J Bras Pneumol. 2023;49(3):e20230147
https://dx.doi.org/10.36416/1806-3756/e20230147

Small samples, big problems: lipoid pneumonia mimicking lung adenocarcinoma

Felipe Marques da Costa[1], Milena Tenorio Cerezoli[1], Augusto Kreling Medeiros[2], Marcos Aurélio Fonseca Magalhães Filho[3], Suellen Nastri Castro[3]

TO THE EDITOR:

Lepidic adenocarcinoma of the lung is a distinct form of lung cancer, characterized by proliferation of neoplastic cells along the alveolar lining without changes in the structure of the alveoli. It is a variant of pulmonary adenocarcinoma, the most common type of lung cancer, and generally has a better prognosis than do other forms of lung cancer, because of its slow growth and more limited pattern of spread.[1]

Sampling of small fragments of lung tissue (e.g., transbronchial biopsy) remains a commonly used diagnostic tool for lung cancer. The main limitations are as follows: 1) samples might not be representative of the entire lesion; and 2) crush artifacts that might not provide enough tissue for a comprehensive histopathological examination, including immunohistochemistry and molecular testing. This can lead to erroneous diagnostic conclusions and unnecessary treatments.[2,3]

A 62-year-old woman who had recently been diagnosed with lung adenocarcinoma—presumably confirmed through a transthoracic biopsy of the right upper lobe, performed at another facility—presented for an oncologic visit for systemic treatment initiation. The patient had no respiratory symptoms. Her medical history included chronic pain secondary to a vertebral fracture in 2015 and constipation secondary to opioids; she used mineral oil laxatives for her constipation. She had never smoked and had no family history of lung cancer.

On physical examination, her RR was = 18 breaths/min, her HR was 80 bpm and her SpO_2 was 93% on room air. Pulmonary auscultation revealed crackles, predominantly in the right hemithorax. Routine blood tests were normal. The patient underwent a PET/CT scan, which showed ground-glass opacities with septal thickening, forming a crazy-paving pattern in the right lung. These opacities were mild in the middle and lower lobes, predominating and coalescing in the upper lobe (Figure 1A). Her previous CT scan was not available. The opacities showed a slightly increased 18F-FDG uptake (maximum standardized uptake value, 3.0), and there were two normal-sized hypermetabolic lymph nodes (right hilar and right upper paratracheal lymph nodes; maximum standardized uptake value, 3.9; Figure 1B).

Before initiation of oncologic treatment, we reviewed the transthoracic biopsy specimens and found no neoplastic cells. In light of this finding, a decision was made to perform a CT-guided transthoracic biopsy of the right upper lobe. The biopsy findings were suggestive of lipoid pneumonia, with no findings suggestive of neoplasia or infection (Figure 1C).

After diagnostic confirmation, treatment with mineral oil was discontinued and nonopioid pain management options were optimized. The patient remained without respiratory symptoms during the follow-up period. The ground-glass opacities remained, showing a slight reduction after 9 months. A follow-up CT scan performed 16 months after the PET/CT scan showed yet another reduction in ground-glass opacities (Figure 1D).

Lipoid pneumonia is a rare lung condition characterized by accumulation of lipid material within the lung parenchyma, resulting from either exogenous (aspiration of oil-based products) or endogenous (disruption of lipid metabolism) sources. Clinical manifestations can vary, ranging from asymptomatic cases to those presenting with cough, dyspnea, chest pain, or fever.[4,5]

Lipoid pneumonia can present as ground-glass opacities, consolidations, or a crazy-paving pattern on chest CT scans. The differential diagnosis includes lung cancer, pulmonary alveolar proteinosis, acute interstitial pneumonia, nonspecific interstitial pneumonia, organizing pneumonia, *Pneumocystis jirovecii* pneumonia, and pulmonary hemorrhage.[6] In the case reported here, an interesting imaging finding was the presence of opacities exclusively in the right lung, predominantly in the upper lobe, an atypical finding for exogenous lipoid pneumonia. The patient later revealed that she had undergone lumbar surgery and slept exclusively on her right side ever since, thus explaining the preferential mechanism by which aspiration of lipid material had occurred. Another interesting imaging finding was an unusually long persistence of parenchymal abnormalities in the context of a lung adenocarcinoma.

In patients presenting with chest CT findings mimicking various pulmonary diseases, including lung cancer, lung biopsy plays a key role in establishing a diagnosis, and the type of biopsy should be carefully selected. The limitations of diagnosing lung cancer from small tissue samples include the risk of sampling errors, which might not capture the full heterogeneity of the tumor, and the possibility of crush artifacts obscuring important histological features. Additionally, small tissue samples might not be enough for comprehensive histopathological examination, immunohistochemistry, and molecular testing, thus limiting the identification of specific tumor subtypes or molecular characteristics crucial for personalized treatment planning.[3,7,8]

1. Serviço de Pneumologia, Hospital Beneficência Portuguesa de São Paulo, São Paulo (SP) Brasil.
2. BP Medicina Diagnóstica, Hospital Beneficência Portuguesa de São Paulo, São Paulo (SP) Brasil.
3. Serviço de Oncologia, Hospital Beneficência Portuguesa de São Paulo, São Paulo (SP) Brasil.

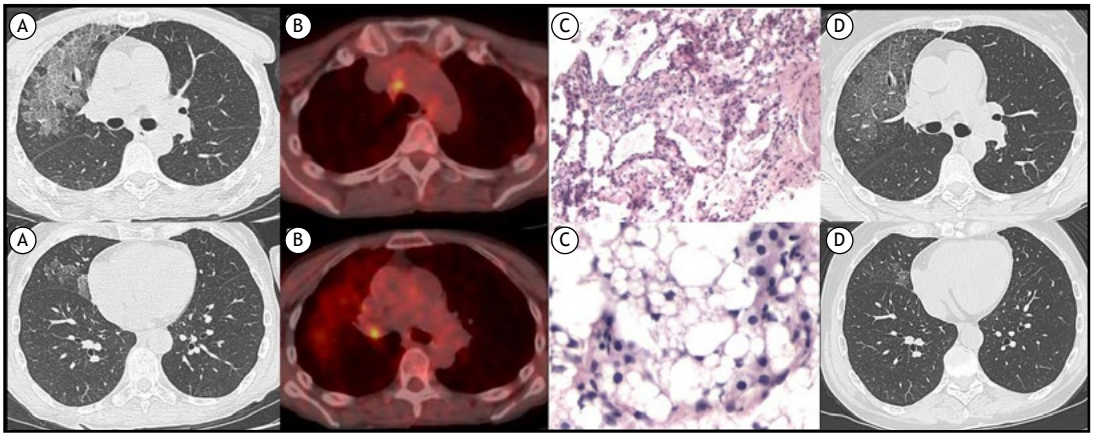

Figure 1. In A, axial CT scans of the chest showing a crazy-paving pattern in the right lung, predominantly in the upper lobe. In B, PET/CT fusion images showing 18-FDG uptake in the lung opacities and in lymph nodes. In C, histopathological images of the pulmonary parenchyma, with the upper image (H&E; magnification, ×10) showing alveolar filling and septal thickening caused by macrophage accumulation and the lower image (H&E; magnification, ×20) showing vacuoles of various sizes in the cytoplasm. In D, follow-up axial CT scans of the chest showing a reduction in ground-glass opacities.

Regarding histopathological findings, lipoid pneumonia and lepidic adenocarcinoma of the lung share some similarities, including lipid-laden macrophages within the alveolar spaces. However, there are key differences between the two. In patients with lepidic adenocarcinoma, malignant glandular epithelial cells line the alveolar walls, but the alveolar architecture is maintained, whereas, in patients with lipoid pneumonia, an alveolar-filling process is accompanied by accumulation of lipid material and a chronic inflammatory response. Immunohistochemically, lepidic adenocarcinoma typically expresses markers of glandular differentiation, such as cytokeratin 7, cytokeratin 20, thyroid transcription factor-1, and napsin A, which are absent in lipoid pneumonia.[4,9]

An alternative to avoid small transbronchial lung biopsy samples, cryobiopsy is a promising method that has proven useful in diagnosing endobronchial and peripheral lung tumors, with increased diagnostic yield and quality of collected samples for histopathological and molecular diagnosis of lung cancer. When used alone or in conjunction with fluoroscopy or radial endobronchial ultrasound, cryobiopsy can improve lung tissue sampling,[10] being similar to transthoracic biopsy or even surgical biopsy (open surgical biopsy or video-assisted thoracoscopic surgery).

Larger biopsy specimens can provide a broader and more detailed view of lung tissue, allowing a more accurate differential diagnosis, especially in cases in which a diagnosis of lung cancer does not seem to match the clinical context or in which other diagnoses are more likely.

AUTHOR CONTRIBUTIONS

FMC, SNC, and AKM: study conception, planning, and design; and data collection. SNC, AKM, MAFMF, and FMC: drafting of the manuscript. FMC, MTC, and MAFMF: revision of the manuscript. All authors read and approved the final version of the manuscript.

CONFLICTS OF INTEREST

None declared.

REFERENCES

1. Lambe G, Durand M, Buckley A, Nicholson S, McDermott R. Adenocarcinoma of the lung: from BAC to the future. Insights Imaging. 2020;11(1):69. https://doi.org/10.1186/s13244-020-00875-6
2. Kage H, Kohsaka S, Shinozaki-Ushiku A, Hiraishi Y, Sato J, Nagayama K, et al. Small lung tumor biopsy samples are feasible for high quality targeted next generation sequencing. Cancer Sci. 2019;110(8):2652-2657. https://doi.org/10.1111/cas.14112
3. Kim L, Tsao MS. Tumour tissue sampling for lung cancer management in the era of personalised therapy: what is good enough for molecular testing?. Eur Respir J. 2014;44(4):1011-1022. https://doi.org/10.1183/09031936.00197013
4. Hadda V, Khilnani GC. Lipoid pneumonia: an overview. Expert Rev Respir Med. 2010;4(6):799-807. https://doi.org/10.1586/ers.10.74
5. Chieng HC, Ibrahim A, Chong WH, Freed H, Fabian T, Saha B, et al. Lipoid Pneumonia. Am J Med Sci. 2022;363(5):452-455. https://doi.org/10.1016/j.amjms.2022.01.019
6. Rossi SE, Erasmus JJ, Volpacchio M, Franquet T, Castiglioni T, McAdams HP. "Crazy-paving" pattern at thin-section CT of the lungs: radiologic-pathologic overview. Radiographics. 2003;23(6):1509-1519. https://doi.org/10.1148/rg.236035101
7. McLean AEB, Barnes DJ, Troy LK. Diagnosing Lung Cancer: The Complexities of Obtaining a Tissue Diagnosis in the Era of Minimally Invasive and Personalised Medicine. J Clin Med. 2018;7(7):163. https://doi.org/10.3390/jcm7070163
8. Nooreldeen R, Bach H. Current and Future Development in Lung Cancer Diagnosis. Int J Mol Sci. 2021;22(16):8661. https://doi.org/10.3390/ijms22168661
9. Zheng M. Classification and Pathology of Lung Cancer. Surg Oncol Clin N Am. 2016;25(3):447-468. https://doi.org/10.1016/j.soc.2016.02.003
10. Simon M, Simon I, Tent PA, Todea DA, Haranguș A. Cryobiopsy in Lung Cancer Diagnosis-A Literature Review. Medicina (Kaunas). 2021;57(4):393. https://doi.org/10.3390/medicina57040393