CASE REPORT

Two Unusual Presentations of Gestational Trophoblastic Neoplasia: Cutaneous Metastasis and a Large Solitary Lung Lesion

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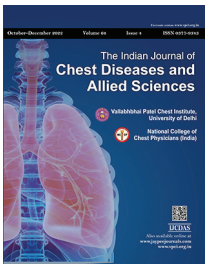

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Abstract

Gestational trophoblastic tumors, an uncommon group of pregnancy-related neoplasms, should be considered in any premenopausal patient presenting with metastatic disease from an unknown primary. A raised hCG and exclusion of pregnancy are often the only requirement in this situation. Although a potentially curable condition, a late diagnosis and the extent of the metastatic disease often determine the prognosis. Here we describe two young women with metastatic GTN, the first presenting with a very unusual finger metastasis and the second with a rare large solitary lung lesion with brain metastasis.

Keywords: Cutaneous metastasis, Gestational trophoblastic neoplasia, Primary pulmonary choriocarcinoma.

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Abbreviations used in this Article

GTN = Gestational trophoblastic neoplasm/tumors; hCG = human chorionic gonadotropin; BMI = Body mass index; CECT = Contrast-enhanced computed tomography; FNAC = Fine needle aspiration cytology; FIGO = International Federation of Gynecology and Obstetrics; EMA-CO = Etoposide, methotrexate, actinomycin-D, cyclophosphamide, and vincristine; MRI = Magnetic resonance imaging; PET-CT = Positron emission tomography-computed tomography.

Highlights

Gestational trophoblastic neoplasm/tumors (GTN), although rare, should be considered in the differential in any young women presenting with pulmonary or other system involvement, particularly in a metastatic disease setting, with the early estimation of human chorionic gonadotropin (hCG) as part of the workup.

Introduction

Gestational trophoblastic neoplasia represents a rare group of malignant neoplasms consisting of abnormal proliferation of trophoblastic tissue, often preceded by a hydatidiform mole or a non-molar pregnancy.[1] Choriocarcinoma characterized by high levels of hCG production and early vascular invasion is the most aggressive variety of GTN. The most common metastatic site is the lungs (in 80% of patients),[2] but because of their rarity, lung deposits from these tumors are encountered infrequently. Gestational trophoblastic neoplasia should be kept in the differential diagnosis in a premenopausal woman presenting with metastatic disease from an unknown primary as patients may have minimal in the way of gynecologic symptoms.[2] Here we report two rare cases of GTN one with skin metastasis and a second case with a rare large solitary lung lesion with brain metastasis, who came to us primarily for evaluation of their chest symptoms.

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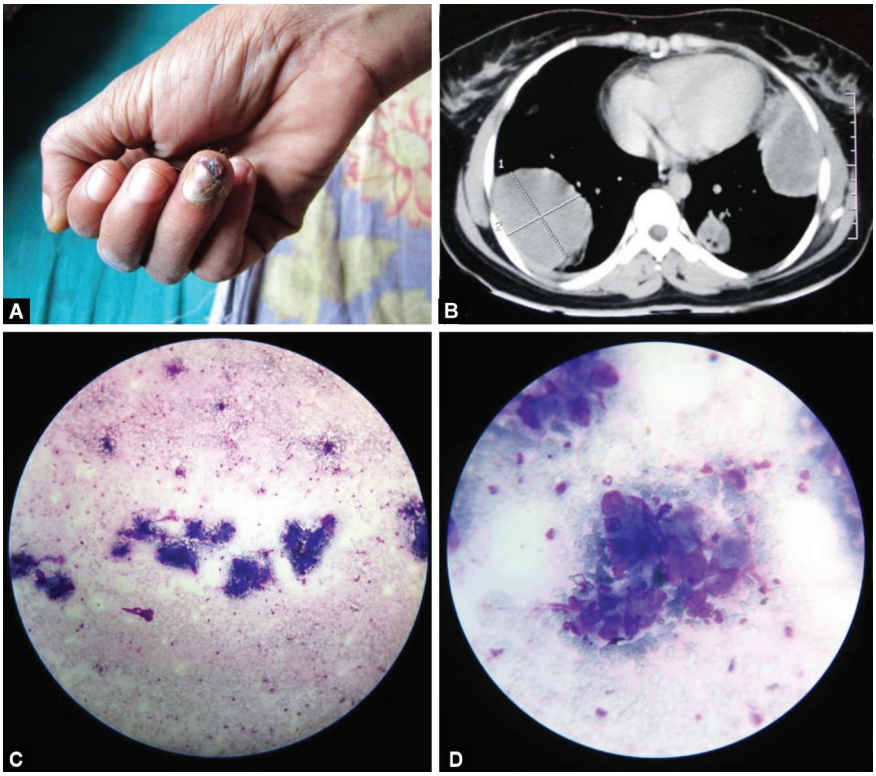
Case Description

Case 1

A 26-year-old female presented with a cough with blood-streaked sputum for three months. She had become breathless over 2 months and had lost weight. There was a history of abortion followed by an emergency sub-total abdominal hysterectomy for vaginal bleeding about a year prior. Histopathology was suggestive of leiomyoma of the uterus with hyaline degeneration and chronic cervicitis.

Her body mass index (BMI) was 14 kg/m^2 and she was anemic. A reddish-black tender nodule was located at the junction of the hyponychium and the nail bed of the right ring finger (Fig. 1A) which she had noticed for several weeks. It had a tendency to bleed on minor trauma. Chest X-ray and contrast-enhanced computed tomography (CECT) of the thorax done before admission showed multiple bilateral well-circumscribed nodular opacities varying in size (some showed cavitation), the largest measuring 83 mm ×



Figs 1A to D: (A) A reddish-black nodule located at the junction of the hyponychium and the nail bed of the right ring finger; (B) The CECT scan of the thorax – multiple bilateral well-circumscribed nodular opacities; (C) Cytotrophoblast and syncytiotrophoblast cells in clusters (low power view, L&G stain); (D) High-power view

53 mm (Fig. 1B). The CT-guided fine needle aspiration cytology (FNAC) from the lesions done elsewhere showed necrotic areas and hemorrhages.

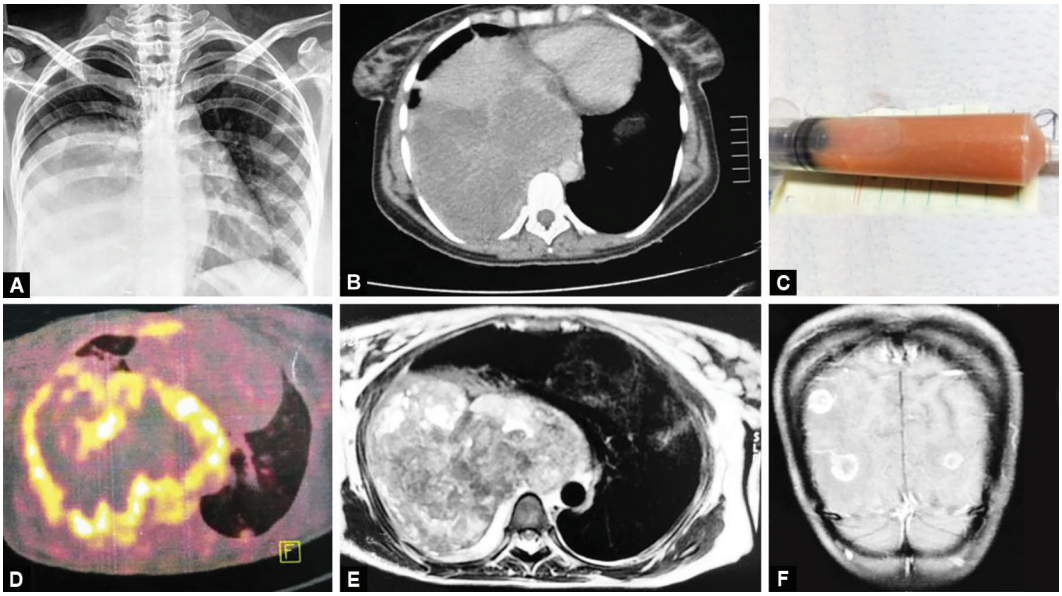
Her serum hCG on admission was 493000 mIU/mL. Pelvic ultrasound showed a cervical stump. The CT scan of the brain showed no abnormality. On gynecology consultation, she was diagnosed as having a high-risk GTN, International Federation of Gynecology and Obstetrics (FIGO) stage III with a World Health Organization (WHO) prognostic score of 11. She was advised of etoposide, methotrexate, actinomycin-D, cyclophosphamide, and vincristine (EMA-CO) chemotherapy. After the second cycle of EMA-CO, hCG dropped down to 22484 mIU/mL. As her right ring finger lesion persisted an FNAC was done which showed syncytiotrophoblast and cytotrophoblast in small groups and isolated fashion along with inflammatory cells suggesting a choriocarcinoma deposit in the digit (Fig. 1C). She was restaged as stage IV:11 and transferred to the gynecology department for further management and follow-up.

Case 2

A 20-year-old female presented with progressive breathlessness and an unproductive cough for five months. She had right chest discomfort, anorexia, nausea, and weight loss. She admitted to occasional vaginal bleeding following a dilation and evacuation procedure done eight months back. She was pale and had no clubbing or lymphadenopathy. Percussion note was impaired and breath sound diminished on the right hemithorax. Chest X-ray was suggestive of an encysted effusion/space-occupying lesion of the right hemithorax (Fig. 2A). A urine pregnancy test, done at admission was positive. Transvaginal ultrasound showed increased myometrial echogenicity but no fetus or adnexal mass. Serum hCG was raised at 34672 mIU/mL.

The CECT thorax was suggestive of a large heterogeneous, non-enhancing opacity in the right hemithorax (Fig. 2B). Only a small amount of fluid could be aspirated from the right hemithorax under ultrasound guidance (Fig. 2C). The fluid was negative for malignant cells but hCG was raised at 16343 mIU/mL. Magnetic resonance imaging (MRI) of the abdomen, pelvis, and brain showed no abnormality. The MRI thorax showed a well-defined heterogenous solid-cystic mass lesion (Fig. 2D). The FNAC and TruCut biopsy of the thoracic mass lesion showed only chronic inflammation with necrotic tissue. A whole-body positron emission tomography-computed tomography (PET-CT) scan was suggestive of a metabolically active large heterogenous malignant growth in the right lung involving the lower and middle lobe, infiltrating pleura and mediastinum showing multiple areas of necrosis (Fig. 2E).

She was diagnosed as having a low-risk GTN (stage III:5) and advised methotrexate-folic acid 8-day regimen on oncology consultation. After three cycles of chemotherapy, the serum β-HCG continued to show a rising trend (103343 mIU/mL). She also had an episode of generalized tonic–clonic seizure, and a repeat MR spectroscopy was suggestive of hemorrhagic metastasis in both cerebral hemispheres (Fig. 2F). She was restaged as stage IV:11, high-risk GTN, and was started on EMA-CO chemotherapy. Unfortunately, she developed a drug-induced erythema multiforme major and septic shock shortly after and succumbed.



Figs 2A to F: (A) Chest X-ray was suggestive of an encysted effusion/space-occupying lesion of the right hemithorax; (B) The CECT thorax was suggestive of a large heterogeneous, non-enhancing opacity in the right hemithorax; (C) Aspirated fluid from the right hemithorax; (D) The MRI thorax showed a well-defined heterogenous solid-cystic mass lesion; (E) The PET-CT scan was suggestive of a metabolically active large heterogenous malignant growth in the right lung involving the lower and middle lobe; (F) Infiltrating pleura and mediastinum showing multiple areas of necrosis

Discussion

Gestational trophoblastic tumors are a clinical diagnosis typically based on an elevated hCG and exclusion of pregnancy or any other rare source of hCG (i.e., ovarian germ cell tumor, ectopic hCG production by a non-trophoblastic tumor).[1] Examination or imaging findings suggestive of metastatic disease support the diagnosis, histologic confirmation is not required for diagnosis or treatment.[1,2] The GTN lesions are very vascular and often biopsies precipitate profuse bleeding.[1,2]

Gestational trophoblastic tumors are uniquely sensitive to chemotherapy with remission approaching 100% in low-risk patients (FIGO stages I–III: WHO risk score 0–4) receiving single-agent chemotherapy (methotrexate or actinomycin D protocols).[3] However, with metastasis outside the lungs or genital tract (FIGO stage IV) or FIGO stages II–III, score above 7 is the high-risk score, and complete remission can be expected in 60–70% with initial multiagent chemotherapy with or without adjuvant radiation or surgery.[4] Adverse prognostic factors are liver or brain metastasis, chemoresistance, delayed diagnosis, or a histologic diagnosis of choriocarcinoma.

Case 1 presented with cough, dyspnea, hemoptysis, and multiple nodular opacities in the lung (Fig. 1B) suggesting a metastatic malignancy. A history of abortion and hysterectomy raised the specter of a gynecologic malignancy which was subsequently found to be GTN when hCG was found to be raised. The most common metastatic sites are the lungs (80%), vagina (30%), brain (10%), liver (10%), and less frequently the kidneys, gastrointestinal tract, and spleen.[2] Skin metastasis as in our case (Fig. 1) is extremely rare with only a handful of cases described in the literature.[5–7]

Discrete nodular opacities are the most common form of metastasis seen in radiographs of patients with GTN (case 1) with the alveolar or "snowstorm" pattern, pleural effusion/hemothorax and an embolic pattern being infrequent.[8]

Case 2 presented with a large solitary lung lesion. Her age and a history of irregular vaginal bleeding prompted a urinary pregnancy test (positive) and hCG estimation (raised). Pregnancy was excluded by pelvic ultrasound. The MRI of the thorax defined the pleural-based heterogeneous solid cystic mass lesion which was difficult to discern on CT thorax (Figs 2B and D). A whole-body PET-CT scan confirmed the isolated hypermetabolic character of the lesion. The pleural and mediastinal extension and the likely vascular nature of the lesion discouraged thoracic surgical procedures.

A solitary lung lesion of choriocarcinoma (case 2) has several hypotheses.[9–12] It may be due to a rare trophoblastic differentiation of primary lung cancer or primary extragenital choriocarcinoma. Also, the lesion in the lung could represent metastases from an undetected GTN, which may have regressed spontaneously leaving only uterine scarring, the "burnt-out" phenomenon, known to occur in choriocarcinomas. Finally, some rare primary lung carcinomas can be simply confused with choriocarcinoma.

In our young females with irregular vaginal bleeding, we tended to prefer the diagnosis of a metastatic GTN, but none of the other hypotheses could be excluded.

To conclude we present a very rare case of GTN with a metastatic deposit in the finger. Also described is a second uncommon case of solitary choriocarcinoma of the lung with brain metastasis. Awareness of GTN and its spectrum of lung involvement will assist in the early diagnosis and treatment of this potentially curable disease.

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