

Case report

Non-gestational choriocarcinoma as a cause of heavy menstrual bleeding-potential: Primary care detection

Allen Chai Shiun Chat¹, Nani Draman^{2}, Siti Suhaila Mohd Yusoff³, Rosediani Muhamad⁴*

Abstract:

Choriocarcinoma is a malignant trophoblastic disease. It can be divided into gestational and non-gestational type. Gestational choriocarcinoma consists of less than 1% of total endometrial malignancy, and usually is diagnosed via histopathological examination preceding a suspected molar pregnancy. In contrast to gestational choriocarcinoma, only a few cases of primary non-gestational choriocarcinoma were reported in literature reviews. The reported locations for primary non-gestational choriocarcinoma were ovarian and uterine cervix. Due to its low incidence, this disease is often overlooked leading, to delayed diagnosis. In primary care practice, heavy menstrual bleeding is a common presentation. Further evaluations, such as full blood count, ultrasound pelvis or hysteroscopy are usually required.

We would like to report a case of potentially earlier detection of non-gestational choriocarcinoma in a 52 years old lady who was presented with heavy menstrual bleeding for a duration of one year. Her symptom persisted despite receiving medical treatment in a few local primary care clinics. She was admitted to a tertiary hospital for symptomatic anaemia which required blood transfusion. Further evaluations, (i.e., laboratory tests, ultrasound, Computed Topography (CT) scan, bone scan, hysteroscopy and laparotomy total abdominal hysterectomy and bilateral salphingo-oophorectomy (TAHBSO) and histological examination) concluded a diagnosis of primary non-gestational choriocarcinoma of fundal uterus with lung metastasis.

Keywords: Abnormal uterine bleeding; Heavy menstrual; Primary non-gestational choriocarcinoma of uterus; Pervaginal bleeding

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Introduction

Gynaecological malignancy is the fourth most commonly diagnosed cancer after breast cancer, colorectal cancer and lung cancer. Endometrial cancer is the second most common gynaecological malignancy after cervical cancer.¹ A 4-years study showed that a total of 4.1 % of women in Malaysia has endometrial carcinoma.

Endometrial cancer can be detected earlier, since 90% of them presented with postmenopausal bleeding

(PMB).² The risk of malignancy is about 9%.² Therefore, women with PMB are recommended to go for further examination. Contrary to premenopausal women with heavy menstrual bleeding, the National Institute for Health and Care Excellent (NICE) guidelines does not recommend routine referral for further investigation (hysteroscopy or pelvic ultrasound).³ The risk of endometrial cancer in premenopausal women with abnormal uterine bleeding is 0.33%.⁴

1. Allen Chai Shiun Chat, e-mail: acsc1988@hotmail.com

2. Nani Draman, e-mail: drnani@usm.my

3. SitiSuhaila Mohd Yusoff, e-mail: drsuhaila@usm.my

4. Rosediani Muhamad, e-mail: rosesyam@usm.my

Department of Family Medicine, School of Medical Sciences, Universiti Sains Malaysia, Health Campus,16150, KubangKerian, Kelantan, Malaysia.

Correspondence to: Nani Draman, Family Medicine Specialist and Lecturer, Department of Family Medicine, School of Medical Sciences, Universiti Sains Malaysia, Health Campus,16150, KubangKerian, Kelantan, Malaysia. email:drnani@usm.my

Choriocarcinoma is a malignant trophoblastic disease. The differentiation between gestational and non-gestational choriocarcinoma is crucial as it affects the treatment choice and prognosis.⁵ The cause of gestational choriocarcinoma is the result of current or previous pregnancy, while non-gestational choriocarcinoma of the uterus, arises from germ cells or transformation of another cancer.⁶ The location of the cancer in the female genital tract were reported to be mainly at the uterus cervix⁶ and ovary.⁵

Heavy menstrual bleeding is a common presentation in primary care practice, with incidence of 9.3 per 1000 person years.⁷ Almost half of them can be managed with hormonal therapy, but the remaining required further evaluation. Delay referral for further investigation and management occurs in clinical practice despite several international and local guidelines were available, and this led to adverse outcome.

We would like to report a case of non-gestational choriocarcinoma of fundal uterus with lung metastasis when diagnosis was made. We showed that proper evaluation and examination is required for woman in the perimenopausal period with prolonged heavy menstrual bleeding.

Case report

A 52 years old housewife, parity 2, last child birth was 16 years ago, presented with prolonged vaginal bleeding for a duration of one year. She described each of her menses lasted for 20-30 days. More often than not, she requires more than 10 pads per day and each pad will be soaked with blood with passing blood clots. She denied any dysmenorrhea, dyspareunia, and urinary symptoms. She denied any low of appetite or loss of weight. There was no chronic cough, no haemoptysis, or shortness of breath. She also did not have nausea, vomiting or morning sickness. Her comorbid include hypertension which was diagnosed one year ago. She has no known allergies toward any drugs or food. Her past obstetric history was uneventful, and her last pap smear was 16 years ago, and the result was normal. Apart from her father who passed away due to lung carcinoma, there is no family history of gynaecological malignancy.

For the one year duration prior to admission, she visited several different primary care clinics. She was informed that her condition was due to hormonal changes (possible menopausal changes) and was prescribed with cyclical tranexamic acid and non-steroidal anti-inflammatory drugs (NSAIDs). Abdominal examination, blood test, urine test, speculum examination or imaging were not performed.

When there were no signs of improvement, she went on to a regime of supplements and traditional herbs. However, her condition remained unchanged.

She presented to us with symptoms of anaemia (lethargy, weakness and her husband noted that she looked pale). Vital signs on arrival revealed: BP; 119/45 mmHg, pulse rate of 110 / minute, RR: 18/min, temperature of 37 °C, and SPO2: 100% under room air. Clinical examination revealed pallor palmar crease and conjunctiva. There was no koilonychias, purpura or petechiae. As for the abdomen, there was a suprapubic palpable mass of 12cm x 8cm. There were no ascites clinically and no palpable lymph node. Per speculum and vaginal examination, the results revealed a healthy cervix, size 2cm x 2cm with close internal os. Blood clot and occasional oozing of blood from internal os were observed.

Transabdominal ultrasound revealed a uterus size of 7.74 cm x 5.62 cm, with endometrial thickness of 18.5mm, mixed echogenicity with vague mass at the fundal region (Figure 1). Blood investigation revealed haemoglobin level of 6.0 g/dL. The tumour markers i.e. CEA, CA-125, alpha fetal protein were within the normal range.

She was transfused with two pints pack cells. Hysteroscopy showed fleshy polypoidal mass with presence of haemorrhagic area and necrotic region. Endometrial lining was fluffy. Biopsy result came back as non-gestational choriocarcinoma. Serum beta-HCG level was 120000 iu/L. Chest X-ray showed clear lung field and no lung nodules were observed (Figure 2). However, the whole body CT scan revealed multiple lung nodules, with the right lung having more nodules than the left lung, suggesting lung metastasis (Figure 3). The bone scan is negative for bone metastasis (Figure 4).

She underwent total abdominal hysterectomy and bilateral salphingo-oophorectomy (TAHBSO). Intraoperative, the uterus size was 16cm X 8cm, with no intra-abdominal metastasis. The endometrial cavity revealed a haemorrhagic mass, irregular surface, triangular in shape, with origin from the uterine fundus (Figure 5A & 5B). Histopathological examination revealed non-gestational choriocarcinoma, FIGO staging 2. Surgery was carried out for diagnostic and therapeutic purposes, followed by six cycles of chemotherapy:

Discussion

Heavy menstrual bleeding is a common gynaecological condition presented to primary care clinic. Clinically, it is defined as blood loss at least

80ml or more per menstrual cycle. The common causes for it include: fibroids, endometrial polyps, endometrial hyperplasia, endocrinology causes and coagulopathy. However, about 40-60% causes of heavy menstrual bleeding are idiopathic.⁸

Careful history taking may give clues to the likely cause for the heavy menstrual bleeding. In our case report, the history of heavy menstrual bleeding, with no other additional risk factors for endometrial malignancy, such as diabetes mellitus, nulliparous, obesity, family history of malignancy and certain medication, such as Tamoxifen. However, repetitive visits for the same symptoms for a year should have raised suspicion of more serious conditions and should have been evaluated further.

Physical examination is fundamental in daily practice. Proper physical examination in this case report may reveal pallor palmar creases and conjunctiva with palpable abdominal mass. Presence of palmar creases indicates severe anemia and requires blood test confirmation.

Full blood count is compulsory for all women with heavy menstrual bleeding.³ However, in this case, full blood count was not performed despite multiple visits to several primary care clinics. Her condition continued until she developed symptomatic anemia (lethargy, tachycardia with haemoglobin level of 6.0 g/dL. Her blood loss was approximately 1.0 to 1.5 L, and required blood transfusion. Early identification the cause of heavy menstrual bleeding would have prevented the need of blood transfusion.

In primary care practice, tranexamic acid and NSAIDs are prescribe to women with heavy menstrual bleeding.³ In a Cochrane review, both are effective in reducing HMB while tranexamic acid being more effective compared to NSAIDs.⁹ Tranexamic acid reduces blood loss approximately 26-60% while NSAIDs 30-40%. However, the regime was not effectively in this case, and warrants reassessment and exploring other causes and other treatment options.

In correlation with history of prolonged heavy menstrual bleeding and low haemoglobin level, further evaluation should be carried out.³ Two options of evaluation can be offered: hysteroscopy or pelvic ultrasound. In this case, a pelvic ultrasound is the preferred option as there is a clinically palpable abdominal mass. There are two methods in assessing pelvic region. Transvaginal ultrasound is the gold standard in detecting uterine structural abnormalities.¹⁰ However, this option is not available in all primary care clinics in Malaysia. Alternatively,

transabdominal pelvic ultrasound is plausible and can be performed in government primary care clinic providing maternal and child health services.

Endometrial sampling is indicated in this case, but was not offered when her heavy menstrual bleeding was not responding to hormonal therapy. There are several methods to get the sample. Pipelle sampling is an in-office procedure preferable for this case. According to NICE guidelines, endometrial sampling is recommended in woman age > 45 years old with persistent intermenstrual bleeding and with no success in previous treatments. Moreover, guideline recommends endometrial sampling with additional risk factors for endometrial carcinoma (e.g. obesity, diabetes mellitus, or polycystic ovarian syndrome (PCOS) for younger woman, age less than 40 years old.¹⁰

Hysteroscopy was mentioned in this case. It is a procedure to inspect the uterine cavity and endometrial biopsy can be obtained in the same setting. This test is offered to women with HMB and suggestive of endometrial pathology, submucosal fibroid or polyps.³ It can be further classified into two types, diagnostic hysteroscopy and operative hysteroscopy. In the UK, diagnostic hysteroscopy can be done as an outpatient basis, which is not the case in Malaysia's setting at the moment. Therefore, all patients with similar indications must be referred to a hospital for hysteroscopy, as shown in our case.

Urine pregnancy test is always perform on all women in the reproductive age group who presented with abnormal per-vaginal bleeding. Unfortunately, it was not performed in this case despite multiple health center visits. If it was performed during her first visit it would warrant urgent referral for further assessment. Potential life-threatening conditions, such as ectopic pregnancy, miscarriage and molar pregnancy should be excluded before directing toward investigations on gynaecological conditions. Assuming abnormal per-vaginal bleeding in perimenopausal woman solely due to hormonal changes is discouraged.

In conclusion, heavy menstrual bleeding is common presentation in primary care and should be evaluated systematically and adhere to local and international guidelines. Multiple visits for unresolved symptoms should have raised a red flag of a more serious condition. Early detection and referral may improve patient's outcome.

Conflict of interest

No potential conflict of interest relevant to this article was reported



Figure 1: Ultrasound pelvic reveals uterus size of 7.74cm X 5.62cm, with endometrial thickness of 18.5mm, mixed echogenicity, and irregular surface within endometrial cavity.

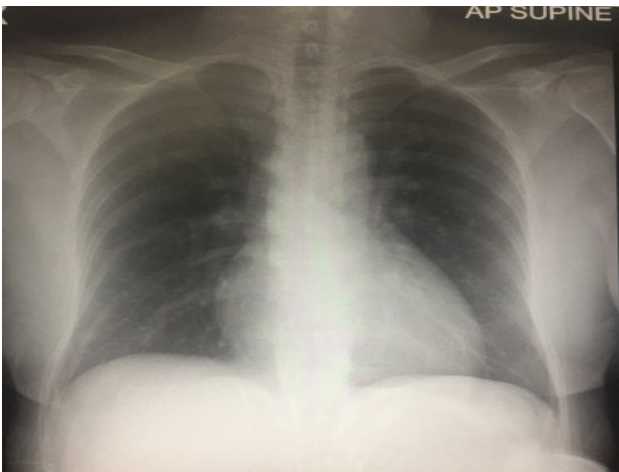


Figure 2: Chest x ray shows clear lung field.



Figure 3: CT thorax shows multiple lung nodules. The right lung shows more Lung Nodules than Left Lung, Suggesting Lung metastasis.

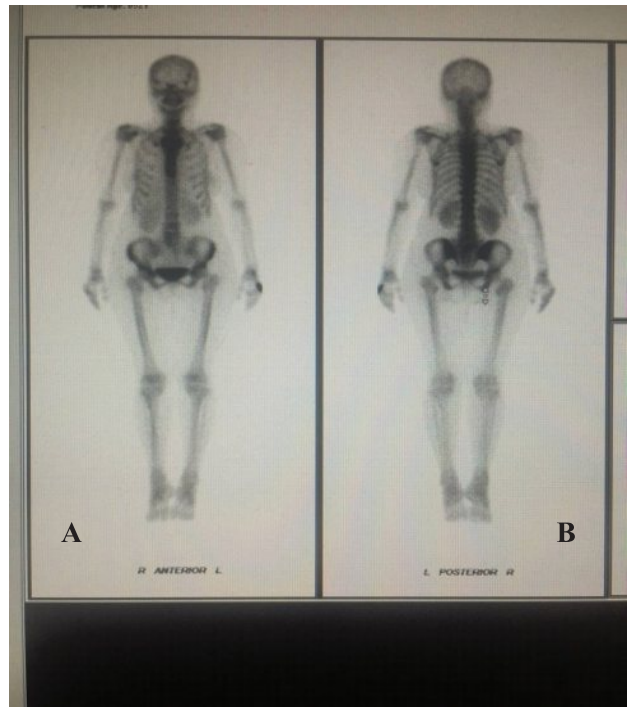


Figure 4: Bone scan with Tc-99m MDP reveals no bone metastasis in this patient. (A): Anterior imaging and (B) posterior imaging.



Figure 5. (A-B) Intraoperative specimen. TAHBSO revealed uterus size of 16cm x 8cm and endometrial cavity revealed a haemorrhagic mass, irregular surface, triangular in shape, with origin from uterine fundus.

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