Case Report

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# Poorly Differentiated Lung Adenocarcinoma with Choriocarcinomatous Features: A Case Report and Literature Review

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**ABSTRACT**

This report describes a rare case of poorly differentiated lung adenocarcinoma with choriocarcinomatous features in a 70-year-old male patient. The initial symptoms included drooling and cough with white sticky sputum. Imaging revealed a mass in the right lower lung lobe and a metastatic lesion in the right frontal lobe. Histopathology and immunohistochemistry confirmed primary poorly differentiated lung adenocarcinoma with choriocarcinomatous differentiation. Serum β-human chorionic gonadotropin (β-hCG) was markedly elevated to 6979.00 mIU/mL. After treatment with platinum-etoposide chemotherapy combined with tislelizumab immunotherapy and local radiotherapy, the serum β-hCG normalized (3.76 IU/mL), and the tumor volume significantly decreased. This case provides novel clinical insights into the diagnosis and management of pulmonary adenocarcinoma with trophoblastic differentiation.

**Keywords:** Poorly Differentiated Lung Adenocarcinoma with Choriocarcinomatous Features; Immunotherapy

**Abbreviations:** β-hCG: β-Human Chorionic Gonadotropin; NSCLC: Non-Small Cell Lung Cancer; SC: secondary choriocarcinoma; CT: Chest Computed Tomography; IHC: Immunohistochemistry

## Introduction

In the histological classification of lung cancer, non-small cell lung cancer (NSCLC) accounts for 85%, with adenocarcinoma being the most common subtype (40%) [1]. Choriocarcinoma, a highly malignant trophoblastic tumor, predominantly arises in the gonads (90%), while extragonadal choriocarcinomas occur in midline structures such as the mediastinum or retroperitoneum (10%) [2]. Pulmonary adenocarcinoma with choriocarcinomatous features is exceedingly rare and must be distinguished from secondary choriocarcinoma (SC). This case, managed through a multidisciplinary approach integrating morphological, immunohistochemical, and molecular features, is the first reported instance of a mixed adenocarcinoma-choriocarcinoma involving both the lung parenchyma and central nervous system.

## Case Report

A 70-year-old male presented with drooling and cough with white sticky sputum. Chest computed tomography (CT) revealed a 73mm×53mm mass in the right lower lung lobe. Subsequent PET-CT confirmed a hypermetabolic right lower lung mass (infiltrating the ipsilateral pleura) and a right frontal lobe lesion, suggestive of lung

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cancer with metastases (Figures 1 & 2). Brain MRI showed a 37mm cystic mass in the right frontal lobe with perilesional edema, likely metastatic. Laboratory tests revealed markedly elevated serum β-hCG (6979.00 mIU/mL), with unremarkable tumor markers. Pathological examination of the lung biopsy demonstrated invasive adenocarcinoma with mucin production. Immunohistochemistry (IHC) results: Napsin-A(-), TTF-1 (focal+), CK20 (focal+), Ki67 (90%+), P63(-), P40(-), P53(+), CK7(+), CDX-2(-), CK19(+), CEA (scattered+), PSA(-), consistent with poorly differentiated lung adenocarcinoma, likely mucinous subtype (Figure 3). Brain lesion biopsy revealed metastatic poorly differentiated carcinoma. IHC: TTF-1(-), Napsin-A(-), CK7 (partial+), CK20 (focal weak+), P40(+), CK5/6(-), P53 (mutant pattern), Ki67 (95%+). Additional markers: GATA3(+), HCG (focal+), Nut(-), INI-1(+), SMARCA4/Brg1(+), S-100(-), CD56 (focal+), Syn(-), CK(+), Vim(-), CEA(-), Glypican-3(-), P63(+), PLAP (rare+), β-catenin(+), HCG (partial+), hPL(-), α-Inhibin(-) (Figure 3). Molecular testing: MAML2 (11q21) gene breakage (FISH) (-).

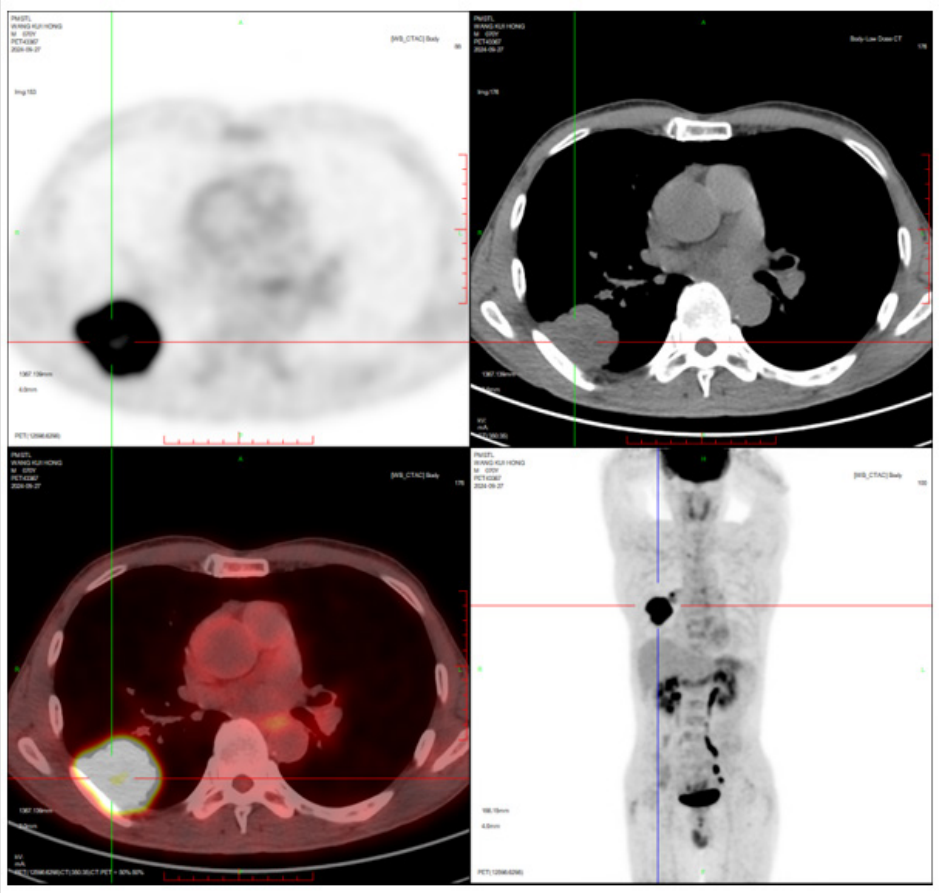

**Figure 1:** PET-CT reveals a lung mass.

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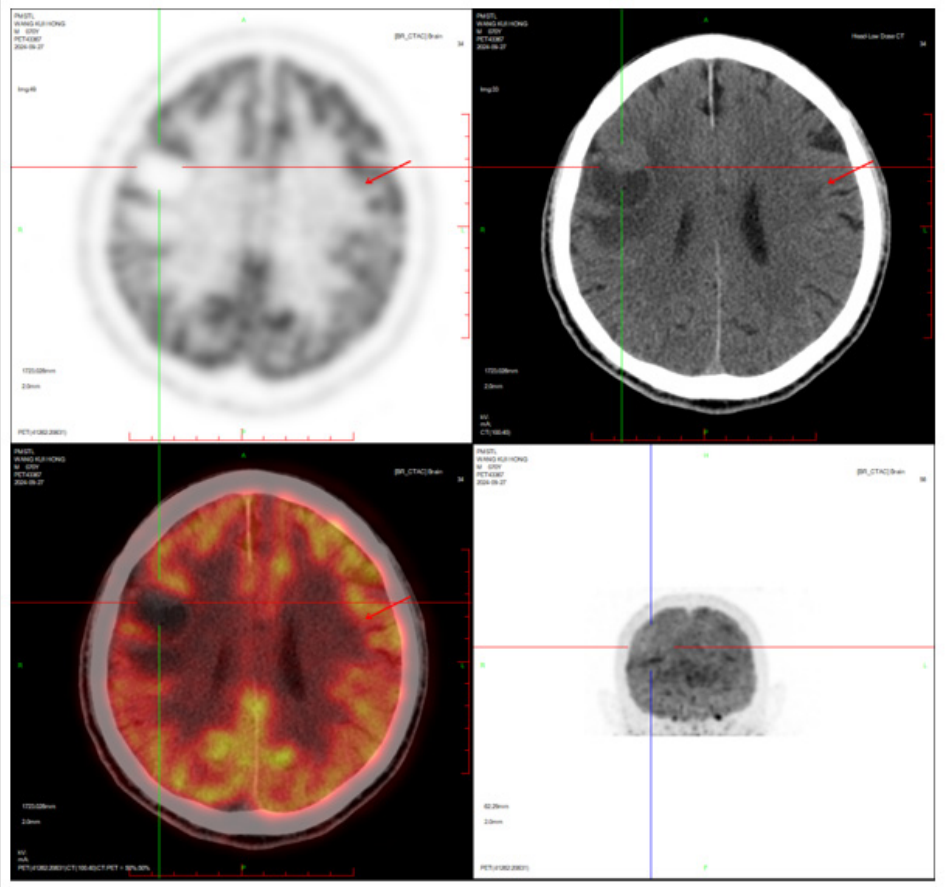

**Figure 2:** PET-CT reveals brain metastases.

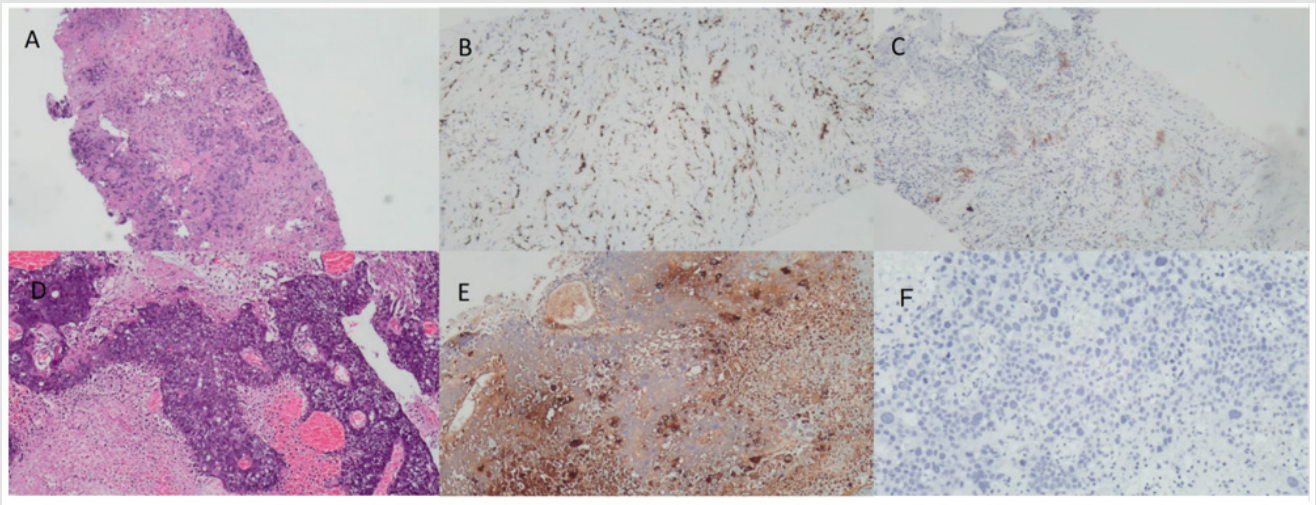


**Figure 3:**
A) HE staining of the lung mass (25x magnification); (D) HE staining of the brain metastatic lesion (50x magnification); (B) Ki-67 positive staining in the lung mass; (C) CEA positive staining in the lung mass; (D) HE staining of the brain metastatic carcinoma (100x magnification); (E) β-HCG positivity in the brain metastatic lesion (IHC, 200x magnification); (F) CEA negativity in the brain metastatic lesion (IHC, 200x magnification).

Based on histomorphology, IHC, and clinical correlation, the brain and lung lesions were diagnosed as synchronous metastases of a primary poorly differentiated lung adenocarcinoma with choriocarcinomatous differentiation. The patient was deemed ineligible for surgery due to metastatic disease. Multigene testing for lung cancer drivers was negative. Treatment included cisplatin-etoposide chemotherapy, tislelizumab immunotherapy, and localized radiotherapy to thoracic and cerebral lesions. After three months, serum β-hCG normalized (3.76 IU/mL), and chest CT demonstrated significant tumor reduction (35 × 26 mm) (Figures 4 & 5).

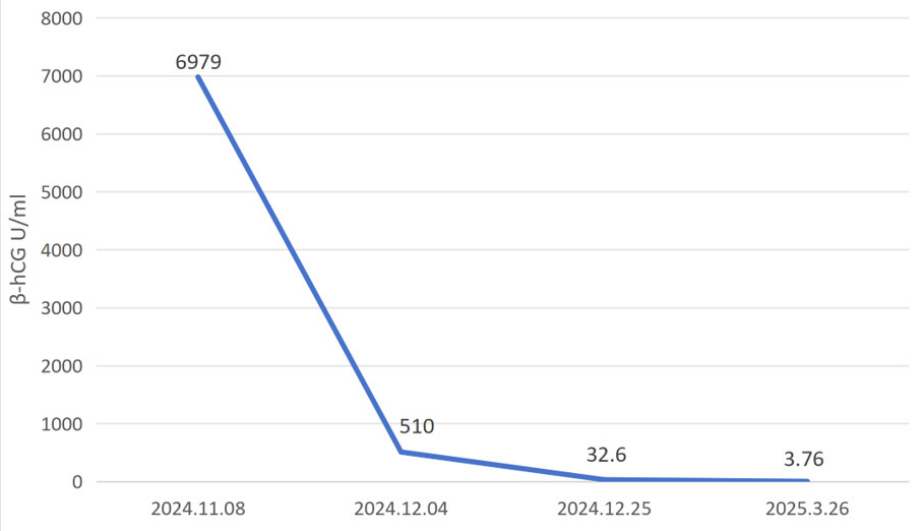


**Figure 4:** Changes in serum β-hCG levels (unit: U/ml) in the patient before treatment (November 8, 2024), after the first treatment course (December 4, 2024), after the second treatment course (December 25, 2024), and after the third treatment course (March 26, 2025).

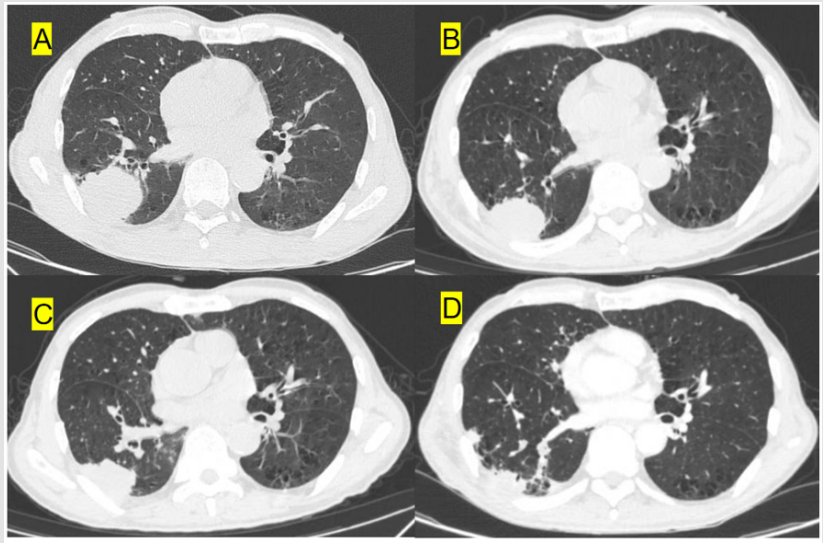


**Figure 5:** Computed Tomography (CT) demonstrates significant regression of the pulmonary tumor following chemotherapy.

A. At initial diagnosis (Oct 2024);
B. Reduction in pulmonary tumor volume 3 months after completion of the first course of chemotherapy and immunotherapy (Dec 2024);
C. Post-second treatment course (Jan 2025);
D. Post-third treatment course (Mar 2025).

## Discussion

Choriocarcinoma is a germ cell tumor containing syncytiotrophoblastic cells that secrete β-hCG and typically occurs following pregnancy. In this case, the male patient ruled out pregnancy-related secondary choriocarcinoma. Lung cancers exhibiting choriocarcinomatous features or trophoblastic differentiation are exceedingly rare. These tumors are fundamentally lung adenocarcinomas but demonstrate trophoblastic differentiation (e.g., syncytiotrophoblast-like morphology) and β-hCG secretion, distinct from conventional lung adenocarcinoma histology. The exact number of primary pulmonary choriocarcinomas or lung adenocarcinomas with choriocarcinomatous features reported in the literature remains unclear, as many studies rely on bronchoscopic specimens, which are often insufficient for comprehensive analysis [3]. Some prior reports have classified these entities under the same disease category. To date, only two cases explicitly defined as "lung adenocarcinoma with choriocarcinomatous features" have been documented [3,4]. One case resembled ours, presenting with a primary lung lesion and cerebellar metastasis pathologically confirmed to be of pulmonary origin, though β-hCG expression was limited to the brain metastasis [3].

In another case, the primary tumor site could not be determined by conventional histopathology or immunohistochemistry (IHC). However, genomic analysis revealed a KRAS G13R mutation (KRAS mutations are the most prevalent cancer drivers in lung adenocarcinoma, accounting for ~35.5% [5], but rare in choriocarcinoma [6,7]), and transcriptomic profiling confirmed pulmonary origin [2]. These findings suggest that molecular markers (e.g., EGFR L858R, EGFR V774M [8,9], and TP53 mutations such as C275G, R273L, V73fs, or D281E [2,8,10,11]) can aid in diagnosing choriocarcinomatous lung tumors. Additionally, the absence of lung-specific IHC markers (e.g., TTF-1, NapsinA) in tumors with choriocarcinomatous features further supports the distinction of lung adenocarcinoma with trophoblastic differentiation [8,9,12,13]. Regarding treatment, surgery or radiotherapy combined with chemotherapy has been used for early-stage lung cancers with choriocarcinomatous features [14]. Chemotherapy regimens such as BEP (bleomycin, etoposide, and cisplatin) and EMA-CO (etoposide, methotrexate, actinomycin-D, cyclophosphamide, and vincristine) are commonly employed [12,14]. Evidence for immune checkpoint inhibitors in these tumors remains limited.

One case report described nivolumab as second-line therapy following pemetrexed, cisplatin, and bevacizumab. The patient's PD-L1 IHC showed positivity in over 50% of cells. Partial response was achieved after four cycles of immunotherapy, but disease progression occurred one year later on CT [3]. In another case, carboplatin, paclitaxel, ipilimumab, and nivolumab were administered. Tumor size decreased by 21% after two cycles, serum β-hCG normalized, and subsequent radiotherapy resulted in no recurrence during follow-up. Due to the paucity of cases, the efficacy of combination therapy remains unclear, but integrating chemotherapy, immunotherapy, and localized radiotherapy may offer a valuable therapeutic strategy for these patients [15].

## Conclusion

This case underscores three key points: First, the primary lung tumor biopsy predominantly exhibited mucinous adenocarcinoma morphology, while the brain metastasis displayed poorly differentiated non-small cell carcinoma features, highlighting significant intratumoral heterogeneity. Thus, abnormal β-hCG elevation warrants suspicion for trophoblastic differentiation. Second, an IHC panel (HCG/GATA3/PLAP) combined with molecular profiling (KRAS/EGFR mutation spectrum) aids in distinguishing primary pulmonary choriocarcinoma from adenocarcinoma with choriocarcinomatous differentiation. Finally, a multimodal approach integrating platinum-based chemotherapy, immune checkpoint inhibitors, and radiotherapy demonstrates potential efficacy in this rare tumor subtype.

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## Data Availability

Not applicable.

## Declarations

### Ethical Approval and Consent to Participate

Not applicable.

### Consent for Publication

Not applicable.

### Competing Interests

The authors declare no competing interests.

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