, the uterus was carefully scanned using colour Doppler sonography for evidence of increased intratu-

moral blood flow, and pulse Doppler was used to obtain a spectral analysis. From the waveform the pulsatility (PI) and resistance (RI) indexes were calculated. Spectral analysis of intratumoral blood flow was performed during three consecutive cardiac cycles and the lowest value obtained was used as the representative value.

The first sonography and colour Doppler flow mapping (Fig. 1), performed before the onset of multiagent chemotherapy with a combination of cisplatin, etoposide and methotrexate, showed a heterogeneous mass located within the myometrium, at the left uterine wall, close to the cornu, containing echolucent lacunar areas and multiple serpiginous sonolucent structures with abnormally increased colour flow. Spectral analysis of sampled vessels demonstrated low PI and RI suggestive of low resistance blood flow. After the second course, the patient exhibited marked decrease of serum β -hCG levels and the second Doppler flow mapping, performed at this time, demonstrated the maintenance of a low impedance pattern. TV-CDS was repeated after four cycles of chemotherapy, when biochemical remission was achieved with β -hCG of 2.6 UI/L. The vessels still appeared prominent and dilated, confirmed by spectral analysis as having increased diastolic flow. The patient underwent two more cycles of chemotherapy, the last one on 14/3/95. The fourth colour Doppler flow mapping of intratumoral blood vessels, performed after the last cycle, showed persistence of abnormal, low resistance blood flow despite the fact that the patient was considered clinically free of disease. Serial β -hCG determination remained negative for 6 months. In September 1994, a little increase of β -hCG levels was noted, 20 UI/L, which dropped to 8 UI/L in a subsequent determination. Colour flow Doppler documented the persistence of dilated and tortuous vessels with decreased vascular impedance which were very similar to the initial pattern (Fig. 2).

The details of serial spectral analysis and of β -hCG values are summarised in table 1. By analysis of table 1, we can see that intratumoral IP and IR remained low and did not correlate with β -hCG titres.

Because of the highly abnormal findings on the Doppler examinations a total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed on 24/10/94. Pathologic examination of the uterus demonstrated within the uterine cavity, in the left antero-lateral uterine wall, a well-circumscribed tumour mass measuring 3 cm in diameter. The tumour was noted to have invaded the myometrium, dissecting between individual muscle fibers and invading the blood vessel walls from the periphery to the lumen. The cellular population was composed mostly of intermediate trophoblast and a few syncytiotrophoblast cells with no evidence of chorionic villi (Figs. 3 & 4). The nuclear atypies were scanty and the mitotic activity was of two mitosis per ten high power fields. These findings are consistent with a placental site trophoblastic tumour.

Immunohistochemical staining for cytokeratin confirmed the histologic finding. A determination of human lactogen placental serum (HPL) was done prior to the operation, but none were identified.

Serum β -hCG levels monitored postoperatively were normal. The patient is alive without any evidence of disease recurrence.

Discussion

The invasion and destruction of myometrium vasculature by trophoblastic tumours cause the formation of blood lacunae and arteriovenous shunts that are responsible for uterine hemodynamic changes which are particularly suitable for blood flow study by TV-CDS. The

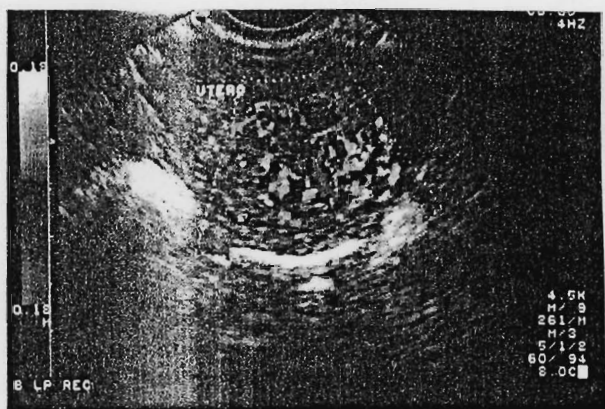


Figure 1. — Transvaginal sonography showing intramyometria hypoechoic channels and spaces exhibiting increased colour flow.

tumour vessels exhibit a low impedance pattern, characterised by a high velocity diastolic component and little systolic/diastolic variation resulting in a decrease of RI and PI values. Lower RI and PI values indicate more severe destruction of the uterine vasculature. Spectral analysis can be assessed in uterine arteries and intratumoral vessels which are dilated with increased blood flow, necessary to meet the demands of the developing tumour [10].

Previous reports have described the role of Doppler ultrasound techniques in identification and localisation of lesions [8] and in investigating the uterine haemodynamic changes in patients with trophoblastic neoplasia requiring chemotherapy. Long *et al.* (1992) [11] used the transabdominal and pulsed-Doppler to assess the uterine arteries prior to the commencement of treatment to help predict those patients who would develop drug resistance for first line chemotherapy. Hsieh *et al.* (1994) [12] used TV-CDS serially at diagnosis and before each course of chemotherapy with the same purpose. Carter *et al.* (1993) [13] analysed the blood flow characteristics in intratumoral vessels in 11 patients known to have persistent

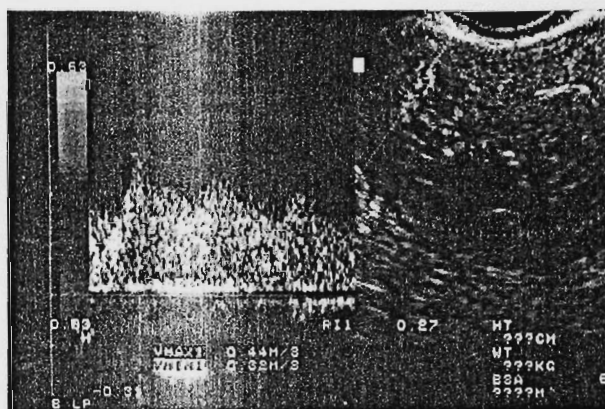


Figure 2. — Transvaginal sonography showing persistence of vascularity of tumour after completion of chemotherapy. A Doppler cursor within the tumour demonstrates a low impedance pattern characterised by a high diastolic component with a very low value of RI.

Table 1. — Serial spectral analysis and details of β -hCG values

| | β -hCG | Doppler examination | |
|------------------------------|--------------|---------------------|---------|
| Prior to the therapy Nov. 93 | 324 UI/L | RI=0.39 | PI=0.50 |
| After 2 cycles 14/12/93 | 57 UI/L | RI=0.32 | PI=0.37 |
| After 4 cycles 21/2/94 | 2.4 UI/L | RI=0.38 | PI=0.50 |
| After the last cycle 14/3/94 | 2 UI/L | RI=0.28 | PI=0.35 |
| On 22/9/94 | 20 UI/L | RI=0.27 | PI=0.35 |
| On 21/10/94 | 8 UI/L | | |

trophoblastic tissue. The PI of uterine and intratumoral vessels were associated with prognosis, and a direct correlation between β -hCG titres and PI was noted. From our experience TV-CDS could be useful in monitoring the response to chemotherapy and as a guide for localisation of residual tumour bulk. When normalisation of β -hCG levels was achieved there was an increase in the vascular resistance in the intratumoral vessels and a subsequent disappearance of intramyometrial blood flow, indicating a non-existent trophoblastic mass.

Because of the difficulty in obtaining tissue for histologic examination the majority of patients are treated on the basis of β -hCG serum determinations, without knowing whether the disease is an invasive mole, a choriocarcinoma or a PSTT. In the case reported, the diagnosis of PSTT was suspected preoperatively because of the persistence of abnormal Doppler findings with the PI and RI values remaining low after apparently successful chemotherapy and a very low increase of β -hCG levels after biological remission was achieved.

To the best of our knowledge, this is the first description of a suspected PSTT because of TV-CDS findings which provided accurate evaluation of residual tumour, remaining for more than six months after the completion of chemotherapy. The colour Doppler was very useful in detecting a persistent focus of the tumour and in guiding the treatment choice. Otherwise, the small increase of β -hCG (20 UI/L), which rapidly dropped to normal values, and lack of symptoms would have been responsible for a delay in performing surgery. This delay in diagnosis and treatment could have been fatal as this tumour had a poor



Figure 3. — Placental-site trophoblastic tumour. The cytotrophoblast and intermediate trophoblast cells have invaded the myometrium, splitting muscle fibers. The neoplasm is composed mostly of large polyhedral mononuclear cells with slight nuclear pleomorphism. (Hematoxylin-eosin stain. 10 X magnification).

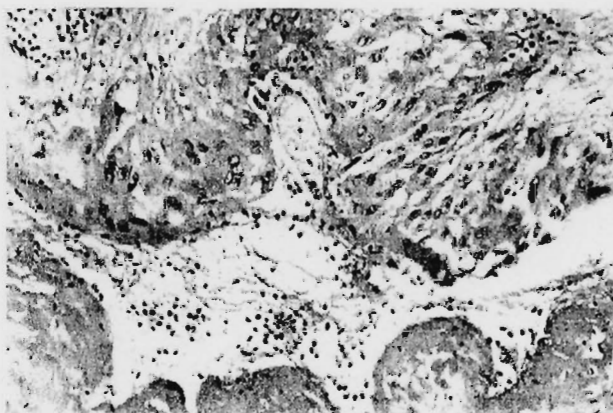


Figure 4. — Placental-site trophoblastic tumour. Large vessel with fibrinoid deposition in the wall, that suffered invasion by intermediate trophoblast from the periphery to the lumen. (Hematoxylin-eosin stain. 10 X magnification).

response to chemotherapy and its biological aggressiveness would have been difficult to predict.

Some reports in the literature illustrate the difficulties encountered in the diagnosis and management of this tumour [4, 14]. Its clinical behaviour is unpredictable; some behave in a benign fashion and can be cured by hysterectomy or curettage alone, whereas others are malignant and approximately 10% are fatal [1, 3, 15]. Although the serum β -hCG remains the most sensitive marker for evaluating chemotherapeutic response in gestational trophoblastic tumours, its sensibility is limited to the tumours composed of syncytiotrophoblast cells. In PSTT, composed mainly of extravillous intermediate trophoblasts, which synthesise mostly human placental lactogen and scanty amounts of β -hCG, this marker cannot be used as a reliable tumour marker because it is detectable only when a large tumour is present [4]. There are five reported cases of PSTT with normal β -hCG levels and one case with 25 UI/L of β -hCG [1, 14].

In terms of prognosis, the most important indicator is mitotic activity. PSTT with a high mitotic count per 10 high power field (HPF) have been reported to have a greater risk of developing metastases [2, 16], however, a metastatic potential exists for tumours with mitotic counts of less than 5 per 10 HPF. One patient developed a pelvic recurrence despite a mitotic count of 3 per 10 HPF and in 10 reported deaths, one patient had a mitotic count of 2 per 10 HPF [1, 4].

This case suggests that TV-CDS performed serially played a role in detecting active residual tumour and should greatly increase the accuracy of diagnosis of PSTT. We believe that this technique should be introduced in pre-treatment assessment of gestational trophoblastic tumours and in evaluating treatment response, especially in tumours that are resistant to chemotherapy.

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