CASE REPORT

Pregnancy presenting as hyperthyroidism with negative urine pregnancy test

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SUMMARY

A 22-year-old lactating mother presented with symptoms of uneasiness, palpitation, tachycardia and exophthalmos. She had an abdominal lump suggestive of 26 weeks uterine size but her urine pregnancy test was negative. Her thyroid profile was suggestive of hyperthyroidism. Gynaecological and ultrasonographic findings revealed a hydatidiform mole. She had a low β -human chorionic gonadotropin level that surprisingly increased after suction and evacuation. The paradoxical findings that appeared as erroneous laboratory results could be explained by the 'high-dose hook effect' after a review of literature. One week after the evacuation, the patient's thyroid profile and symptoms resolved completely without any treatment for hyperthyroidism.

BACKGROUND

Molar pregnancies comprise a spectrum of diseases varying from benign partial hydatidiform mole (H. Mole) on one hand to malignant choriocarcinoma on the other. These patients most commonly present with vaginal bleeding. Uterine size is larger than the period of gestation, usually by around 4 weeks. Excessive uterine size is often associated with markedly increased levels of β -human chorionic gonadotropin (β HCG) from trophoblastic overgrowth. Abdominal pain, toxemia and hyperemesis gravidarum are other associated features. Clinically evident hyperthyroidism is uncommon, though laboratory evidence of hyperthyroidism is frequently found.¹

We present a case of complete H. Mole that presented with features of hyperthyroidism to the department of internal medicine. The patient had an unreliable menstrual history as she was lactating. She had a negative urinary pregnancy test (UPT). Her gynaecological examination and ultrasonography led to correct diagnosis and treatment. This case illustrates the possibility of a false-negative urine HCG point of care assay in a case of H. Mole due to the 'high-dose hook effect'.² Lack of knowledge of this important phenomenon can be misleading and can lead to delayed diagnosis. A high index of suspicion of a molar pregnancy for women in the reproductive age group presenting with hyperthyroidism is required even if (UPT) is negative, especially if her menstrual history is not reliable.

CASE PRESENTATION

A 22-year-old woman came to the medical outpatient department of a hospital with symptoms of palpitation and uneasiness for 10 days. She was

married for 6 years, had delivered a child normally 1 year ago and was lactating. She had her menstrual period around 2 months ago for the first time after the delivery and then spotting for 1 day 10 days ago.

On examination she had pallor, mild pedal oedema and exophthalmos. The lid-lag sign was positive. She was afebrile but had tachycardia with a heart rate of 110/m and her BP was 120/80 mm Hg. She was found to be having abdominal mass suggestive of a 26 weeks gravid uterine size enlargement. Her ECG showed tachycardia with sinus rhythm. Her (UPT) was found to be negative. On investigation she was found to be having a thyroid-stimulating hormone (TSH) of less than 0.1 mIU/mL with T3 and T4 near upper limit of normal. She was diagnosed as a case of hyperthyroidism but before proceeding further with the management of hyperthyroidism, it was considered prudent to take a gynaecological opinion for her abdominal enlargement. She attended the gynaecology department of another hospital where she had delivered her last child. Her gynaecological examination revealed an anteverted, 26 weeks size uterus with slight blood staining on the gloved finger during per vaginum examination. Her UPT was negative once again. Ultrasonography revealed an intrauterine heterogenous mass with numerous anechoic spaces showing snow storm appearance with absence of fetus in the uterine cavity suggestive of a complete H. Mole (figure 1). Bilateral ovaries were bulky and cystic suggestive of theca lutein cysts. Repeat UPT was also clearly negative.

Her β HCG level was only 45 mIU/mL to add to the dilemma, as β HCG levels are expected to be very high in a molar pregnancy. However, since her

Figure 1 'Snow storm appearance' with absence of fetal parts suggestive of a complete hydatidiform mole.

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Figure 2 Grape-like vesicles obtained on suction evacuation.

diagnosis was certain because of the ultrasonographic findings, the laboratory reports were considered erroneous. Suction and evacuation of the molar pregnancy was performed and the evacuated grape-like vesicles were sent for histopathological examination (figure 2). Twenty-four hours post evacuation, her β HCG level was found to be 161 mIU/mL. The increase in her β HCG level after the suction and evacuation was perplexing.

A review of literature was undertaken to understand these findings. It was found that there is a phenomenon known as 'high-dose hook phenomenon' where very high levels of β HCG may lead to falsely low β HCG values and also a negative UPT. Guided by the literature, dilution of the same sample with normal saline was requested and this interestingly resulted in the a β HCG level of greater than 175 200 mIU/mL.

DIFFERENTIAL DIAGNOSIS

The 'high-dose hook effect' leading to falsely low values of β HCG may be seen in other conditions, such as choriocarcinoma and twin pregnancy.³ These conditions are actually associated with very high levels of β HCG but may lead to error in diagnosis as explained below. History of amenorrhoea, negative UPT and mildly raised β HCG levels in the reproductive age group may be seen in ectopic pregnancy and missed abortion. Uterine enlargement with negative UPT as occurred in this case may be mistaken for condition such as uterine fibroid.² Hyperthyroidism with abdominal lump, as seen in this case, may be seen in struma ovarii, where thyroid tissue is present in the ovarian tumour or a thyroid carcinoma with abdominal wall metastasis.⁴ All of these conditions can be differentiated from molar pregnancy on ultrasonography and confirmed on histopathology.

OUTCOME AND FOLLOW-UP

Two days post evacuation, the patient was doing well with a heart rate of 80/m and BP of 114/70 mm Hg. Uterus was well contracted and of 12–14 weeks size. The patient was discharged with contraception advice and asked to follow-up after 1 week with the reports of thyroid profile, serum β HCG levels and histopathology report. One week after evacuation, serum β HCG showed significant decline with the diluted sample showing a value of 28 280 mIU/mL and direct sample of 1749 mIU/mL. Histopathology report revealed complete H. Mole. Her thyroid profile returned to normal after a week of evacuation. The patient was asked to follow-up with weekly β HCG levels.

DISCUSSION

Menstrual history during lactation is unreliable and a UPT is the standard method to determine pregnancy. UPT is considered highly reliable except for a very early pregnancy, where a repeat UPT after some interval becomes positive. However, UPT may be negative in ectopic pregnancy or miscarriage.

A patient presenting with features of hyperthyroidism may not undergo an abdominal examination in a busy medical out patient department (OPD). Our case underscores the importance of complete physical examination in a patient and reminds that H. Mole should be kept as a differential diagnosis of hyperthyroidism in women of reproductive age group. H. Mole produces large quantities of β HCG. β HCG is structurally similar to pituitary TSH and can mimic its actions when present in large quantities. This patient presented with features of hyperthyroidism with a negative UPT. The patient was referred for gynaecological opinion in spite of a negative UPT because of her abdominal lump. It was her gynaecological examination followed by ultrasonography that confirmed her molar pregnancy.

Hundred per cent of patients with molar pregnancy have very high levels of β HCG and hence are expected to have a strongly positive UPT.⁵ This patient was found to be having negative UPT repeatedly and low β HCG levels in spite of molar pregnancy. Conditions such as molar pregnancy that produce large amounts of β HCG may interestingly cause a false-negative UPT and low β HCG levels due to oversaturation of the assay system, known as 'hook effect'.² In a UPT, free and fixed antibodies bind HCG to form a 'sandwich', which is detected because of a colour change. When in great excess, intact HCG can saturate the antibodies to prevent the formation of the 'sandwich'. The 'hook effect' may be seen with various other assays besides β HCG like prolactin, IgE, ferritin, thyrotropin, prostate-specific antigen, albumin and tumour markers such as CA 125, alpha-fetoprotein, etc. This, however, can lead to misdiagnosis and delay in treatment. Negative UPT with low β HCG on serum quantification should be further evaluated by sample dilution in patients with high suspicion of pregnancy.² Cases have been reported where exclusion of pregnancy due to false negative UPT because of high-dose hook effect leads to initial misdiagnosis of a molar pregnancy as degenerative fibroid, delayed diagnosis or even death in cases of choriocarcinoma.^{2 3 6 7}

Learning points

- ▶ Hydatidiform mole (H. Mole) should be considered as a differential diagnosis in women of reproductive age group who present with features of hyperthyroidism.
- ▶ H. Mole may present with a negative urine pregnancy test (UPT) and low β human chorionic gonadotropin (HCG) levels because of 'hook effect'. It can also lead to paradoxical increase in the β HCG values after removal of the trophoblastic disease. This phenomenon can be confirmed by dilution of the serum sample.
- ▶ In patients with a high index of suspicion for molar pregnancy, a negative UPT should be followed by ultrasonographic examination.
- ▶ A complete physical examination should be undertaken in all patients to avoid diagnostic inaccuracies. Opinion of another specialty may be helpful if one is unable to understand the signs and symptoms confidently.
- ▶ Unexpected investigation results should prompt one to review the literature rather than presuming erroneous report.

Competing interests None.

Patient consent Obtained.

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