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40-year-old female with menorrhagia and abdominal pain: A case of metastatic gestational trophoblastic neoplasia

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Choriocarcinoma is part of a rare spectrum of placental abnormalities known as gestational trophoblastic disease (GTD). It is the most invasive form of GTD, with a mortality rate approaching 100% if left untreated. It spreads predominantly hematogenously to multiple target sites, most commonly the lungs. Due to its hypervascular nature, it is often complicated by bleeding. We describe a case of choriocarcinoma in a 40-year-old female with metastases to the lungs, brain, and bilateral kidneys resulting in large retroperitoneal hematomas.

Case report

A 40-year-old female presented to the emergency department at an outside facility with symptoms of vaginal bleeding, abdominal pain, headaches, dizziness, double vision, and epistaxis. The patient had been experiencing heavy vaginal bleeding with abdominal pain for a period of several months after a normal C-section delivery of a healthy female infant. Her placental pathology revealed a small nodular placental lesion consistent with trophoblastic disease (Fig. 1).

She was seen postoperatively in the clinic; however, there was no workup at that time, as her visit was prior to the reporting of the pathology results. In the interim, she was seen at multiple emergency departments for persistent vaginal bleeding and abdominal pain, with diagnoses of spontaneous abortion with retained products of conception. She was administered misoprostol for evacuation with

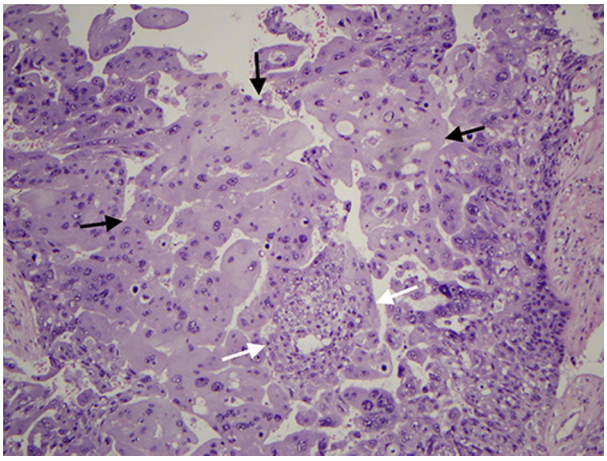

Fig. I. Placental pathology revealed a small (2.5 cm x 2.0 cm x 2.0 cm) nodular placental lesion consistent with trophoblastic disease. Choriocarcinoma is characterized by abnormal trophoblastic hyperplasia and anaplasia (black arrows), absence of chorionic villi, hemorrhage, necrosis (white arrows), and direct invasion into the myometrium. (H&E stain, 100x magnification)

plans for followup in the clinic with beta-hCG levels; however, she was again lost to followup. During her most recent visit to an outside emergency department, her beta-hCG was 225,000 mIU/ml, and a pelvic ultrasound revealed pelvic free fluid, but no intrauterine pregnancy or abdomi-

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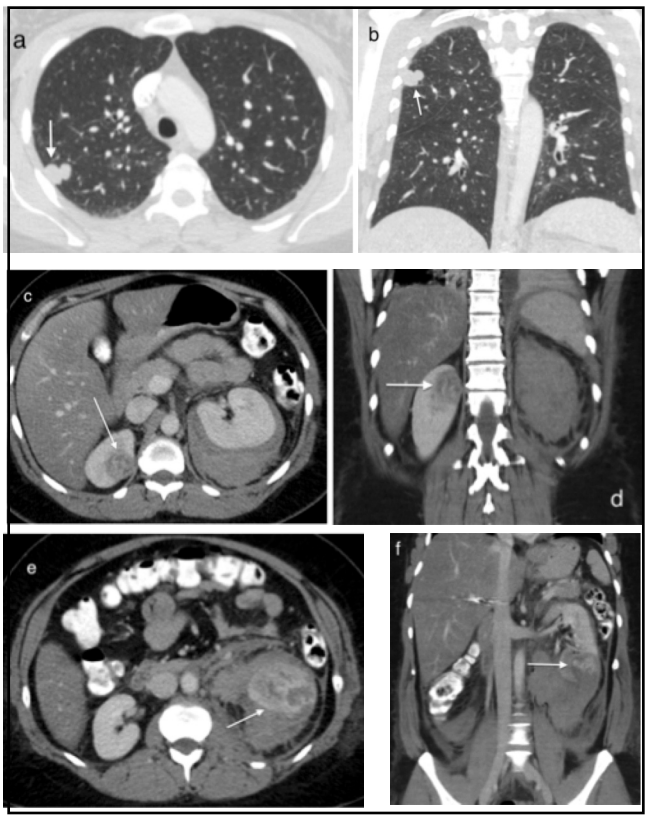

Fig. 2. Diagnostic CT scan of the chest (a, b) revealed a bilobed right-upper-lobe pulmonary lesion measuring 1.4 cm AP x 2.1 cm TV x 1.8 cm CC. Lungs are the most common site of metastasis for choriocarcinoma, accounting for 76%-87% of metastases, and it is rare to have additional metastatic sites in the absence of lung metastases. CT scan of the abdomen also demonstrated bilateral contrast-enhancing renal lesions measuring 2.7 cm AP x 2.6 cm TV x 3.5 cm CC in the right upper pole (c, d) and 2.7 cm AP x 2.4 cm TV x 4.2 cm CC in the left lower pole (e, f). The left renal lesion was also associated with a large retroperitoneal hematoma measuring approximately 22 cm in CC dimension. Choriocarcinoma is a hypervascular tumor and is often associated with bleeding; as a result, biopsy of metastatic lesions is not routinely performed, as it may result in excessive bleeding.

nal masses. Due to high suspicion for an ectopic pregnancy, she was taken to the operating room for a diagnostic laparoscopy, which revealed a small hematoma in the retroperitoneum, but no etopic pregnancy. She required multiple blood transfusions, as her hemoglobin had dropped from 11 to 7 g/dL. She also underwent diagnostic CT scans of the chest, abdomen, and pelvis that revealed a right-upper-lobe pulmonary lesion, bilateral renal lesions, and an associated left-sided retroperitoneal hematoma (Fig. 2).

Due to concern for malignant gestational trophoblastic disease with hemorrhage, the patient was transferred to our institution for a higher level of care. She was admitted to the gynecologic-oncology service for further workup and treatment. A pelvic ultrasound revealed no intrauterine pregnancy, no focal mass lesions, normal adnexa, and a thickened endometrium measuring up to 2 cm with a small amount of flow. As part of the metastatic workup, the patient underwent a head CT scan that revealed a 4-mm contrast-enhancing focus in the left parietal lobe. A subsequent MRI demonstrated the solitary lesion, with no other intracranial metastases identified (Fig. 3). A diagnosis of metastatic gestational trophoblastic neoplasm was made with a WHO score of 14, or Stage IV disease, with renal and brain metastases. The patient was started on induction chemotherapy with etoposide and cisplatin, plus whole brain radiation, and was subsequently discharged.

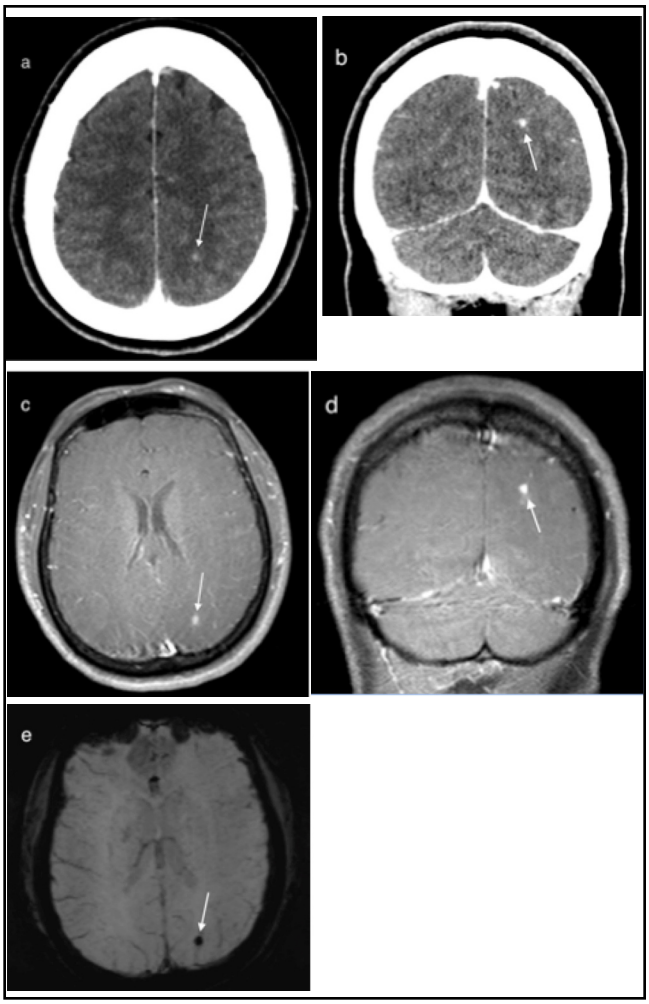

Fig. 3. A head CT scan revealed a 4-mm contrast-enhancing focus in the left parietal lobe (a, b). Subsequent MRI demonstrated the solitary lesion (c, d). A susceptibility-weighted sequence (e) revealed that the lesion was associated with hemorrhage, further raising concern for metastatic choriocarcinoma. No other intracranial metastases were identified.

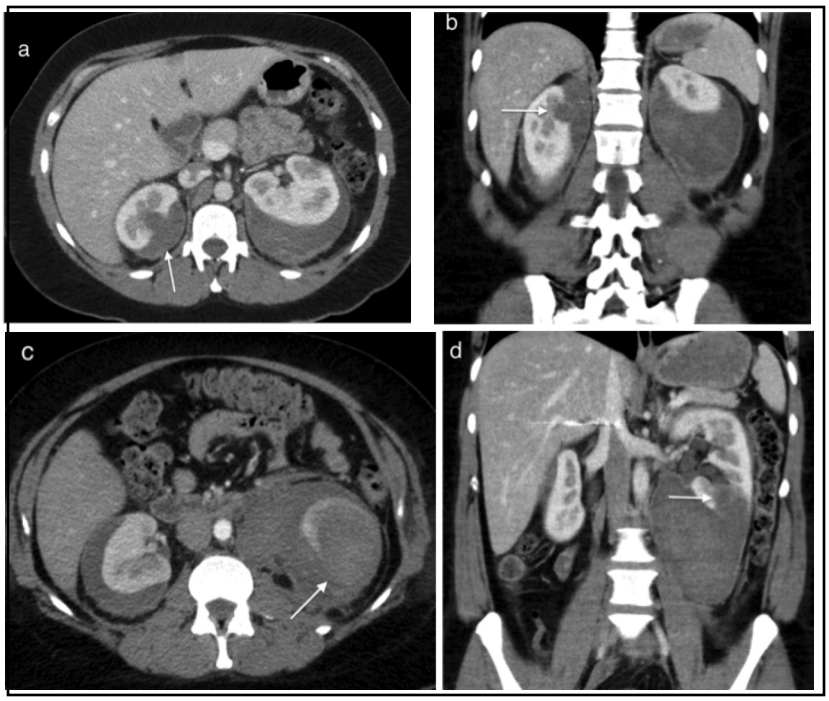

Fig. 4. An abdomen/pelvis CT scan was performed after the patient represented to the emergency department two days after discharge with symptoms of nausea, vomiting, severe abdominal pain radiating to the left flank, weakness, and a hemoglobin drop from 10.0 g/dL on discharge to 8.4 g/dL on readmission. Imaging revealed interval development of a right-sided subcapsular hematoma extending from the previously visualized right renal lesion (a, b) and interval increased size of the large left renal mass (c, d), now measuring approximately 5.2 cm AP x 3.7 cm TV x 5.3 cm CC, with interval increase in associated retroperitoneal hematoma now measuring 27 cm in CC dimension. The patient was subsequently taken to interventional radiology for possible embolization; however, renal arteriography did not reveal a hypervascular lesion or active extravasation.

Unfortunately, the patient represented to the emergency department two days later with symptoms of nausea, vomiting, severe abdominal pain radiating to the left flank, and weakness. Her hemoglobin had dropped from 10.0 g/dL on discharge to 8.4 g/dL on readmission to the emergency department. An abdomen/pelvis CT scan revealed increased size of the large left retroperitoneal hematoma and interval development of a new retroperitoneal hematoma (Fig. 4). The patient was readmitted to the gynecologic-oncology service. Due to concern for active bleeding, interventional radiology was consulted for possible embolization. After bilateral renal arteriography, however, no active extravasation or hypervascular tumors were identified, and embolization could not be performed. The patient was managed supportively and remained hemodynamically stable during the subsequent course of her hospitalization and discharged home with a plan to continue on an EMA/CO (etoposide, methotrexate, actinomycin D, cyclophosphamide, vincristine/oncovine) chemotherapy regimen, and whole brain radiation.

Discussion

Gestational trophoblastic disease (GTD) includes a spectrum of abnormalities arising from the placental villous trophoblast and consists of four main types: hydatidiform mole, invasive mole, placental site trophoblastic tumor (PSTT), and choriocarcinoma. Gestational trophoblastic neoplasia (GTN) implies metastatic potential, and refers to the latter three abnormalities, which have a high mortality rate if untreated. Prior to chemotherapy, invasive moles carried a mortality rate of approximately 15%, and choriocarcinoma resulted in a mortality rate of almost 100%. The outcomes of GTN improved drastically after the introduction of chemotherapy, with cure rates of greater than 90% (1-4).

There is limited data regarding the incidence of choriocarcinoma due to its rarity and challenging clinical distinction from invasive mole. Choriocarcinoma has an incidence of approximately 1 in 40,000 pregnancies in Europe and North America, and a higher incidence in Southeast Asia and Japan of approximately 9.2 and 3.3 in 40,000 pregnancies. Incidence rates for both hydatidiform mole and choriocarcinoma have declined over the latter part of the 21st century (5, 6).

Pathologically, choriocarcinoma is characterized by abnormal trophoblastic hyperplasia and anaplasia, absence of chorionic villi, hemorrhage, necrosis, and direct invasion into the myometrium (Fig. 1) (1, 7). Vascular invasion (hematogenous spread) results in distant metastases that most commonly include the lungs (76%-87%), vagina (30%), brain (10%), liver (10%), pelvis, kidney, intestines, and spleen, although metastases have been reported in virtually every body site (8). It is rare, however, to have additional metastatic sites in the absence of lung metastases (9). Vaginal metastases are an exception, as spread is contiguous rather than hematogenous (10). Although metastatic disease has been reported in up to 19% of all GTN, choriocarcinoma accounts for the majority of cases (9). Central nervous system metastases may produce neurologic symptoms, intracranial hemorrhage, or mass lesions. Biopsy is rarely necessary and may result in excessive bleeding, with serum beta-hCG and exclusion of pregnancy being the main diagnostic criteria required for GTN in the presence of metastases (11-13).

Ultrasound is the imaging study of choice for the initial diagnosis of GTN. In addition to identifying a molar pregnancy, ultrasound is primarily used to exclude an intrauterine pregnancy before initiation of chemotherapy. Although transvaginal ultrasound results in greater resolution and can potentially demonstrate more findings, it is not routinely done at all centers due to the risk of bleeding from

possible vaginal metastases. Choriocarcinoma is markedly hypervascular on Doppler ultrasonography; however, endometrial, myometrial, and parametrial invasion can be difficult to demonstrate (9).

Magnetic resonance imaging (MRI) of the pelvis can be helpful in such cases, but it is seldom clinically indicated in the routine assessment of GTN and is typically used in challenging cases such as relapsed patients, suspected PSTT, or very advanced disease. MRI of the brain, however, is recommended for staging, especially in the presence of lung metastases and neurologic symptoms, as these patients are at significant risk for CNS metastases (9, 14, 15).

Although a chest radiograph is recommended as the initial radiographic staging for patients with malignant GTN, a computed tomography scan (CT) is more routinely performed, as approximately 41% of patients have lung metastases that are not detected on plan radiograph (16). Contrast-enhanced CT is the diagnostic modality of choice for the assessment of metastatic disease, as choriocarcinoma is characteristically hypervascular and tends to bleed (8, 9).

As with our patient, choriocarcinoma can be complicated by hemorrhage from the tumor itself or from vascular malformations. GTN is the most common cause of uterine vascular malformations, and when hemorrhage occurs as a complication, the lesions are amenable to endovascular management, as these lesions are supplied by the uterine arteries (17). Our case, however, resulted in a negative bilateral renal arteriography, which precluded embolization of a self-resolved retroperitoneal bleed.

In summary, choriocarcinoma is a challenging diagnosis to make during a single presentation. Prolonged menorrhagia and markedly elevated beta-hCG should raise suspicion for choriocarcinoma and prompt further workup, especially in the setting of neurologic symptoms. Choriocarcinoma accounts for the majority of metastatic GTN and predominantly demonstrates hematogenous spread. Most common sites of hematogenous metastases include lungs, brain, liver, pelvis, and kidneys. Vaginal metastases are also common and occur via contiguous spread. Biopsy is rarely necessary for diagnosis and can result in excessive bleeding. Urgent specialist consultation with induction of chemotherapy can significantly improve prognosis.

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