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Placental site trophoblastic tumour: Clinical features and management

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Abstract

Objective. To describe the clinical features, treatment and outcome of all consecutive patients with placental site trophoblastic tumour (PSTT) treated at the Sheffield Trophoblast Centre and to compare these findings to other reports.

Method. All cases of PSTT on the Sheffield Trophoblastic Tumour Centre database from 1984 to 2004 were reviewed. Data obtained included age at diagnosis, antecedent pregnancy (AP), interval from antecedent pregnancy until diagnosis, presenting features, presenting serum human chorionic gonadotrophin hormone (hCG) level, number and sites of metastases, treatment received, outcome and follow-up.

Results. Seventeen patients with PSTT were identified from the database which incorporates a total of 7489 cases of trophoblastic disease. Fourteen (70.6%) were more than 30 years old at presentation; 5 were over 40. The median interval from pregnancy to diagnosis was 18 months (range 6 months to 22 years). The outcome of antecedent pregnancy was a female in 11 out of the 13 patients where the sex was known. Eleven (70.6%) of patients presented with irregular vaginal bleeding, with or without a preceding period of amenorrhoea. All 8 patients with non-metastatic (Stage I) disease were alive and well after hysterectomy (6), chemotherapy alone (1) or hysterectomy and chemotherapy (1) whereas only 4 of 9 patients with metastatic (Stage III/IV) disease were alive and well after treatment with chemotherapy and hysterectomy.

Conclusion. PSTT is rare and accounts for 0.23% cases of gestational trophoblastic disease referred to this centre. It has a variety of presenting features and its course is unpredictable. Metastatic involvement and antecedent pregnancy interval greater than 4 years are poor prognostic factors. Hysterectomy is the primary mode of treatment in the majority of cases. However, chemotherapy can still play a major role when curative surgery is not feasible.

Keywords: Placental site trophoblastic tumour; Features

Background

Placental site trophoblastic tumour (PSTT) is a rare form of gestational trophoblastic disease (GTD). The first observations were made in 1895 and 1910 by Merchand and Ewing, respectively, and the clinical and pathological characteristics of PSTT were described in 1976 by Kurman and Scully when the term 'trophoblastic pseudotumour' was adopted to characterise the apparently benign nature of the disease [1]. Subsequent case reports described evidence of a sometimes aggressive, malignant and fatal course of the disease and the nomenclature was changed to placental site trophoblastic tumour in 1981 [1,2]. Histopathologically, it is characterised by a neoplastic monomorphic population of implantation-like intermediate trophoblastic cells, often as sheets of polyhedral, rounded or occasionally spindle-shaped cells extensively infiltrating the myometrium. Due to the rarity of this type of tumour, there is little information about its epidemiology and aetiology and few large series on diagnosis and treatment have been published [3]. It is seen

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mostly in patients of reproductive age and can follow a normal pregnancy, miscarriage or gestational trophoblastic disease [4–7]. Irregular vaginal bleeding has been the most commonly reported presenting feature, but a wide range of other symptoms have also been reported including galactorrhoea, virilization [8], nephrotic syndrome [9,10] and polycythaemia [11]. In view of the scarcity of PSTT, we have reviewed the clinical features and management of consecutive patients presenting to the Sheffield Trophoblastic Tumour Centre.

Method

All UK patients with GTD are consented and registered with one of three Trophoblast Centres. During the period of study (1984–2004), 7489 were registered at the Sheffield Centre. In those with PSTT data obtained included patient age at diagnosis, antecedent pregnancy (AP), interval from antecedent pregnancy until diagnosis, presenting features, presenting serum β human chorionic gonadotrophin (hCG) levels, metastases (number and sites), new FIGO [12] stage and score, treatment received, outcome and follow-up.

Results

Seventeen patients with PSTT were identified. In all cases, the pathology specimen was centrally reviewed. In 12 cases, PSTT had been suspected locally and was confirmed on central review. In 5 cases, the diagnosis made locally was changed to PSTT on central review.

Clinical features

The median age of patients at presentation was 35 years (range 26–52), 14 patients were over 30 years of age; 5 were over 40. Previous pregnancy was recorded in 16 patients; the antecedent pregnancy was normal term delivery in 13 cases resulting in 11 females and 2 male offspring, miscarriage in 2 cases, elective termination in 1 case and unknown in 1 case. The median interval from pregnancy to diagnosis was 18 months (range 6 months–22 years). All the patients in this series were symptomatic at presentation. Irregular vaginal bleeding was the most common presenting feature occurs in 8 (47%) of 17 patients. Other presentations included (in order of decreasing frequency) amenorrhoea (4 cases), ruptured uterus (2 cases), abdominal pain (2 cases), post menopausal bleeding (1 case) and an enlarged neck node (1 case).

Extent of disease

Eight patients had widely metastatic disease at presentation and one patient had regional disease. Eight patients had negative staging investigations including abdominal ultrasound scan, CT scan of the head, abdomen and pelvis, chest X-ray, clinical chemistry and haematology and MRI scan in selected patients. The lungs were the most common site of metastases in this series. In fact, all patients who presented with distant metastases had pulmonary deposits. Other sites of metastases included liver (3 cases), vagina (2 cases), brain (1 case), pancreas (1 case) and kidneys (1 case). The median serum ßhCG at diagnosis was 13,923 iu/l (range 6–107,600 iu/l), but 10/17 had levels of less than 500 iu/l. A breakdown of various clinical factors thought to be of prognostic import is given in Table 1.

Treatment and outcome

All patients are summarised in Table 2. Eight patients presented with disease confined to the uterus at diagnosis. Total abdominal hysterectomy was the primary treatment in 6/8 patients with ovarian conservation in 5/6. All six patients are well and alive with no evidence of disease (follow up 0.25–11 years). Two patients were initially treated with methotrexate. One, treated with 'low risk' methotrexate (methotrexate 50 mg im on alternate days ×4; folinic acid 7.5 mg oral 24 h after MTX; 7 days between cycles), is disease free at 5 years. The other was initially treated with methotrexate after presenting with a suspected ectopic pregnancy. However, her hCG levels remained high so she underwent total abdominal hysterectomy with subsequent normalisation of her beta hCG levels. She is currently free of the disease with 8 years follow up.

Nine patients had metastatic disease at the time of presentation; four patients have died of their disease and one is alive but with active disease. Four patients are alive and well (follow up 2.5–11 years). Two were treated with 'low risk' methotrexate and both needed treatment with second line chemotherapy. One patient received dactinomycin and

Table 1
Patient groups according to risk factors

		Dead	Alive
Risk score	Low (13)	1	12
	High (4)	3	1
Stage	I (8)	0	8
	II (1)	0	1
	III (5)	1	4
	IV(3)	2	(1)
HCG (iu/L)	Low <500 (10)	1	8 (1)
	Medium (3)	0	3
	High >10 k (4)	3	1
Interval to antecedent pregnancy (months)	≤6 (4)	0	4
	≤24 (6)	1	5
	≤48 (2)	0	1 (1)
	>48 (5)	3	2
Age (years)	≤39 (12)	1	11
	≥40 (5)	3	1 (1)
Outcome of AP	Term (13)	4	8 (1)
	Unknown (1)	0	1
	Miscarriage (2)	0	2
	Termination (1)	0	1