

Case report

A rare case of metastatic choriocarcinoma to multiple organs causing intractable bleeding.

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Abstract

Choriocarcinoma is the most aggressive form of gestational trophoblastic disease (GTD). It has rapid growth and metastatic potential. Patients with this disease presented with bleeding manifestation in certain organs such as vaginal, gastrointestinal tract, lungs or brain. We report an unusual case of multiple organs bleeding in a patient with metastatic carcinoma.

Key words: bleeding, metastasis, choriocarcinoma

Introduction

Choriocarcinoma is an aggressive germ cell tumour that is characterized by rapid proliferation and the potential for rapid development of widespread metastases. Common metastatic sites are the lung liver, gastrointestinal tract and brain (1). Metastases are highly vascular and frequently result in local bleeding complications. We report a case of metastatic choriocarcinoma to multiple organs causing disastrous and interminable bleeding which ultimately resulted in patient's death. To our best knowledge, this is a first in the literature that report a patient with multi-organ bleeding.

Our patient was a young 41yo female, Para 2, without a significant past medical history who was initially investigated at a secondary care institution for lower abdominal pain and vomiting, associated with loss of appetite, cough and haemoptysis over 3 weeks.

Blood investigations showed an elevated beta HCG of 508017.9 mmol/dm and haemoglobin levels of 5.5 g/dl. Bedside focused abdominal ultrasound for trauma (FAST) scan revealed free fluid in Morrison's pouch. The initial impression was of ectopic pregnancy. She was reviewed by O & G team in the emergency department where she had generalized tenderness and guarding of the abdomen. Diagnostic laparoscopy was performed, which revealed haemoperitoneum with bleeding left corpus luteum

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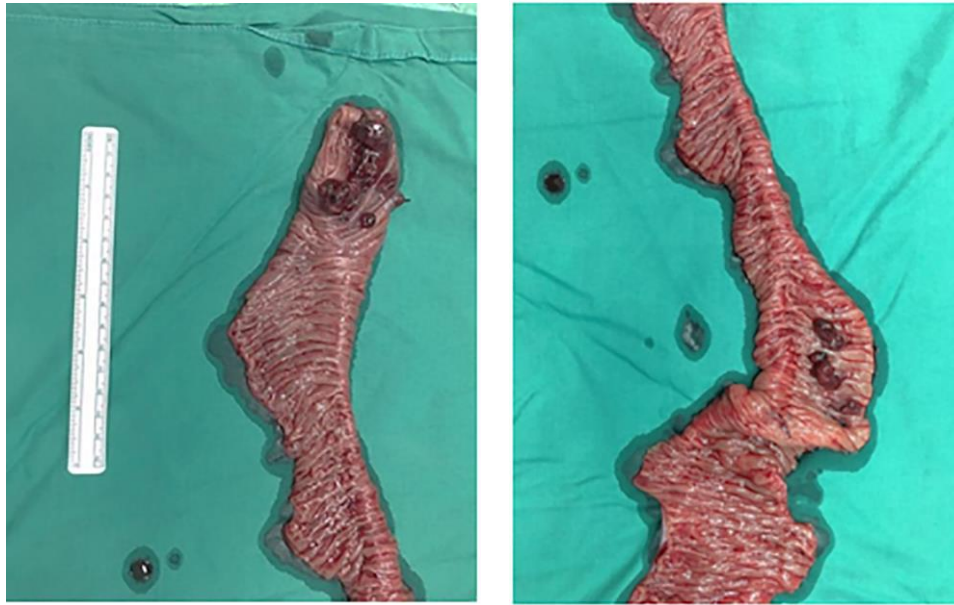


Figure 1 (left) & figure 2 (right): Tumour deposits at D3, proximal jejunum 30cm (left) and 70cm (right) from duodenal jejunal flexure.

cyst. Ligation of bilateral uterine tubes and evacuation of retained products of conception was performed.

Post operatively, an ultrasound pelvis was performed which showed an endometrial cavity with multiple cystic spaces. Histology of the uterus returned as metastatic choriocarcinoma. Computed tomography (CT) scan of thorax, abdomen and pelvis showed multiple pulmonary nodules and lesions in the liver and kidneys as well as splenic rupture. An exploratory laparoscopy was performed at which splenic metastasis with rupture and bleeding was found for which she had splenectomy. Histology of the spleen returned metastatic choriocarcinoma. Thereafter her haemoglobin levels remained persistently low requiring multiple blood transfusions, for which she underwent oesophagogastroduodenoscopy on post op day 2. This revealed a bleeding tumour at the third portion of duodenum. This was injected with adrenaline. A follow up computed tomography mesenteric angiogram (CTMA) showed multiple masses in liver, partial thrombosis in right portal vein and tumour deposits at proximal jejunum without evidence of further bleeding.

She was transferred to our institution for further management of her metastatic choriocarcinoma.

Upon arrival, she immediately had coffee ground vomitus and fresh malaena and a fall in haemoglobin from 7.3 to 4.9 g/dl. Repeat OGD revealed a bleeding D3 tumour with adherent clot which was controlled using Hemospray. She then received a dose of etoposide 110mg and methotrexate 330mg. The next day she rebled. A computed tomography mesenteric angiogram (CTMA) performed showed a blush from a branch of the superior mesenteric artery (SMA) so she underwent selective superior mesenteric artery angiography and angioembolization of the first jejunal artery with apparent hemostasis. 2 days later, her haemoglobin fell from 9.6 g/dl to 6.2 g/dl. Repeated OGD showed rapid oozing from the previous lesions and repeated Hemospray application was attempted however this failed to arrest the bleeding. She became hemodynamically unstable and underwent aggressive resuscitation. An urgent mesenteric angiogram performed showed no active bleeding to angioembolize.

Overnight her haemoglobin continued to fall despite aggressive transfusion with packed red blood cells. On day 4 she had an OGD in emergency operating theater. Unexpectedly no bleeding was seen in the stomach or duodenum to D3, and the previously seen tumor was not bleeding. An exploratory laparotomy was

performed at which we found brisk bleeding from a nodule at segment 6 of the liver, and multiple subcapsular tumours. Several tumour deposits were palpable in the jejunum.

After a day of initial stability, she became hypotensive and anemic again. A repeat OGD showed blood clots in stomach and duodenum. A decision was made for small bowel resection and temporary abdominal closure. Upon entering the abdomen, we found 3 distinct areas of ulcerated tumour deposits at D3, proximal jejunum 30cm and 70cm from duodenal jejunal flexure (Figure 1& 2).

She underwent a second look laparotomy and reconstruction with duodenojejunostomy and closure of abdomen 2 days later. On post op day 5, she developed hospital acquired pneumonia requiring reintubation and readmission to ICU. Antibiotics were escalated to IV meropenem, caspofungin and levofloxacin.

She begun to pass motion 5 days later and was extubated. Unfortunately, she collapsed and became unresponsive with GCS 3 and anisocoric pupils and left sided hemiparesis. Urgent CT brain showed a large acute intra-parenchymal haematoma in left cerebral hemisphere from a brain metastasis causing mass effect and intraventricular extension of the haematoma with hydrocephalus.

She underwent an emergency left decompressive craniectomy and evacuation of intra-cerebral haemorrhage and insertion of intracranial pressure monitor but continued to decline postoperatively with escalating ventilator requirements and increasing coagulopathy. A joint decision was made between the family and attending surgical and anesthetic teams for comfort care in view of medical futility given the multi-organ failure and relentless bleeding with immunosuppression despite aggressive management. She subsequently succumbed and passed away. Condolences were passed to the family.

Discussion

Choriocarcinoma of the testis was the first case described by Tsuchiya et al in 1980. It is a germinal tumour arising from testicular cells in men and from fetal trophoblast in women (2). It frequently presents

late after haematogenous spread to lung, liver, gastrointestinal tract (GIT) and brain (3). This tumour is characterized by high levels of beta- human chorionic gonadotrophin (HCG). The effect of this pregnancy hormone can be instantaneous such as in our case (vomit) or delayed such as secondary tumor occurrence later in life (4). We initially had the wrong diagnosis of ectopic pregnancy: a prompt diagnosis of choriocarcinoma can be sometimes challenging, as supported by other authors (5). Choriocarcinoma generally has good response to chemotherapy, even in advanced stages (6).

The high metastatic rate (30%) at presentation is likely due to the high affinity of trophoblastic cells towards blood vessels with disruption of normal vascular architecture leading to bleeding (7). Patients frequently present with bleeding from either the primary tumour or from the metastases. Aside from malaena, per rectal bleeding and haematemesis, other presentations include stroke, epistaxis and intra-peritoneal bleeding (8).

We performed a PubMed search using the keywords "choriocarcinoma, bleeding, metastatic". The results are displayed below (Table 1). Notably, bleeding complications are most often limited to a single organ. This case was unusual in presenting with such a rapid

Table 1: Number of cases with sites of bleeding

Site	Cases	Percentage (%)
Upper GIT	19	31.7
Brain	16	26.6
Lung	9	15
Renal	6	10
Liver	5	8.3
Lower GIT	2	3.3
Vertebra	1	1.7
Cardiac	1	1.7
Nasal mucosa	1	1.7
Total	60	100

succession of overlapping bleeding at short time points from the liver, gastrointestinal tract and brain due to metastases.

Although gastrointestinal metastases from choriocarcinoma are uncommon (less than 5% of patients have gastrointestinal involvement), upper GI bleeding is the most common site of when it does occur (9). Most patients only had isolated upper GIT bleeding. One patient had metastasis to the brain without any bleeding (10). Another patient had both upper and lower GI bleeding (11). An isolated case described upper GIT bleeding with intussusception (12).

The second most commonly reported site of bleeding was the brain with 16 cases reported. Metastasis to both brain and lungs in the same patient had been reported by Sierra et al with haemoptysis the only bleeding complication (13).

Other sites of bleeding include lower GIT, liver, genital tract, lung, heart, vertebral, kidney, spleen and nasal mucosa. A rare case of metastasis to lung, brain and lumbar spine was reported, presenting with back pain, haemoptysis and headache (14). One particular case of pericardiac tamponade was reported as a complication of bleeding from metastatic choriocarcinoma (15). Although some of the patients had multiple sites of metastasis, they did not have bleeding complications from more than one organ.

Patients with upper GIT bleeding are usually managed via endoscopic intervention with surgical intervention reserved for failure of hemostasis. Lewis et al reported that the most common reason for surgery is haemorrhage control (16). Embolization is the preferred choice of treatment to control bleeding in liver metastasis (17). Metastases to the brain have a poorer prognosis (18). Vugrin et al reported 5 patients

who died with median survival of only 1 month despite treatment with multi-agent chemotherapy (19). Brain metastases usually require a combined strategy of whole-brain radiation, early neurosurgical intervention and combination chemotherapy. In the absence of brain metastases a combined approach of hemorrhage control and multi-agent chemotherapy yields cure rates as high as 75% (20). In our case, we attempted several measures to arrest bleeding such as endoscopy, angioembolization as well as surgical intervention.

Conclusion

Although choriocarcinoma is very aggressive, cure is possible if it is detected early and appropriate treatment initiated. 75% of patients are expected to achieve complete or prolonged remission. Death when it happens is due to bleeding. Our patient suffered from frustratingly torrential bleeding from one site after another in rapid succession and ultimately succumbed after a long and exhausting battle through numerous invasive procedures and operations. We hope that others may learn from our experience and able to detect this disease early.

Abbreviations:

CT, computed tomography;
CTMA, computed tomography mesenteric angiogram;
FAST, focused abdominal ultrasound for trauma;
GIT, gastrointestinal tract;
GTD, gestational trophoblastic disease;
HCG, human chorionic gonadotropin;
O&G, obstetrics and gynaecology;
OGD, oesophagogastroduodenoscopy;
SMA, superior mesenteric artery

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