Case Report

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One needle, two diagnoses: a dual finding of adenocarcinoma and granulomatous reaction after EBUS-TBNA in lung cancer staging – a case report

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Introduction and importance: Coexistence of malignant and granulomatous pulmonary lesions can represent a diagnostic and therapeutic challenge. Distinguishing between tumor recurrence, infectious, or iatrogenic conditions is crucial for guiding appropriate management.

Case presentation: We report the case of a 69-year-old woman referred to our center for evaluation of a 6-mm solid nodule in the left lower lobe, incidentally discovered during a coronary computed tomography scan. Endobronchial ultrasound-guided transbronchial needle aspiration confirmed invasive adenocarcinoma, whereas granulomatous inflammation was identified exclusively in the postoperative surgical specimen. The postoperative course was uneventful, and the patient was discharged in good condition.

Clinical discussion: This case highlights the importance of considering differential diagnoses when encountering granulomatous changes adjacent to malignant tumors. The overlap between iatrogenic, infectious, and tumor-related findings can complicate the diagnostic process. Our experience underscores the importance of histopathological confirmation to avoid misinterpretation, ensure adequate oncological treatment, and prevent overtreatment.

Conclusion: Granulomatous lesions concomitant with lung cancer are rare but clinically relevant. Awareness of this possibility is essential for accurate diagnosis and optimal patient management.

Keywords: diagnostic accuracy, EBUS-TBNA, histopathology, lung cancer, thoracic oncology

INTRODUCTION

Multimodal imaging and histological sampling frequently guide the evaluation of solitary pulmonary nodules. In this context, endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) has become a cornerstone for minimally invasive tissue acquisition. However, instances in which dual pathology is identified from a single biopsy are rare and pose a diagnostic challenge. We report the case of a patient whose EBUS-TBNA demonstrated cytological features consistent with invasive pulmonary adenocarcinoma, without evidence of granulomatous inflammation, raising essential considerations regarding biopsy-induced tissue changes and the interpretation of diagnostic results. This case report has been reported in line with the SCARE checklist[1].

HIGHLIGHTS

- Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) enabled the diagnosis of lung adenocarcinoma in a 69-year-old woman
- Simultaneous finding of adenocarcinoma and granulomatous inflammation in one slide
- Granulomatous reaction likely biopsy-induced, mimicking systemic disease or malignancy
- The case emphasizes interpretive challenges of PET-positive hilar uptake without malignancy
- EBUS-TBNA confirmed as a precise, minimally invasive tool in thoracic oncology diagnostics

Case report

A 69-year-old former smoker and retired schoolteacher was referred to our center for evaluation of a 6-mm solid nodule in the left lower lobe (LLL), incidentally discovered during a coronary computed tomography (CT) scan. Her medical history was significant for treated breast cancer two decades prior, chronic obstructive pulmonary disease, hypertension, dyslipidemia, and bilateral carotid stenosis. A high-resolution

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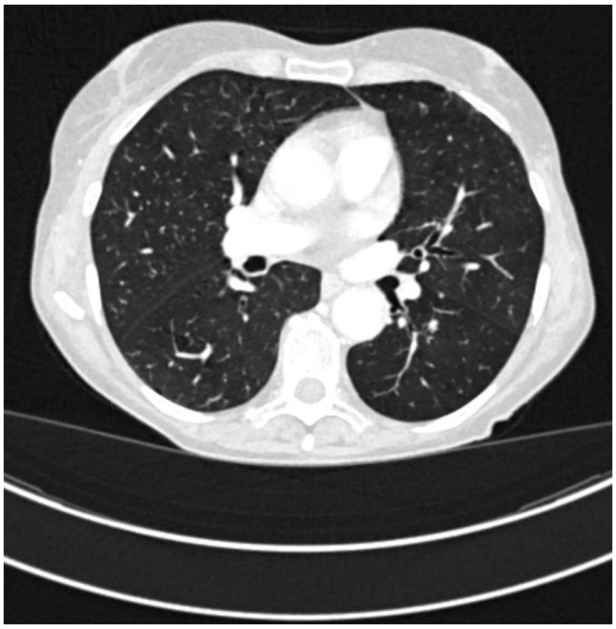

Figure 1. Axial high-resolution computed tomography (HRCT) image showing a solid, 6-mm pulmonary nodule in the perihilar region of the left lower lobe with irregular margins..

CT and subsequent positron emission tomography (PET)-CT scan confirmed the presence of a stable, perihilar LLL nodule without hypermetabolic activity in the lesion itself but with mild uptake (SUV max 4.4) (Figs. 1, 2). Although the primary pulmonary nodule did not show FDG uptake, the PET-CT demonstrated moderate metabolic activity in the left hilar region. This finding raised the suspicion of possible N1/N2 involvement.

Pulmonary function tests revealed mild obstructive impairment with a diffusing capacity of the lungs for carbon monoxide at 69% of predicted. Cardiological evaluation indicated no contraindications for surgery. The case was discussed within a multidisciplinary tumor board, where neoadjuvant therapy was considered due to the clinical stage T1aN1M0 (stage II). Ultrasound-guided sampling of the left hilar station yielded adequate material for rapid onsite evaluation and subsequent histological analysis.

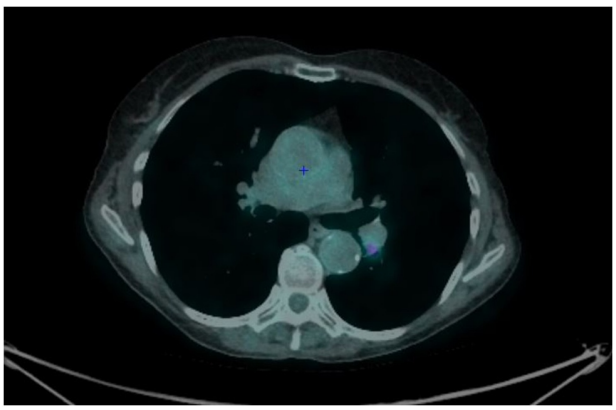

Figure 2. Fused PET-CT image revealing mild metabolic activity in the hilar region (SUV max 4.4), with no uptake in the pulmonary nodule itself.

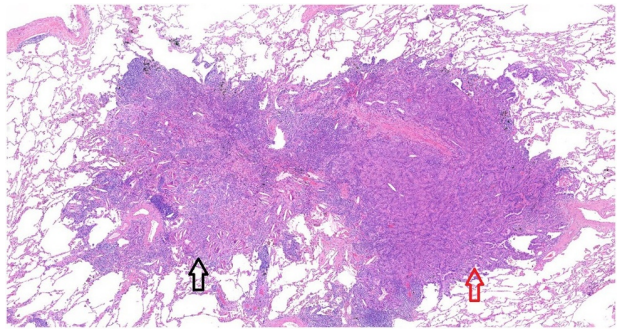

Figure 3. Low-power histological view (hematoxylin and eosin stain, 40×) of the resected surgical specimen showing adjacent foci of invasive adenocarcinoma (red arrow) and granulomatous inflammation (black arrow).

Cytopathologic examination of the transbronchial needle aspirate revealed cohesive clusters of epithelial cells consistent with primary lung adenocarcinoma, which were positive for TTF-1 and napsin A and negative for GATA-3, TRPS1, and p40. As mediastinal involvement was not confirmed on EBUS, the Multidisciplinary Team recommended proceeding directly with surgical resection.

Postoperative histopathological analysis revealed an invasive, non-mucinous pulmonary adenocarcinoma of intermediate differentiation, characterized by acinar, papillary, and focal lepidic patterns, measuring 6 mm in diameter. Adjacent to the neoplastic focus was an area of granulomatous inflammation characterized by multinucleated giant cells and cholesterol clefts, consistent with a foreign body-type reaction (Figs. 3 and 4). The visceral pleura was uninvolved (PL0), and a single hilar lymph node metastasis (pN1) was identified. All other nodal stations were free of tumor. The final pathological stage was pT1aN1M0.

The postoperative course was uneventful, and the patient was discharged in stable condition with instructions for follow-up. Molecular testing for EGFR mutations, ALK rearrangement, and PD-L1 expression was recommended to guide potential adjuvant therapy.

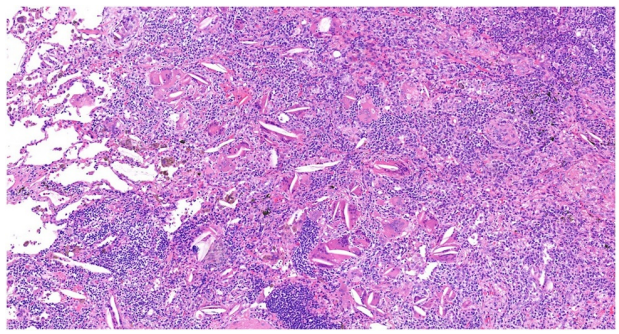

Figure 4. High-power view (H&E, 200×) highlighting the juxtaposition of adenocarcinoma and multinucleated giant-cell granulomatous reaction, consistent with a foreign-body-type inflammation, likely secondary to preoperative EBUS-TBNA.

Discussion

This case illustrates an unusual histological finding: the coexistence of invasive adenocarcinoma and granulomatous inflammation within the same specimen. Granulomatous inflammation in patients with lung cancer may arise from infectious, autoimmune, or sarcoid-like reactions; however, in rare cases, it may be iatrogenic, reflecting a foreign-body-type reaction to fine-needle aspiration biopsy. As reported, granulomatous inflammation may be diagnosed by fine-needle aspiration biopsy (FNAB); however, reports of granulomas induced by FNAB are exceedingly rare. Our case likely represents a procedure-related granulomatous reaction rather than granulomatous disease sampled during biopsy[2].

In our case, the presence of multinucleated giant cells and cholesterol clefts near the neoplastic tissue is compatible with a granulomatous response to foreign material, such as cellular debris or needle fragments introduced during EBUS-TBNA. Although this phenomenon is uncommon, it has been histologically documented in both the lymphatic and parenchymal compartments[3]. Moreover, the finding underscores the importance of distinguishing reactive granulomatous inflammation from granulomas associated with systemic disease, such as sarcoidosis or tuberculosis, particularly in small biopsy specimens. The coexistence of granulomatous inflammation and adenocarcinoma is well documented in the literature and should not be considered an unusual finding.

Importantly, EBUS-TBNA remains a highly sensitive and specific technique for diagnosing lung malignancies and mediastinal lymphadenopathy, with reported diagnostic sensitivities exceeding 85% for malignancy, and has an excellent safety profile[4,5]. In the current case, the procedure yielded not only diagnostic tumor tissue but also captured the adjacent inflammatory reaction, demonstrating the technical precision of EBUS-guided sampling.

Radiologically, the case also exemplifies the interpretative challenges when PET-positive hilar findings do not correlate histologically with malignancy but instead with reactive or iatrogenic inflammation. This phenomenon, termed "false-positive FDG uptake," has been observed in patients with both infectious and iatrogenic granulomatous processes and may complicate staging or prompt unwarranted interventions if not carefully correlated with histological evidence[6]. This case underscores that a procedure-related granulomatous reaction occurring shortly after EBUS-TBNA can mimic nodal involvement on PET-CT, representing a clinically relevant diagnostic pitfall.

Conclusion

This case demonstrates that granulomatous inflammation may develop along the trajectory of a recent EBUS-TBNA and coexist with malignant pathology, creating uncertainty in PET-CT interpretation. Recognizing this phenomenon is crucial to avoid overstaging and to interpret early post-biopsy imaging findings within their procedural context.

Ethical approval

Written patient informed consent was obtained.

Consent

Written patient informed consent was obtained.

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Author contributions

C.D.: study concept, data collection, drafting of the manuscript. M.L.: histopathological analysis, data interpretation, drafting of the manuscript. V.L.d.L.: pathology data collection, critical revision of the manuscript. J.G.: interventional pulmonology procedure, clinical data acquisition, manuscript revision. L.S.: study supervision, critical revision of the manuscript for important intellectual content. L.B.: study design, clinical case management, data interpretation, drafting and final approval of the manuscript.

Conflicts of interest disclosure

The authors declare that they have no conflicts of interest.

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Data availability statement

The data underlying this article will be shared on reasonable request to the corresponding author.

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