CASE REPORT

Testicular Metastasis as a Sanctuary Site Detected on 18F-FDG PET-CT in Disseminated Small-Cell Lung Cancer: A Diagnostic and Management Dilemma

Metástase Testicular como Local Santuário Detetada por PET-TC com 18F-FDG em Cancro do Pulmão de Pequenas Células Disseminado: Um Dilema Diagnóstico e Terapêutico

Alok Mandal [1], *Preeti Sharma* [2], *Parneet Singh* [3], *Sachet Saxena* [4]

1 - DEPARTMENT OF NUCLEAR MEDICINE, HCG-CURIE ABDUR RAZZAQUE ANSARI CANCER INSTITUTE, RANCHI, JHARKHAND, INDIA.
2 - DEPARTMENT OF OTORHINOLARYNGOLOGY, GOVERNMENT MEDICAL COLLEGE, RAJOURI, JAMMU AND KASHMIR, INDIA.
3 - DEPARTMENT OF NUCLEAR MEDICINE, AMERICAN INTERNATIONAL INSTITUTE OF MEDICAL SCIENCES, UDAIPUR, RAJASTHAN, INDIA.
4 - DEPARTMENT OF MEDICAL ONCOLOGY, AMERICAN INTERNATIONAL INSTITUTE OF MEDICAL SCIENCES, UDAIPUR, RAJASTHAN, INDIA

https://doi.org/10.82582/thorac.83

Autor Correspondente/Corresponding Author:
Dr. Parneet Singh (MBBS, MD, FABNM, FEBNM)
https://orcid.org/0000-0003-2149-9077
American International Institute of Medical Sciences,
Near Airport Rd, Bedwas, Transport Nagar, Udaipur, Rajasthan, Pin – 313001, India
Email: parneetsingh999@gmail.com

Declaração de Contribuição/Contributorship Statement:

AM: Was involved in literature review and manuscript drafting.
PSharma: Was involved in the collection of clinical details and manuscript editing.
PSingh: Contributed to the interpretation of the PET-CT images, conception of the case report, and critical revision of the manuscript.
SS: Contributed to the preparation of the figures and final proofreading of the manuscript.
All authors read and approved the final manuscript to be published.

AM: Participou na revisão da literatura e na redação do manuscrito.
PSharma: Participou na recolha de dados clínicos e na edição do manuscrito.
PSingh: Contribuiu para a interpretação das imagens de PET-CT, a conceção do relato de caso e a revisão crítica do manuscrito.
SS: Contribuiu para a preparação das figuras e a revisão final do manuscrito.
Todos os autores leram e aprovaram o manuscrito final a ser publicado.

Recebido/Received: January 16th, 2026
Aceite/Accepted: May 18th, 2026
Publicado online/Published online: July 10th, 2026
Publicado / Published: August 18th, 2026

ABSTRACT

Testicular involvement in the systemic disease is rarely encountered owing to its blood-testis barrier (BTB), making it an immune-privileged site as well as a sanctuary site. Metastasis to the testis from small-cell lung cancer (SCLC) is a rare phenomenon, typically indicating advanced systemic disease and breakdown of the BTB. We present the case of a 64-year-old male with left-sided small-cell lung cancer who underwent 18F-FDG PET-CT for staging. Staging 18F-FDG PET-CT revealed widespread nodal & skeletal metastases and an incidental hypermetabolic focus in the left testis, which was confirmed to be metastatic on HPE. This case highlights the importance of evaluating the scrotum in patients with disseminated malignancy and the potential of PET-CT to evaluate the whole body in a single study and to identify metastases even in rare sites.

RESUMO

O envolvimento testicular na doença sistémica é raramente observado devido à barreira hematotesticular (BST), o que o torna um local imunologicamente privilegiado e um local santuário. A metastização para os testículos no cancro do pulmão de pequenas células (CPPC) é um fenómeno raro, geralmente indicativo de doença sistémica avançada e de disrupção da barreira hematotesticular. Apresentamos o caso de um homem de 64 anos com CPPC que realizou PET-TC com 18F-FDG para estadiamento. O exame revelou metástases nodais e esqueléticas disseminadas, bem como um foco hipermetabólico incidental no testículo esquerdo, posteriormente confirmado como metastático no exame histopatológico. Este caso destaca a importância da avaliação do escroto em doentes com neoplasia disseminada e o potencial da PET-TC para avaliar todo o organismo num único exame e identificar metástases mesmo em locais raros.

Keywords:
Blood-Testis Barrier; Fluorodeoxyglucose F18; Positron Emission Tomography Computed Tomography; Small Cell Lung Carcinoma/diagnostic imaging; Testicular Neoplasms/secondary

Palavras-chave:
Barreira Hematotesticular; Carcinoma do Pulmão de Pequenas Células/diagnóstico por imagem; Fluordesoxiglucose F18; Neoplasias Testiculares/secundária; Tomografia por Emissão de Positrões Combinada à Tomografia Computorizada

INTRODUCTION

Metastatic involvement of the testis is rarely encountered (0.1%–3.6% of all testicular tumors) owing to its relatively lower scrotal temperature and the blood-testis barrier, which serves as a pharmacological, immunological and biological sanctuary.[1,2] While common metastatic sites for SCLC include the brain, bone, liver, and adrenals, testicular involvement is often a harbinger of widespread hematogenous dissemination & BTB breakdown and indicates a poor prognosis.[3] We hereby report a case of small cell lung cancer, where testicular metastasis was identified alongside extensive skeletal and nodal disease identified on staging 18F-FDG PET-CT scan.

CASE REPORT

A 64-year-old male smoker presented with chronic cough, severe back pain, and significant weight loss (7 kg) over three months. A chest X-ray was performed, which revealed a mass in the left lung upper lobe. The patient then underwent HRCT chest for characterization of the lesion. It revealed a large soft tissue mass (6.3 x 4.7 x 3.9 cm) with spiculated margins in the left lung upper lobe, along with mediastinal lymphadenopathy. Subsequently, endobronchial ultrasound-guided biopsy of the lung mass confirmed small cell lung cancer (strong and diffuse positivity for synaptophysin & chromogranin with dull and diffuse positivity for TTF-1). The patient then underwent whole-body 18F-FDG PET-CT for staging and it revealed extensive disseminated disease, including a FDG-avid LUL mass, few right lung nodules, along with left supraclavicular, mediastinal and abdominal lymphadenopathy and skeletal metastases. The scan also revealed an intensely FDG-

avid heterogeneously enhancing lesion involving the left testis, measuring 3.1 x 2.8 cm with SUVmax 7.1.

Despite the widespread disease confirming stage IV status, the testicular lesion posed a diagnostic dilemma. A possibility of synchronous primary testicular germ cell tumor with abdominal lymphadenopathy (a potentially curable pathology) needed to be ruled out versus metastatic lung cancer (prognostically poor). Although testicular germ cell tumors typically occur in younger men, it has been reported in older patients and therefore cannot be excluded based on age alone. In our case, the presence of abdominal lymphadenopathy raised the possibility of a synchronous primary testicular germ cell tumor, warranting definitive histopathological evaluation. To confirm the diagnosis, the patient underwent a scrotal USG, which revealed a hypoechoic vascular lesion. Subsequently, the patient underwent left radical inguinal orchiectomy. This was deemed necessary for definitive tissue diagnosis and local palliation, as testicular metastases are resistant to many systemic chemotherapies due to the blood-testis barrier. HPE confirmed metastatic involvement from lung cancer with immunohistochemistry positive for synaptophysin, chromogranin and TTF-1.

DISCUSSION

Testicular metastasis from lung cancer is extremely rare and has been infrequently reported in the literature[3-6] including a case of large cell lung carcinoma associated with synchronous pleural mesothelioma.[7] The present case is distinct in demonstrating small cell lung carcinoma with testicular involvement detected by staging 18F-FDG PET-CT scan in the background of widespread systemic dissemination.

In our case, the presence of an FDG avid testicular lesion along with extensive nodal and skeletal metastases raised a significant diagnostic dilemma, particularly in differentiating metastatic disease from a synchronous primary testicular malignancy, which carries significantly different therapeutic and prognostic implications. This case emphasizes the value of whole-body 18F-FDG PET-CT in identifying uncommon metastatic sites and highlights the importance of histopathological confirmation to guide appropriate management in advanced small-cell lung cancer.

The presence of testicular metastasis in the context of widespread bone and abdominal disease suggests a high tumor burden with probable breakdown of BTB.[3,4] This barrier often prevents adequate penetration of chemotherapeutic agents, allowing the testis to serve as a “sanctuary site” where cancer cells can proliferate even while other systemic sites respond to treatment.[2,8]

Testicular metastasis is generally associated with a poor prognosis, with a mean survival of 6–12 months post-diagnosis.[4,5] It reflects the aggressive heterogeneous behavior of the tumor, as demonstrated in this case by extensive skeletal and nodal involvement. Hence, precise diagnosis and site-specific management are critical, as they directly affect the overall treatment strategy.

Also, due to its rare involvement, a testicular mass cannot be presumed to represent metastatic disease without proper investigation, even in the presence of disseminated lung cancer, to ensure appropriate management.

This case illustrates that although unusual, testicular metastasis can occur in disseminated small cell lung cancer and highlights the importance of 18F-FDG PET-CT for staging, identification of rare sites of metastasis, as well as guiding the appropriate management.

Ethical Disclosures:

Conflicts of Interest: The authors have no conflicts of interest to declare.

Financing Support: This work has not received any contribution, grant or scholarship.

Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of patient data.

Patient Consent: Consent for publication was obtained.

Provenance and Peer Review: Not commissioned; externally peer-reviewed.

Responsabilidades Éticas:

Conflitos de Interesse: *Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.*

Fontes de Financiamento: *Não existiram fontes externas de financiamento para a realização deste artigo.*

Confidencialidade dos Dados: *Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.*

Consentimento: *Consentimento do doente para publicação obtido.*

Proveniência e Revisão por Pares: *Não comissionado; revisão externa por pares.*

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FIGURE LEGENDS

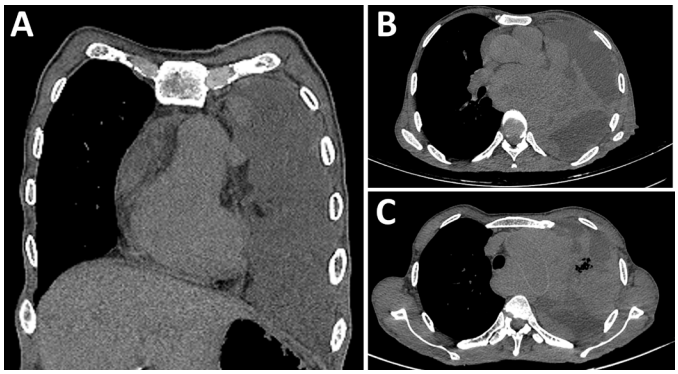

Figure 1 **Non-contrast CT images of the chest demonstrating the primary thoracic disease.** (**A**) Coronal image showing a soft-tissue mass in the left lung upper lobe with associated collapse–consolidation of the adjacent lung. (**B, C**) Axial images showing the left lung upper lobe mass with associated pleural effusion, consistent with advanced primary lung malignancy.

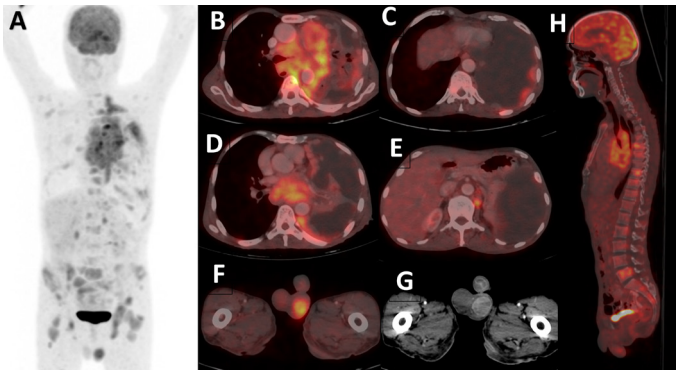

Figure 2 **Whole-body 18F-FDG PET-CT images demonstrating disseminated metastatic disease** (**A**) Maximum intensity projection (MIP) image showing increased FDG uptake in the left hemithorax, along with multiple foci of increased FDG uptake in the left supraclavicular, mediastinum, upper abdomen, visualized skeleton and left testicular region. (**B-D**) Axial fused PET-CT images showing intense FDG uptake in the left lung upper lobe primary tumor and mediastinal nodal metastases. (**E**) Axial fused PET-CT image showing FDG-avid abdominal lymphadenopathy. (**F-G**) Axial fused PET-CT and corresponding CT images showing an intensely FDG-avid heterogeneously enhancing lesion in the left testis. (**H**) Sagittal fused PET-CT image showing extensive FDG-avid skeletal metastases involving the axial skeleton.