A perplexing case of gastrointestinal haemorrhage

Prabhu M M, Baxi J, Malhotra A, Setty M, Sharma P

ABSTRACT

Choriocarcinoma is a gestational trophoblastic tumour with a high metastatic potential but presentation with gastrointestinal haemorrhage due to jejunal mucosal metastasis is very rare. A 25-year-old Nepali woman presented with severe anaemia and massive gastrointestinal haemorrhage after normal pregnancy following evacuation of a hydatiform mole. During laparotomy, the patient was found to have extensive jejunal mucosal metastases.

Keywords: choriocarcinoma, gastrointestinal haemorrhage, hydatiform mole, jejunal mucosal metastasis

Singapore Med J 2006; 47(2):159-162

Department of Medicine
Manipal College of Medical Sciences
Manipal Teaching Hospital
Pokhara
Nepal

Prabhu M M, MD
Associate Professor

Malhotra A, MD
Lecturer

Setty M, MD
Assistant Professor

Sharma P, MBBS
Resident

Department of Surgery
Manipal College of Medical Sciences

Baxi J, MS
Associate Professor

Correspondence to:
Dr Mukhyaprana Prabhu Manuru
Kasturba Medical Colege
Madhavnagar
Manipal 576104
India
Tel: (91) 820 257 3627
Fax: (91) 820 257 0062
Email: mmukhyaprana@yahoo.com

INTRODUCTION

Choriocarcinoma is a rapidly-invasive, widely metastatic human chorionic gonadotropin (HCG)-producing neoplasm, and is usually intrauterine and gestational. Other sites of origin include ectopic pregnancies and gonads. As a teratoma, it arises from the mediastinum, retroperitoneum, and pineal gland[1]. Only rarely has this neoplasm been reported in organs such as the prostate, liver, lung, urinary bladder, nose, and gastrointestinal (GI) tract[2]. We describe a young lady who presented with severe anaemia, massive GI haemorrhage due to choriocarcinoma with jejunal mucosal metastases and bleeding duodenal ulcer two years four months after evacuation of a hydatiform mole.

CASE REPORT

A 25-year-old Nepali woman first presented to our hospital in January 2004 at 34 weeks gestation with severe pain on the right chest and back. On physical examination, she was found to have a right pleural effusion. She gave a history of hydatiform mole two years ago, which was evacuated at about 12 weeks of gestation. She was on regular follow-up at another healthcare facility, and was subsequently considered fit to be pregnant.

Chest radiograph showed a massive right haemopneumothorax. Intercostal drainage was done and about two litres of haemorrhagic fluid was drained. Work-up for bleeding and clotting disorders was negative. Emergency Caesarian section was done and a baby boy was born. Investigations, including computed tomography (CT) of the thorax, to find the cause of haemorrhagic pleural effusion at that time could not conclusively confirm its aetiology. CT did not show a mass lesion. The patient did not consent to have a pleural biopsy. Thorocoscopy was not available in our hospital. Subsequently, both mother and child recovered and were discharged. Haemoglobin at discharge was 12.9 g/dL. Patient did not return for follow-up, in spite of advice.

The patient next presented to our emergency room four months later with complaints of multiple episodes of vaginal bleeding and an episode of epistaxis. On examination, she was markedly pale with haemoglobin at admission of 5 g/dL, with a haematocrit of 21%. There was minimal bleeding per vaginum. Otherwise, systemic examination was essentially normal. Her peripheral smear showed evidence of microcytic hypochromic anaemia. Initial clinical impression was severe anaemia due to chronic genital blood loss.

The patient was diagnosed to have iron deficiency anaemia due to genital blood loss, as her history of minimal vaginal bleeding started after discharge from hospital. The patient was also investigated for bleeding and clotting disorders. Coagulation profile, and liver, renal and thyroid function tests were normal. Ultrasonography (US) of the abdomen was normal while pelvic US showed minimal fluid in the endometrial cavity. Hysteroscopy could not be done as facilities were not available. Bone marrow aspiration showed refractory anaemia. The patient was then started on multiple blood transfusions and oral iron therapy.

On the third day of admission, the patient developed several episodes of haematemesis and malaena. Upper GI endoscopy showed a

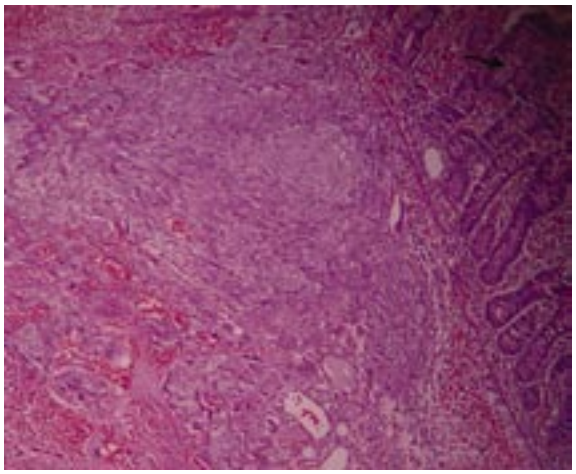

Fig. 1 Photomicrograph of the jejunal specimen shows intact mucosal surface lined by columnar cells, submucosal cells nests and trabecular pattern with a bilaminar picture. Mononuclear trophoblastic and syncytiotrophoblastic cells are seen along with intermediate trophoblast with nuclear pleomorphism with necrosis and haemorrhage (Haematoxylin & eosin, x 100).

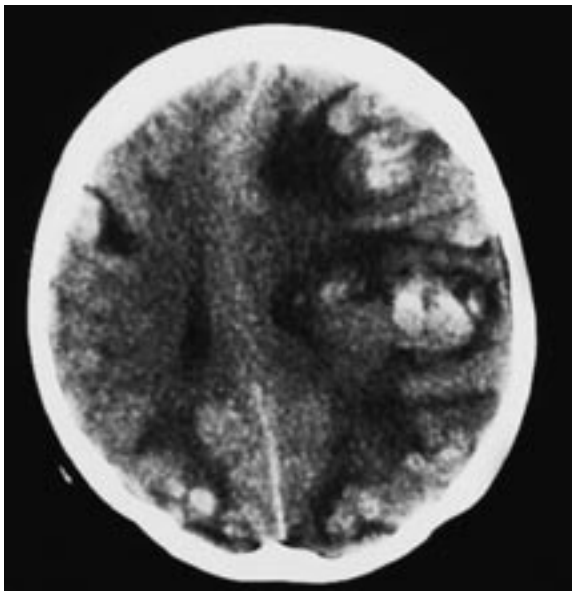

Fig. 2 Axial CT image of the brain shows multiple haemorrhagic secondaries with midline shift to the right.

superficial bleeding duodenal ulcer, not justifying the amount of haemorrhage the patient was having. Upper GI haemorrhage was managed conservatively, including high doses of proton pump inhibitors, sucralfate, antacids and multiple blood transfusions. A total of 32 pints of blood was transfused. Endoscopical intervention was not done as injection and thermal therapy were not available in our hospital. Due to failure of medical management to stop the GI haemorrhage, an emergency laparotomy was done.

During the operation, multiple polypoidal masses spread throughout the jejunum and a jejuno-jejunal intussusception due to large papillomatous growth were found. Multiple small (less than 5 mm) nodular deposits on the liver surface and mesenteric lymphadenopathy were seen. 80 cm of involved jejunum was resected, liver nodules and lymph nodes were sent for histopathology, and the bleeding was controlled. All intestinal polypoidal masses (Fig. 1), mesenteric lymph nodes and liver nodules showed metastatic choriocarcinoma.

Preoperative serum β-HCG level was >500mIU/mL. On the seventh postoperative day, the patient developed sudden loss of consciousness, global rigidity, decortication and respiratory failure requiring mechanical ventilation. CT of the head showed multiple haemorrhagic secondaries in both cerebral hemispheres (Fig. 2). She deteriorated further and died the next day.

DISCUSSION

Anaemia is the commonest haematological disorder worldwide. Challenges in managing anaemia include making an accurate diagnosis and treating the underlying cause. The first step is doing a peripheral smear examination. Based on red cell morphology, anaemia is classified as microcytic, normocytic or macrocytic. Iron deficiency is the commonest cause of microcytic hypochromic anaemia, with other causes being thalasaemia, sideroblastic anaemic and anaemia of chronic disease. Common causes of iron deficiency include excessive demand during pregnancy and lactation, and chronic blood loss from the GI tract and uterus[3].

In females in the reproductive age group, menorrhagia, increased demand during pregnancy and lactation are aetiological factors implicated in iron deficiency. In post-menopausal females and older males, occult GI haemorrhage due to bleeding peptic ulcer, and stomach and colonic carcinomas have been implicated to cause chronic blood loss. Iron deficiency anaemia is characterised by a microcytic hypochromic blood picture and low serum ferritin. The definitive diagnosis is by demonstrating low iron store in the bone marrow. Diagnosis of iron deficiency anaemia is easy but the challenge lies in finding the cause of blood loss.

Clues for planning of investigations in microcytic hypochromic anaemia are based on the history and clinical presentation. In females of reproductive age with a history of menstrual or genital bleeding, pelvic investigations (pelvic US and hysteroscopy) are planned initially. In males, in post-menopausal females with no definite history of GI haemorrhage, and in both sexes with a history suggestive of GI haemorrhage, investigations like stool occult

blood, upper GI endoscopy, colonoscopy and barium enema, should be conducted to find out the cause of blood loss.

Common causes of upper GI haemorrhage are peptic ulcer, oesophageal varices, Mallory-Weiss tear, gastritis, and gastric carcinoma, whereas causes of small intestinal haemorrhage include angiodysplasia, haemangioma, telangiectasia, Crohn's disease, Meckel's diverticulum, lymphoma and small bowel carcinoma[4]. Treatment of anaemia due to acute GI haemorrhage is by repeated blood transfusion, high dose proton pump inhibitors for ulcer, sclerotherapy for bleeding varices, and endoscopic haemostatic techniques for bleeding ulcers. Bipolar probe coagulation, argon plasma coagulation or laser therapy may be used to ablate angiodysplasia. If bleeding continues in spite of the above measures, laparatomy is indicated.

Our patient had chronic vaginal blood loss and presented to us with severe anaemia, While investigating for anaemia, the patient started having severe GI haemorrhage manifested by haematemesis and malaena. Upper GI endoscopy showed a bleeding duodenal ulcer which added to the confusion. The patient was treated with standard medical therapy (i.e. high dose proton pump inhibitors, antacids, sucralfate, multiple blood transfusions). In spite of these measures, the GI haemorrhage continued, necessitating laparotomy. Laparatomy showed extensive jejunal mucosal metastases due to choriocarcinoma.

Choriocarcinoma is a malignant tumour derived frm trophoblasts that have a high metastatic potential. Choriocarcinoma and placental site trophoblastic tumours are considered as gestational trophoblastic tumours (GTT). GTT are unique in cancer biology in that they follow either a normal or abnormal pregnancy. The most common antecedent pregnancy to GTT is a complete or partial hydatidiform mole. Both complete and partial moles remit spontaneously in most cases, following evacuation of the uterine cavity. However, either persistent trophoblastic disease or a frank trophoblastic tumour can follow a complete hydatidiform mole, with an incidence of approximately 8%, and after a partial hydatidiform mole with an incidence of approximately 0.5%. The incidence of GTT after normal pregnancy is one in 40,000 and 50,000 deliveries[5].

GTT occurring following a full-term pregnancy are always choriocarcinomas histologically, and frequently are the highly aggressive variant of this disease. Patients presenting within a few months of delivery have widespread pulmonary and, not uncommonly, cerebral metastases. 50% of metastatic choriocarcinoma cases follow evacuation of a hydatidiform mole, 25% after abortion, and 20% following full-term delivery while 5% follow ectopic gestation. Presentation may occur several years after pregnancy, usually with persistent or irregular uterine bleeding[5].

The disease may also present with signs and symptoms of metastasis, usually affecting the lungs. Deposits are frequently found in kidneys[6], brain and liver. Lung metastasis presenting as pneumothorax and haemothorax have been reported in the literature[7-9]. GI involvement is rare, being present in less than 5% of cases. Locating and therapy of these lesions can be achieved by endoscopy, angiography or surgery. Despite being a highly curable malignant disease, the occurrence of GI bleeding worsens the prognosis[10].

Choriocarcinoma is a tumour composed both of cytotrophoblastic and syncytiotrophoblastic cells. It is an unusual tumour in that it stimulates virtually no stromal reaction and is therefore essentially a mixture of haemorrhage and necrosis with tumour cells scattered within the mass. Tumour cells can be scanty and present problems of pathological interpretation. The pathology of choriocarcinoma is reflected in its clinical behaviour, with widespread intravascular dissemination to lungs, brain and other sites. It has a characteristic haemorrhagic tendency due to its trophoblastic origin.

There are very few case reports of choriocarcinoma presenting as GI bleeding, either as primary GI malignancy, bleeding duodenal ulcer or metastatic deposits[10-12]. Our patient had a hydatiform mole. After its evacuation, her serial β-HCG levels were normal, so she was cleared for planned pregnancy again. The patient presented with haemothorax at 34 weeks pregnancy and at this stage, her serum β-HCG was negative for choriocarcinoma. After a few months, the patient presented with severe anaemia and minor bleeding manifestations initially, then massive GI haemorrhage.

This case is unusual as even at the stage of metastases, the patient had only a modest rise in serum β-HCG (500mIU/ml). Endoscopy done during massive GI haemorrhage showed superficial bleeding duodenal ulcer, adding to the confusion in diagnosis. Laparotomy done showed multiple jejunal polypoidal growths with deposits of choriocarcinoma in the liver which, to our knowledge, has not been reported in literature.

Choriocarcinoma, though rare in developed countries, is still a major problem in developing countries, especially Southeast Asia[5]. Since it has

varied presentations with metastases at various sites including unusual sites, it has to be considered in the differential diagnosis of unexplained anaemia with bleeding manifestations in females, especially those with a past history of hydatiform mole even many years earlier. The unusual presentation of this entity is highlighted in this reported case.

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