Bullae-Forming Pulmonary Metastasis from Choriocarcinoma Presenting as Pneumothorax

Kwanyong Hyun, M.D.¹, Hyeon Woo Jeon, M.D.², Kyung Soo Kim, M.D.¹, Kook Bin Choi, M.D.¹, Jae Kil Park, M.D.¹, Hyung Joo Park, M.D.¹, Young Pil Wang, M.D.¹

Gestational trophoblastic disease (GTD) is a condition of uncertain etiology, choriocarcinoma, or placental-site hydatidiform moles, invasive moles, choriocarcinoma, and placental-site trophoblastic tumors. It arises from the abnormal proliferation of trophoblastic tissue and spreads beyond the uterus hematogenously. The early diagnosis of GTD is important to ensure timely and successful management and the preservation of fertility. We report the unusual case of a metastatic choriocarcinoma that formed bullae on the lung surface and presented as recurrent pneumothorax in a 38-year-old woman with elevated beta-human chorionic gonadotropin (hCG) levels. She underwent thoracoscopic wedge resection of the involved lung and four subsequent cycles of consolidation chemotherapy. No other evidence of metastatic disease or recurrent pneumothorax was noted during 22 months of follow-up. GTD should be considered in the differential diagnosis of spontaneous pneumothorax in reproductive-age women with an antecedent pregnancy and abnormal beta-hCG levels.

Key words: 1. Pneumothorax 2. Choriocarcinoma 3. Lung metastasis 4. Chemotherapy

CASE REPORT

A 38-year-old multipara woman was admitted to Seoul St. Mary’s Hospital for the evaluation and treatment of persistently elevated human chorionic gonadotropin (hCG) levels over the previous three years, with the presumptive diagnosis of a persistent gestational trophoblastic tumor (GTT). Four years previously, she was diagnosed with a hydatidiform mole and had shown persistently elevated hCG levels since her last normal gestation. To treat this condition, she underwent three cycles of methotrexate treatment and subsequent laparoscopic total hysterectomy. At the time, she was suspected to have a carcinoma or ectopic beta-hCG production, and positron emission tomography (PET) showed two bullae-like lesions in the right lower lung base with no definitive indications of increased metabolic activity. Therefore, it was difficult to conclude that these lesions were malignant.

For the treatment of persistent GTT, she was started on etoposide, methotrexate, and actinomycin D alternating with cyclophosphamide and vincristine (EMA/CO) chemotherapy...
Fig. 1. (A) An initial X-ray and (B) computed tomography imaging of the chest showed right pneumothorax and two cavitory lesions on the base of the right lower lobe.

Fig. 2. A small bullous lesion was identified during video-assisted thoracoscopic surgery.

and was referred to the department of thoracic and cardiovascular surgery for the treatment of asymptomatic recurrent pneumothorax. Although she had no signs of dyspnea or chest pain, a routine chest X-ray was performed, revealing right-sided pneumothorax with small amount of pleural effusion (Fig. 1). The patient was a non-smoker with no underlying lung disease, but had a previous history of pneumothorax, which was managed conservatively at the local hospital six months previously. As she was hemodynamically stable at presentation, we proceeded to a comprehensive work-up instead of placing a chest tube. Computed tomography (CT) images also revealed two bullae-like lesions in the right lower lung base with no other solitary lung nodules.

For the simultaneous treatment of the pneumothorax and the lung lesions that were identified, the patient underwent video-assisted thoracoscopic wedge resection of the bullae using a linear endostapler. No pleural pathology was observed intraoperatively, and we found multiple bullae on the lower margin of the basal segment of the right lower lobe (Fig. 2). Since the bullae were located in an unusual site of the lung for pneumothorax, we collected frozen pathology sections during surgery. The frozen sections showed severe inflammation, necrosis, and atypical cells of unknown origin. The margin was adequate and negative for malignancy, so the remaining lung was not further resected. Postoperatively, the right lung remained fully expanded, and the patient was advanced to adjuvant chemotherapy immediately after the removal of chest tube drainage on postoperative day 3.

Permanent histological examination of the lung specimen revealed multinucleated and eosinophilic syncytiotrophoblastic cells lining large cystic spaces (Fig. 3D). All tumor cells stained strongly for cytokeratin and hCG (Fig. 3B, C). This finding further supported the diagnosis of metastatic chorionicarcinoma.

On postoperative day 7, laboratory studies confirmed that the patient’s hCG level had dropped to 15 mIU/mL and daily follow-up chest X-rays also showed complete resolution of the right-sided pneumothorax. The patient was discharged from the hospital, and after an uneventful discharge, she underwent a total of four cycles of EMA/CO adjuvant consolidation chemotherapy on a regular basis in an inpatient hospital unit. No other evidence of metastatic disease or re-
Bullae-Forming Pulmonary Metastasis

Fig. 3. (A) Gross specimen of the 0.5-cm whitish bullous nodule. (B) A bullous tumor nodule positive for beta-human chorionic gonadotropin staining was observed on the left side. Normal lung parenchyma was also noted on the right side (×200). (C) Positive beta-human chorionic gonadotropin staining (×400). (D) High-power microscopy showing multinucleated and eosinophilic syncytiotrophoblastic cells interwoven with monocytes (H&E, ×400).

current pneumothorax have been noted over 22 months of postoperative follow-up.

DISCUSSION

Choriocarcinoma is a rare type of gestational trophoblastic disease, with an incidence rate of one per 50,000 deliveries [1]. Clinically, the neoplasms may present after hydatidiform moles, normal pregnancy, or abortions. Of these, hydatidiform moles are the most common, occurring in about half of patients. Gestational trophoblastic disease is derived from the placenta, and choriocarcinoma arises from villous trophoblasts. Choriocarcinoma is a malignant hCG-producing epithelial tumor that has anaplastic cuboid cytotrophoblast epithelium and syncytiotrophoblasts. It is the most aggressive form of gestational trophoblastic disease, and presents not only as a local invasion but frequently also as distant hematogenous metastases. At the time of diagnosis, 30% of patients are found to have the disease extending beyond the uterus, with the lung being the most common site of metastasis [1,2]. Hence the lung accounts for 50% to 70% of cases with distant metastasis [2].

Choriocarcinoma is characterized by rapid proliferation and high vascularity of the tumor cells. Therefore, hemorrhage and necrosis of the tumors in primary or metastatic lesions can create varying imaging results. Several case reports have
reported the finding of prominent arteriovenous shunts in pulmonary metastatic tumors from choriocarcinoma [3]. Although Ouellette [4] previously documented unsuspected metastatic choriocarcinoma presenting as unilateral spontaneous pneumothorax, pneumothorax is an unusual complication of choriocarcinoma. In a review of 1,143 patients with spontaneous pneumothorax, 10 cases were attributed to metastases to the lung, and five of these cases were secondary to metastatic sarcomas [5]. As stated previously, pulmonary metastasis from choriocarcinoma is characterized by necrosis and hemorrhage, and hence one of the proposed mechanisms is necrosis of the metastases, resulting in pleural defects. Pleural metastatic involvement and cystic degeneration may add to the risk of developing pneumothorax.

Fluorodeoxyglucose (FDG)-PET has generally been considered to be a sensitive tool for detecting distant metastases, with a reported sensitivity of 87% for the detection of lung metastases [6]. However, in some cases, low FDG uptake has been found in metastatic nodules from choriocarcinoma. It is well known that the partial volume effect phenomenon affects the quantitative measurement of FDG uptake, particularly in small lesions [7]. Therefore, the reason why the cystic lesion in our case showed low or absent FDG accumulation may have been the underestimation of FDG accumulation as a result of the partial volume effect.

The optimal therapy for metastatic tumors is currently uncertain. However, chemotherapy plays an important role in the treatment of metastatic choriocarcinoma. Although pulmonary resection is not recommended for patients with a satisfactory response to chemotherapy in the initial treatment period, the surgical resection of pulmonary metastatic lesions is indicated when clinical evidence suggests that pulmonary metastatic disease caused relapse, and when these lesions are localized [8]. If pulmonary metastatic lesions present as bullous lesions and cause pneumothorax, as in our case, the thoracotomic or thoracoscopic resection of bullae may be necessary for patients with recurrent or persistent pneumothorax.

In conclusion, we report a case of lung metastasis from choriocarcinoma that presented as recurrent pneumothorax, making diagnosis difficult using preoperative imaging studies. As choriocarcinoma is the most aggressive GTD, characterized by early vascular invasion and widespread metastasis, and can have a range of clinical presentations, a meticulous pulmonary work-up including CT and PET-CT should be performed for bullae-like pulmonary lesions as well as for solitary masses. When a woman in her reproductive years with an antecedent pregnancy shows persistent hCG elevation and recurrent pneumothorax, pulmonary metastasis from a persistent GTT should not be excluded, even if the bullae show only faint FDG accumulation. Furthermore, subsequent pathologic confirmation via bulllectomy should be considered.

**CONFLICT OF INTEREST**

No potential conflict of interest relevant to this article was reported.

**REFERENCES**

1. Ngan S, Seckl MJ. Gestational trophoblastic neoplasia management: an update. Curr Opin Oncol 2007;19:486-91.
2. Small W Jr, Lurain JR, Shetty RM, Huang CF, Applegate GL, Brand WN. Gestational trophoblastic disease metastatic to the brain. Radiology 1996;200:277-80.
3. Choi SH, Goo JM, Kim HC, Im JG. Pulmonary arteriovenous fistulas developed after chemotherapy of metastatic choriocarcinoma. AJR Am J Roentgenol 2003;181:1544-6.
4. Ouellette D, Inculet R. Unsuspected metastatic choriocarcinoma presenting as unilateral spontaneous pneumothorax. Ann Thorac Surg 1992;53:144-5.
5. Dines DE, Cortese DA, Brennan MD, Hahn RG, Payne WS. Malignant pulmonary neoplasms predisposing to spontaneous pneumothorax. Mayo Clin Proc 1973;48:541-4.
6. Pastorino U, Veronesi G, Landoni C, et al. Fluorodeoxyglucose positron emission tomography improves preoperative staging of resectable lung metastasis. J Thorac Cardiovasc Surg 2003;126:1906-10.
7. Soret M, Bacharach SL, Buvat I. Partial-volume effect in PET tumor imaging. J Nucl Med 2007;48:932-45.
8. Liu Y, Yang J, Ren T, et al. The encouraging prognosis of nongestational ovarian choriocarcinoma with lung metastases. J Reprod Med 2014;59:221-6.