CASE REPORT

Placental site trophoblastic tumour: An unpredictable clinical course

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SUMMARY

Placental site trophoblastic tumour (PSTT) is a rare entity within the spectrum of gestational trophoblastic neoplasia (GTN). This condition is known for its rare occurrence and unpredictable clinical course. The diagnosis of this condition is complicated further by its lack of specific clinical or imaging features or biochemical markers for its diagnosis. We report a case of PSTT following a normal pregnancy with a previous history of molar pregnancy in the past which was treated with chemotherapy due to persistent gestational trophoblastic disease.

INTRODUCTION

Placental site trophoblastic tumour (PSTT) is a very rare disease belonging to gestational trophoblastic neoplasms (GTNs).[1] It constitutes from 0.23%[2] to 3.00%[3] of all gestational trophoblastic disease (GTD). Notably, none have been reported in Malaysia.[4] PSTTs differ from other GTNs as they grow more slowly and produce less ß-hCG relative to other GTN and are relatively resistant to chemotherapy.[5,6] This disease is significant because it has a higher disease-specific mortality compared to other GTD subtypes (16.1% for PSTT compared to 13.4% for choriocarcinoma).[7]

CASE REPORT

A 31-year-old woman (gravida 4, para 2) was referred to our centre 3 months postpartum with continuous per vaginal staining and elevated beta human chorionic gonadotrophin (ß-hCG) levels at 1371 mIU/mL compared to a normal level of less than 2 mIU/mL. She was diagnosed with a molar pregnancy (FIGO risk score 2; low-risk GTD) 3 years prior for which she required chemotherapy for persistent GTD and had completed 2 years of follow-up. This latest pregnancy and delivery was uncomplicated but unfortunately, she did not have her placental tissue sent for histopathological examination. A CT scan on first encounter with us showed a rounded intrauterine lesion measuring about 2 × 2 cm.

Subsequently, a decision to initiate chemotherapy was made as her ß-hCG levels had plateaued at about 300–400 mIU/mL (Figure 1). The patient was treated with eight cycles of methotrexate and folinic acid – the initial response was promising with ß-hCG levels declining dramatically after the first few cycles. However, the levels again plateaued but this time at between 30 and 40 mIU/mL during her last four cycles (Figure 1). She was subjected to another CT scan which showed a smaller intrauterine lesion measuring 0.4 × 0.4 cm in comparison to before. At this point, the diagnosis of PSTT was suggested as although the intrauterine lesion was smaller than before, it was relatively chemo-insensitive and her ß-hCG levels were persistently elevated. To confirm the diagnosis, the patient was subjected to imaging with positron emission tomography–computed tomography (PET-CT). A serum human placental lactogen (hPL) was done as well. The serum hPL was elevated while the PET-CT showed a hypermetabolic linear focus in the endometrium with SUVmax of 2.63 and did not detect any presence of metastasis.

After extensive counselling and discussion with the patient, she consented to a laparotomy, total hysterectomy with bilateral salpingectomy and ovarian conservation. The intraoperative survey was otherwise unremarkable. Post operatively, the cut section of the hysterectomy specimen revealed a smooth endometrial lining with no obvious tumour visible. The patient recovered well following surgery and the histopathological report showed a circumscribed intramural lesion 12 × 10 mm beneath the endometrial stroma, the tumour was infiltrating less than half of the myometrial thickness with two mitotic figures seen per high-power field. No lymphovascular permeation was seen. The immunohistochemical staining was positive for hPL (Figure 2) while being focally positive for PLAP and ß-hCG. Ki-67 proliferation index was reported as less than 20%. The final histopathological examination was reported as PSTT. Subsequently, the patient did not have any post-operative chemotherapy and ß-hCG levels normalized following surgery.

DISCUSSION

PSTT was first described in 1976 when it was first described as a "trophoblastic pseudotumour of the uterus" because of its apparent benign nature.[8] The term PSTT was adopted only in the year 1981 after evidence of its malignant behaviour emerged.[9] PSTT is a slow growing malignant tumour mainly arising from the placental intermediate trophoblasts.[5] This condition is a subtype of GTD, which also includes partial mole, complete mole, invasive mole, choriocarcinoma (CC), PSTT and epithelioid trophoblastic tumours (ETT).[1] Of these conditions, CC, PSTT, and ETT are also called gestational trophoblastic neoplasia due to their malignant potential.[1]

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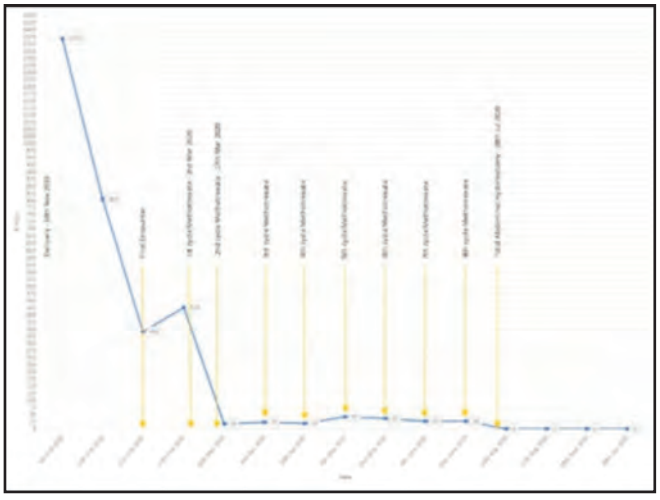

Fig. 1: ß-hCG trend on treatment.

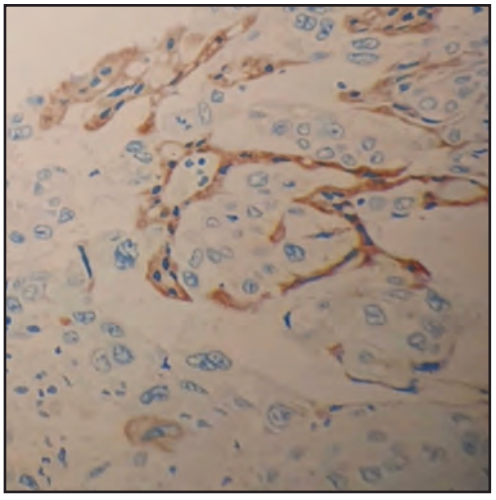

Fig. 2: Immunohistochemical staining positive for hPL.

PSTT usually occurs in women of childbearing age.[6] Typically, PSTT follow normal term pregnancies but can occur after any pregnancy event including molar pregnancy and choriocarcinoma and can present from months to several years after the antecedent pregnancy event.[5,6] Most PSTT develops within 1 year after the antecedent pregnancy.[6] Early stage PSTT exhibits slow growth rates and remain confined to the uterus.[5,6] Due to this, there are not many symptoms other than vaginal bleeding or amenorrhea.[3,5,6] Rarely, some women may present with nephrotic syndrome, haemoptysis, and ascites.[3]

PSTT can also metastasize, and common sites of metastasis include lung, and central nervous system.[5,6] The retroperitoneal lymph nodes, especially the paraaortic lymph nodes, are the most frequent sites of lymphatic metastasis.6 The presenting symptoms are non-specific, and a high index of suspicion plays an important role in diagnosis.

Compared to other trophoblastic tumours, the serum ß-human chorionic gonadotropin (ß-hCG) levels are usually (about 85%) only mildly elevated (ß-hCG < 1000 IU/L) in PSTT patients.[3] In fact, there is no direct correlation between tumour burden and ß-hCG value.[2] This, in addition to the usually low levels of ß-hCG make using ß-hCG a less reliable tumour marker. While PSTT tissue itself generally strongly stains for human placental lactogen (hPL), serum hPL has not been proven to be useful in monitoring the disease or guiding clinical management.[5]

Imaging modalities used in the diagnosis of PSTT include ultrasound which may highlight features shared by GTNs, such as echogenic and vascular masses involving the endometrium and the myometrium.[10] The presence of myometrial invasion can be confirmed using pelvic magnetic resonance imaging (MRI).[10] PET-CT is not a regular imaging tool, but it has great potential in assessing and excluding metastases.[10]

Following diagnosis, treatment depends on the stage of the disease. In early-stage disease (Stage 1) a simple hysterectomy would suffice considering PSTT's relative resistance to chemotherapy.[5,6] The role for lymphadenectomy in Stage I disease is controversial.[5] Patients with Stage II–IV disease are advised for hysterectomy followed by adjuvant chemotherapy.[5,6] Although there are several chemotherapy regimens to treat PSTT, the optimal one has not been identified due to the rarity of this disease. EP/EMA (etoposide and cisplatin with etoposide, methotrexate, and dactinomycin) however seems to be the preferential first-line therapy as studies show it leads to a higher remission rate.[6]

On histopathological examination, PSTT shows intermediate trophoblastic cells without chorionic villi infiltrating the muscle fibres. One of the main tools in the diagnosis of this condition is immunohistochemistry – it is diffusely positive for hPL and Mel-CAM (CD146) while being focally positive for placental alkaline phosphatase (PLAP) and hCG.[5,6] Ki-67 proliferation index could reach 15% compared to choriocarcinoma which can exceed 50%.[6] There is potential for the use of liquid biopsy in the diagnosis of PSTT in the future.[6]

CONCLUSION

PSTT is difficult to diagnose. The approach to the diagnosis requires a combination of serum ß-hCG levels, imaging, tissue biopsy if feasible for histopathological examination with immunohistochemistry testing. Of course, a high degree of suspicion should always be present when encountering persistent GTD that is chemo-insensitive especially in combination with modestly elevated ß-hCG levels. Surgery is the mainstay of treatment. This generally means a hysterectomy. There is no current consensus available on the type of chemotherapy to be given for metastatic disease or disease recurrence.

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