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Case Report

A metastatic intermediate trophoblastic tumor of unspecified subtype presenting as pneumothorax

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Introduction

Intermediate trophoblasts, a subtype of trophoblastic tissue arising from the cytotrophoblast can give rise to four distinct lesions which include the exaggerated placental site (EPS), placental site nodule (PSN), placental site trophoblastic tumor (PSTT), and epithelioid trophoblastic tumor (ETT). Rare and usually benign, these tumors reveal malignant potential in 10–15% of cases. Two particularly malignant lesions include the placental site trophoblastic tumor and the epithelioid trophoblastic tumor that arise from the chorion laeve (Shih and Kurman, 2001; Soper et al., 2004). The average age at time of diagnosis is 30 years with a range of 19–62 years (Schulz-Bischof and Scheidel, 2007). Most commonly, these patients present with abnormal uterine bleeding and low serum levels of β-HCG, preceded by a normal pregnancy or a spontaneous abortion (Baergen et al., 2006; Kurman, 1991). Diagnosis can be difficult and delayed. By the time of patient presentation, frequently there is already evidence of metastatic disease. Pneumothorax is a rare form of initial presentation in the patient with metastatic lung disease (Biran et al., 1992).

Case

A 47 year old African-American multipara (G4P3013) woman without any significant past medical history presented to the emergency room with complaints of worsening shortness of breath and right-sided chest pain. She reported that this episode was similar to a previous episode 15 months ago when she presented to a different hospital at which time diagnosis of a spontaneous right pneumothorax was made. She had a chest tube placed at that time followed by a 4-day hospitalization prior to release with no further evaluation. The patient acknowledged a history of cigarette smoking and denied a history of tuberculosis, or any prior lung disease.

Evaluation in the emergency room revealed radiologic evidence of a recurrent pneumothorax (Fig. 1). A chest tube was placed and she was admitted to the cardiothoracic surgery service. On admission, she had a computed tomography scan which revealed multiple cystic lesions in her lungs, a hypo-dense lesion in her liver, and a pelvic mass concerning for a necrotic fibroid. Internal medicine, Obstetrics/Gynecology and Interventional Radiology were consulted.

She underwent trans-bronchial biopsies and bronchoalveolar lavage, which returned non-diagnostic. Serum studies for infectious processes also returned negative. The pulmonary service recommended surgical lung biopsy for diagnosis of a pulmonary process. Given the characteristics of the lesions, the leading differentials were between metastatic processes versus septic emboli.

To the Gynecology consult service, the patient reported a 2-year history of irregular vaginal bleeding. She stated that recently the bleeding had been lighter than in the past. She stated that for the past two years she had also noted a slow increase in abdominal girth and a 15 lb weight gain in the past 5 months.

Also, the patient gave a history of having a positive urine pregnancy test during an annual exam 3 months ago. She had a positive urine pregnancy and quantitative HCG blood test two years ago prior to that exam at her family medicine clinic, which was not further evaluated. The patient reported that her last pregnancy was 12 years ago, which resulted in the cesarean delivery of a term male infant. She had not been on any form of contraception since.

An endometrial biopsy was performed which returned with features of both an epithelioid trophoblastic tumor and a placental site trophoblastic tumor, making the more general diagnosis of an intermediate trophoblastic tumor appropriate. A β-HCG obtained at the time of the endometrial biopsy was noted to be 59.7 IU/L. An IR biopsy of the liver lesion was found to be consistent with metastatic trophoblastic disease. She underwent exploratory laparotomy with total abdominal hysterectomy, bilateral salpingo-oophorectomy and omentectomy on day 12 of her hospital admission. No gross disease other than a necrotic uterus was noted in the abdomen, and close inspection of the liver revealed no gross exophytic lesions. At completion, no residual disease burden was noted in the abdomen or pelvis.

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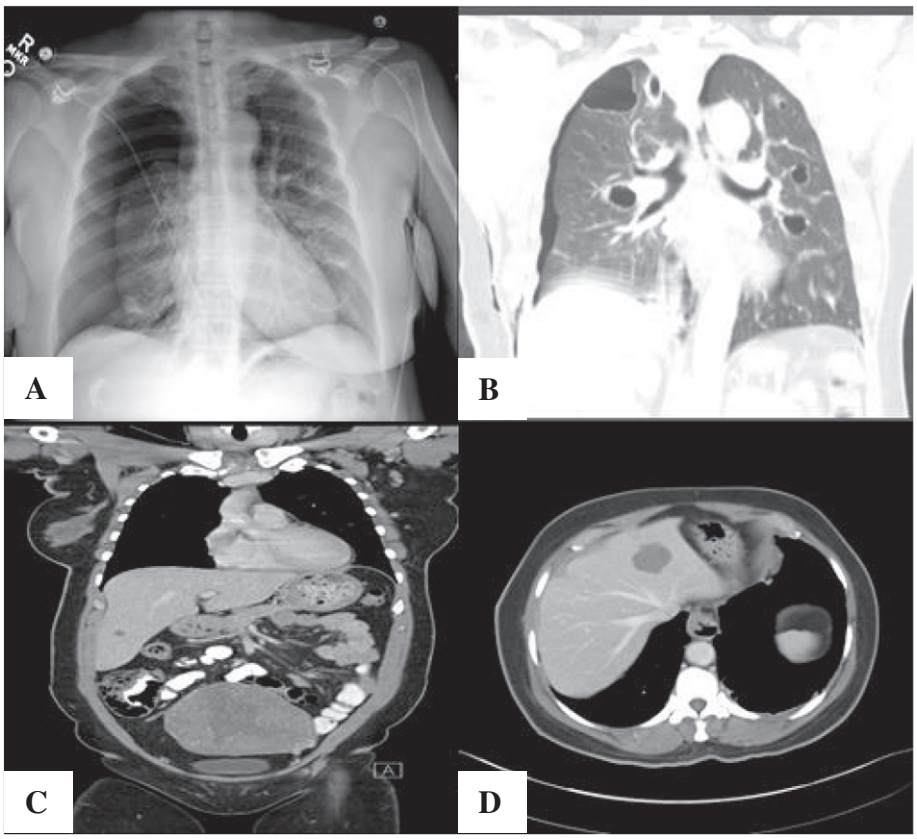

Fig. 1. A. Right pneumothorax. B. Multiple cystic lesions of varying size in both lungs with mildly thickened walls. C. Enlarged uterus with heterogeneous enhancement. D. Metastatic liver lesion.

Her postoperative β-HCG was noted to be 17.8 IU/L. Pathology results of the surgical specimen confirmed initial diagnosis obtained by endometrial biopsy. Her final diagnosis was FIGO Stage IV intermediate trophoblastic disease.

Her right pneumothorax had been resolved by postoperative day 5 and the chest tube was removed. However, the patient's postoperative course was complicated by a left sided pneumothorax for which she underwent left sided chest tube placement by IR on postoperative day 6. Prior to discharge the patient underwent placement of a chemoport and left pigtail chest tube. Her pneumothoraces were believed to be secondary to the extensive pulmonary metastatic disease. She was discharged from the hospital on postoperative day 15 with no further sequelae.

She underwent a VATS procedure with cardiothoracic surgery in June 2013 after her first cycle of chemotherapy due to persistent pneumothorax on the left side as well as recurrent pleural effusions on the right side, which were treated with left chest tube placement, right lung decortication and pleurodesis.

She underwent chemotherapy treatment with 10 cycles of EMA-CO (etoposide, methotrexate, actinomycin D, cyclophosphamide and vincristine) from May 2013 to November 2013. The patient was then noted to have an increasing HCG of 3.3 IU/L in February 2014 to 8.3 in May 2014 with negative imaging. The patient then underwent 6 cycles of 2nd line EMACO, last on 8/26/14. On 9/9/14, her HCG was 2.3 IU/L, however, has now started rising again, most recently 21 IU/L in November 2014. The patient tolerated the cycles of chemotherapy well with minimal side effects; however, she has had persistent pulmonary complaints of a dry cough and recently pulmonary abscesses. Her course has been followed by B-HCG as HPL was not available at our institution and imaging was performed for rising HCG or worsening symptoms.

Discussion

Trophoblastic tumors remain a rare and elusive disease process. Diagnosis of these tumors can prove difficult, as most often the symptoms at the time of presentation are often vague. Diagnosis of this rare form of trophoblastic disease has proven difficult due to very few cases having been reported in literature.

As proven to be the case in our scenario, a thorough history of the patient's presentation can prove useful in establishing a comprehensive list of differential diagnoses. Pneumothorax is a rare presentation of GTN and still a more uncommon complication with metastatic lung disease of any etiology (Aggarwal et al., 2010; Brufman et al., 1977).

In the setting of abnormal uterine bleeding and a positive urine pregnancy test, consideration should be given to the possibility of gestational trophoblastic diseases. In our patient, an earlier diagnosis could have been achieved if the patient was referred to an Ob/Gyn for evaluation.

Further separating this case from previously published case reports are the patient's histologic findings. This intermediate trophoblastic tumor is composed of two cell populations (Fig. 2). One population is the chorionic-type intermediate trophoblast, and the other is the implantation site intermediate trophoblast. The chorionic-type intermediate trophoblast comprises the epithelioid trophoblastic component of this tumor, and the implantation site intermediate trophoblast comprises the placental site trophoblastic component of this tumor.

Her antecedent pregnancy having been 12 years prior to her presentation is also an uncommon occurrence with placental site trophoblastic tumors. Very few studies are published regarding mortality risks in patients with these tumors. To date, the only correlate that has been found between overall survival rates of the patient has been FIGO staging, with

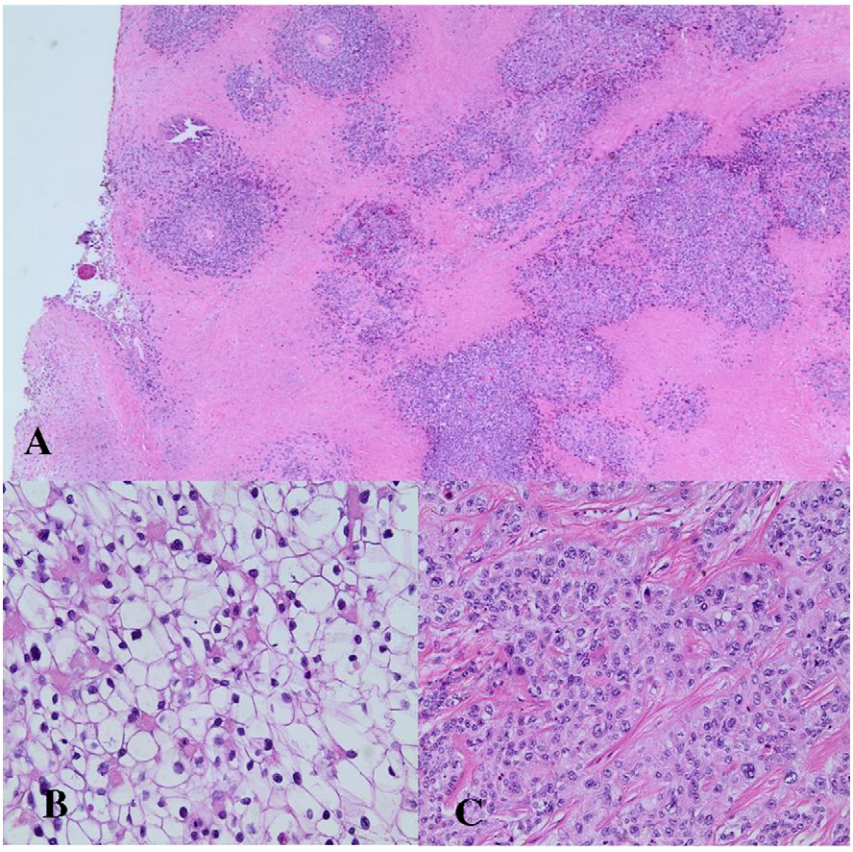

Fig. 2. A. An area of geographic necrosis is present with islands of tumor cells. B. The epithelioid trophoblastic portion of this tumor is composed of relatively uniform epithelioid cells. These cells are mononuclear with abundant eosinophilic cytoplasm. Occasional populations of tumor cells contain clear, glycogen-rich cytoplasm. C. Additionally there is a second population of cells, which comprise the placental site trophoblastic component of this tumor. These cells are large and polygonal with irregular, hyperchromatic nuclei. There are characteristic areas of myoinvasion present.

Stage IV predicting an overall worse survival. Time from antecedent pregnancy played no role in survival rates (Baergen et al., 2006).

To the best of our knowledge, our patient is the fifth reported case with the presentation of a spontaneous pneumothorax (Schulz-Bischof and Scheidel, 2007). None of the other four cases had an antecedent pregnancy occurring longer than two years prior to presentation with this constellation of symptoms. Also, unlike previous case reports, the final pathologic diagnosis in our patient displayed features of both an epithelioid trophoblastic tumor and a placental site trophoblastic tumor, a finding that has not been previously reported.

A placental site trophoblastic tumor, though a rare form of GTN, can prove difficult to treat as we have learned in the course of our patient. It requires a multidisciplinary approach. Though the patient may have an initial response to chemotherapy, the pulmonary sequelae may persist as in the case of our patient.

Conflict of interest

The authors have no conflicts of interest or financial disclosures.

References

Aggarwal, N., Sawhney, H., Vasishta, K., Pathak, N., Saran, R.K., Nijhawan, R., 2010. Metastatic placental site trophoblastic tumor: a case report. J. Obstet. Gynaecol. Res. 27 (1), 49–52.

Baergen, R.N., Rutgers, J.L., Young, R.H., Osann, K., Scully, R.E., 2006. Placental site trophoblastic tumor: a study of 55 cases and review of the literature emphasizing factors of prognostic significance. Gynecol. Oncol. 100 (3), 511–520.

Biran, H., Dgani, R., Wasserman, J.P., et al., 1992. Pneumothorax following induction chemotherapy in patients with metastases treatment: a case report and literature review. Ann. Oncol. 3, 297–300.

Brufman, G., Krasnokuki, D., Schwartz, A., Biran, S., 1977. Spontaneous pneumothorax complicating lung metastases from carcinoma of the breast. Radiol. Clin. (Basel) 46 (1), 38–41.

Kurman, R.J., 1991. The morphology, biology, and pathology of intermediate trophoblast: a look back to the present. Hum. Pathol. 22 (9), 847–855.

Schulz-Bischof, K., Scheidel, P., 2007. Metastatic placental site tumor: diagnosis during a spontaneous pneumothorax. Pathologe 28 (3), 229–234.

Shih, I.M., Kurman, R.J., 2001. The pathology of intermediate trophoblastic tumors and tumor-like lesions. Int. J. Gynecol. Pathol. 20 (1), 31–47.

Soper, J.T., Mutch, D.G., Schink, J.C., 2004. Diagnosis and treatment of gestational trophoblastic disease: ACOG Practice Bulletin No. 53. Gynecol. Oncol. 93 (3), 575–585.