Diagnostic challenge of aneurysmal dermatofibroma mimicking cutaneous metastasis in a patient with lung cancer: A case report

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Received August 28, 2025; Accepted October 15, 2025

DOI: 10.3892/etm.2025.13014

Abstract. While cutaneous metastasis from lung cancer is rare, its recognition is critical. Benign mimics like aneurysmal dermatofibroma (ADF) complicate diagnosis, particularly in patients with known malignancy. A 71-year-old man with non-small cell lung cancer presented with a chest wall nodule. Positron emission tomography-CT revealed hypermetabolic activity (maximum standardized uptake volume, 6.9), prompting excision. Histopathology showed spindle-like cells in storiform patterns, blood-filled spaces and CD34/human herpesvirus-8 negativity. Ki-67 (5%) confirmed ADF. This case illustrates the diagnostic challenge of distinguishing ADF from cutaneous metastasis in patients with known malignancy. Improper workup through imaging or clinical impression without pathologic confirmation may lead to unsuitable treatment. Histologic confirmation with immunohistochemical assessment is essential for accurate diagnosis. ADF as a potential mimic of metastatic disease is necessary to prevent upstaging. Histopathological confirmation should always be considered for ambiguous cutaneous lesions.

Introduction

Cutaneous metastasis as the initial manifestation of visceral malignancy is a rare but clinically significant event, occurring in ~0.8% of patients with solid tumors (1). Among solid organ malignancies, lung carcinoma metastasized to the skin is associated with a poor prognosis. The clinical presentation is often non-specific, with skin nodules or plaques that may be mistaken for benign dermatologic conditions such as dermatofibromas or inflammatory lesions (2). This diagnostic challenge is further confounded by imaging findings, as various benign entities can mimic malignancy even with advanced imaging techniques (3). Therefore, knowledge of false-positive nuclear imaging findings in benign skin and soft tissue conditions is crucial to avoid misdiagnosis.

Aneurysmal dermatofibroma (ADF), a rare variant of dermatofibroma, is notable for its histologic overlap with malignant skin tumors and its potential to mimic metastasis on imaging (4). This mimicry highlights the importance of careful histopathologic evaluation and the integration of clinical and radiologic data when evaluating patients with suspected cutaneous metastasis.

The aim of this work is to highlight the diagnostic challenge posed by a rare neoplasm presenting as possible cutaneous metastasis in a patient with lung carcinoma. The present study outlines the multidisciplinary approach, integrating clinical, radiologic and pathologic findings to facilitate accurate diagnosis and optimal patient management.

Case report

A 71-year-old male with a prior diagnosis of non-small cell lung cancer (NSCLC) presented to Seoul St. Mary's Hospital (The Catholic University of Korea, Seoul, Republic of Korea) in March 2024, with a 3-month history of a painless, slowly growing cutaneous nodule located on the right chest wall. The patient had a significant smoking history of 50 pack-years and no history of other malignancies or chronic diseases, such as hypertension or diabetes. Histologic examination of the lung cancer revealed squamous cell carcinoma, clinically staged as cT1cN3M1c, stage IVB. The patient had undergone video-assisted thoracoscopic surgery, including lobectomy and mediastinal lymph node dissection, followed by adjuvant chemotherapy consisting of vinorelbine (22.5 mg/m^2) and cisplatin (60 mg/m^2) administered at 75% of the standard dose for three cycles. On physical examination, a two-centimeter, non-ulcerated, blackish nodule with intermittent contact bleeding was observed at the upper right chest (Fig. 1A). Satellite lesions were not identified. The lesion initially raised no suspicion until positron emission tomography-CT (PET-CT) demonstrated hypermetabolic activity (maximum standardized uptake volume, 6.9; Fig. 1B), although the primary lung

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Abbreviations: NSCLC, non-small cell lung cancer; ADF, aneurysmal dermatofibroma; DFSP, dermatofibrosarcoma protuberans; PET, positron-emission tomography; H&E, hematoxylin and eosin

Key words: lung neoplasms, dermatofibroma, histiocytoma, neoplasm metastasis, immunohistochemistry, false positive reactions, positron-emission tomography

lesion remained present on imaging. The cutaneous lesion was subsequently identified during a focused physical examination that followed the PET-CT scan, prompted by the imaging studies. The hypermetabolic activity detected by PET-CT raised suspicion of cutaneous metastasis, prompting surgical excision of the skin lesion.

No other distant metastases were identified at the time of the initial evaluation. Given that cutaneous metastasis of lung cancer was suspected, an excisional biopsy was performed for pathologic diagnosis. Wide local excision with 5-mm safety margins was carried out (Fig. 1C). Unexpectedly, histopathologic evaluation revealed features consistent with ADF. Histopathologic examination revealed a well-circumscribed dermal lesion composed of spindle-like cells arranged in a storiform pattern, with multiple large, blood-filled pseudovascular spaces characteristic of ADF (Fig. 2A and B). Formalin-fixed (10% neutral-buffered formalin; room temperature; 24 h), paraffin-embedded tissue sections were cut to 4 μm thickness, deparaffinized in xylene and rehydrated through a decreasing series of ethanol solutions (100, 95 and 70%; each for 3 min). The sections were stained with hematoxylin (at room temperature for 5 min) to visualize cell nuclei, followed by counterstaining with eosin (at room temperature for 2 min) to visualize the cytoplasm and extracellular matrix. After staining, the slides were dehydrated, cleared and mounted for microscopic examination under a light microscope. The overlying epidermis was intact, and no significant cytologic atypia or increased mitotic figures were identified. Immunohistochemical staining was performed at the pathology laboratory of the Catholic University of Korea (Seoul, Korea; part of Seoul St. Mary's Hospital) using a BenchMark ULTRA autostainer (Roche Tissue Diagnostics). Formalin-fixed (10% neutral-buffered formalin; room temperature; 24 h), paraffin-embedded tissue sections (4 μm thick) were deparaffinized in xylene and rehydrated with a descending ethanol series (100, 95 and 70%). Heat-induced epitope retrieval was carried out using Cell Conditioner 1 (pH 8.0; Roche Tissue Diagnostics) at 95˚C for 36 min. Endogenous peroxidase was blocked with a hydrogen peroxide solution (ready to use; Roche Tissue Diagnostics) at room temperature for 4 min. After blocking with a commercially available antibody diluent (ready to use; applied undiluted according to the manufacturer's instructions; Roche Tissue Diagnostics) at room temperature (20-25˚C) for 10 min, the tissue sections were incubated with the following primary antibodies at room temperature for 32 min (BenchMark ULTRA standard protocol): Anti-CD34 (clone QBEnd/10; ready to use; cat. no. MA1-10202; Dako; Agilent Technologies, Inc.), anti-HHV-8 (clone 13B10; ready to use; cat. no. 359A-14; Cell Marque; Merck KGaA) and anti-Ki-67 (clone 30-9; ready to use; cat. no. 790-4286; Roche Tissue Diagnostics). The ultraView Universal DAB Detection Kit (ready to use; cat. no. 760-500; Roche Tissue Diagnostics) was used as a secondary detection reagent. This system utilizes an HRP-labeled multimer antibody complex that does not require further dilution. Incubation with the secondary HRP-conjugate was performed for 8 min at room temperature, as per the manufacturer's standard protocol. Hematoxylin counterstaining (Roche Tissue Diagnostics; room temperature; 12 min) and bluing reagent incubation (Roche Tissue Diagnostics; room temperature; 4 min) were applied sequentially. Slides were examined under a light microscope. The Ki-67 proliferation index was assessed manually by a board-certified pathologist. The pathologist selected a representative high-proliferation 'hot spot', defined as an area containing a high density of positively stained nuclei. Within this selected region, >1,000 tumor cells were visually evaluated under a light microscope, and the proportion of Ki-67-positive nuclei among total tumor cells was estimated to derive the proliferation index. All staining procedures and evaluations were conducted by a board-certified pathologist according to the institution's standard protocols. CD34 immunohistochemistry showed staining limited to the endothelial lining of vascular spaces, while the spindle-like cells remained negative (Fig. 2C). HHV-8 immunostaining was negative (Fig. 2D), excluding Kaposi sarcoma. The Ki-67 proliferation index was low at 5% (Fig. 2E). These findings confirmed the diagnosis of ADF.

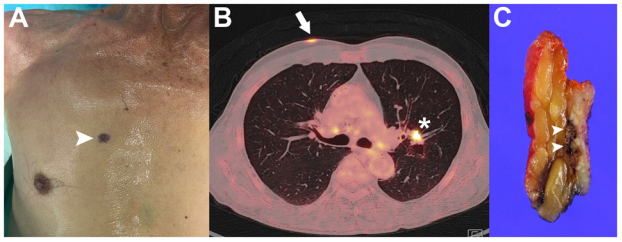

Figure 1. Clinical presentation, imaging and gross specimen of aneurysmal dermatofibroma. (A) Clinical photograph showing a well-circumscribed, blackish nodule on the right chest wall (arrowhead). (B) Positron emission tomography-CT demonstrating increased fluorodeoxyglucose uptake (maximum standardized uptake volume, 6.9) in the cutaneous lesion (arrow) with concurrent hypermetabolic nodule in the left lower lobe of the lung (asterisk). (C) Gross specimen after wide local excision showing the well-demarcated lesion with hemosiderin deposition in the deep dermis (arrowheads).

With this definitive diagnosis, the patient was ruled out for cutaneous metastasis, allowing for accurate tumor staging and appropriate surgical management.

After surgical removal of ADF, the patient was monitored every 3 months at the outpatient clinic through clinical examination. No evidence of recurrence or new lesions was observed during 1 year of follow-up. The patient continues to be managed conservatively with regular clinical evaluations. The patient's overall condition remained stable and there were no complications related to the disease in March 2025.

Discussion

This case draws attention to the diagnostic uncertainty that can arise when evaluating new skin lesions in patients with a known diagnosis of cancer. Although skin metastases from lung cancer are not common, their presence usually signals advanced disease and often requires a change of the treatment plan. In this case, the clinical and imaging findings initially pointed toward metastatic disease, particularly given the patient's recent diagnosis of NSCLC and the increased uptake of the lesion seen on PET-CT.

Importantly, the patient was diagnosed with stage IVB (cT1cN3M1c) squamous cell carcinoma of the lung and had undergone prior surgical resection and adjuvant chemotherapy. This advanced-stage lung cancer background added

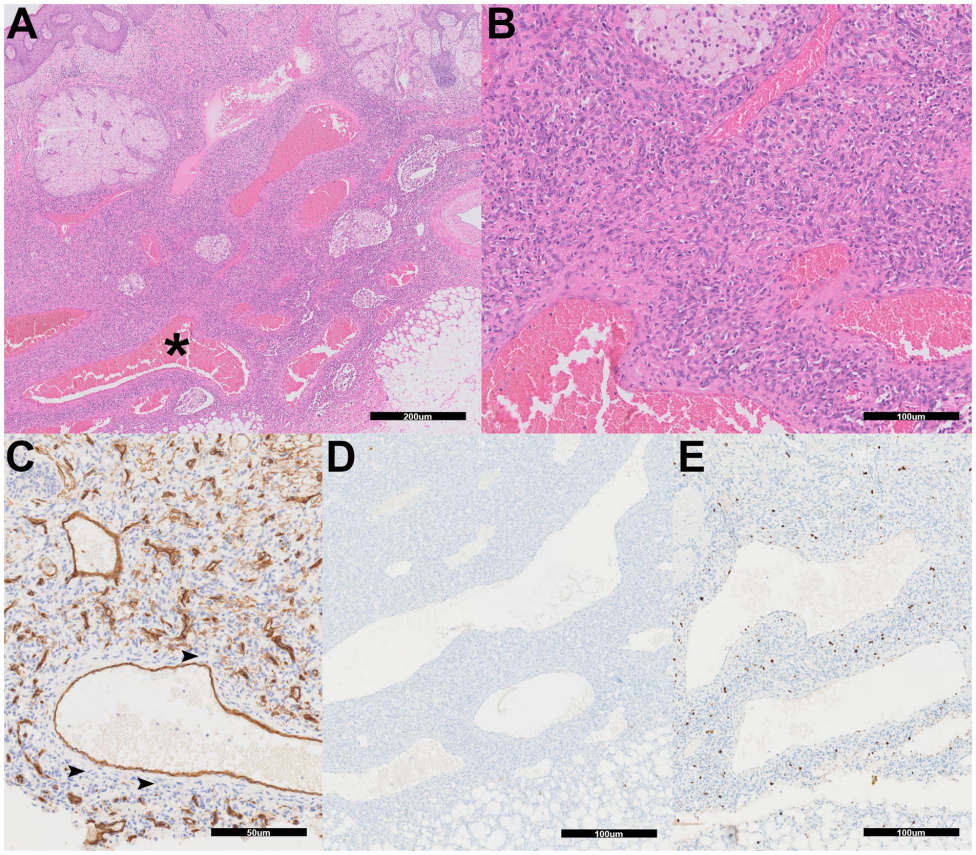

Figure 2. Histopathologic and immunohistochemical features of aneurysmal dermatofibroma. (A) The specimen demonstrates a dermal-based spindle-like cell proliferation with multiple blood-filled pseudovascular spaces (asterisk) characteristic of aneurysmal dermatofibroma (H&E; magnification, x40; scale bar, 200 μm). (B) Higher magnification shows the storiform arrangement of spindle-like cells surrounding the aneurysmal spaces (H&E; magnification, x200; scale bar, 100 μm). (C) CD34 immunohistochemistry reveals positive staining limited to endothelial cells lining vascular structures, while the spindle cell component remains negative (arrowheads; scale bar, 50 μm). (D) Human herpesvirus-8 immunohistochemistry is negative throughout the lesion, excluding Kaposi sarcoma. (E) Ki-67 immunohistochemistry demonstrates low proliferative activity with scarce positive nuclei (magnification, x100; scale bars, 100 μm). H&E, hematoxylin and eosin.

complexity to the clinical suspicion of metastasis, making differentiation from benign mimics crucial to avoid unnecessary alterations in treatment.

Fluorodeoxyglucose (FDG) uptake in the lesion resulted in a false-positive PET-CT scan interpretation, suggesting metastasis. Benign tumors with FDG uptake are rare, and the reported cases in the literature are predominantly of tumors other than dermatofibroma (5,6). To the best of our knowledge, dermatofibroma showing FDG uptake has only been reported in one previous case (7).

ADF is a rare subtype, accounting for <2% of all dermatofibromas, and 0.8% of all solid tumors (8). Recent studies emphasize the histopathologic overlap between ADF and malignancies, necessitating rigorous immunohistochemical evaluation to avoid misdiagnosis (3,9). Recent large series and reviews emphasize the importance of thorough histopathologic and immunohistochemical evaluation to avoid misdiagnosis and unnecessary aggressive treatment, particularly in oncology patients presenting with new or atypical skin lesions (3,10).

On gross morphology, the lesion of the present case appeared as a two-centimeter, non-ulcerated, blackish nodule on the upper right chest, with intermittent contact bleeding. The differential diagnosis for this lesion includes cutaneous metastasis, angiosarcoma, Kaposi sarcoma, spindle cell hemangioma, malignant melanoma and other benign or malignant spindle cell neoplasms such as ADF (11).

ADF can closely resemble malignant tumors both in radiologic and histological aspects (12). In this patient, the lesion's metabolic activity on PET-CT was within the range seen in malignancies, which raised high suspicion for cutaneous metastasis of the lung lesion or other primary malignancy. The presence of blood-filled spaces and spindle-like cells may be mistaken for angiosarcoma or metastatic carcinoma (13). This is particularly the case if tissue samples are limited due to partial skin and soft tissue excision or punch biopsy performed in the outpatient setting for diagnostic evaluation of potential malignancy (14); however, in the present study, a full excisional biopsy with clear margins was performed at the initial surgery. To rule out other primary malignancies, differential diagnosis with immunohistochemical staining was made. The absence of CD34 immunoreactivity ruled out dermatofibrosarcoma protuberance and negativity for HHV-8 expression ruled out Kaposi sarcoma, along with a low proliferation index (15,16). These findings finalized the diagnosis of ADF (3). This outcome prevented the patient from being incorrectly classified as having metastatic disease or a double primary malignancy, which would have affected the overall treatment plan.

The main limitation of this report is that it describes a single patient case; therefore, it is not possible to generalize the findings to a broader population. Further research with a larger cohort study is necessary to validate these findings and support conclusions.

This case shows that a high FDG uptake lesion in a cancer patient may not represent metastasis. Benign tumors and tumor-like conditions are often incidentally detected on FDG PET/CT during workup and should be differentiated from metastasis. Over-reliance on imaging or clinical impression, without tissue confirmation, can lead to inappropriate changes in treatment plans. Careful evaluation, including histopathology and appropriate immunostains, remains essential when the diagnosis is uncertain.

In conclusion, this case emphasizes the critical importance of histopathologic evaluation in distinguishing benign lesions from true metastatic disease. To avoid misdiagnosis due to the tendency of ADF to mimic malignancy in cancer patients, multidisciplinary integration of imaging, histopathology and immunohistochemistry is essential.

Acknowledgements

Not applicable.

Funding

The present study received financial support from the Catholic Medical Center Research Foundation in the program year of 2024 (grant no. 5-2024-B0001-00104).

Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

JYC was involved in the conceptualization and investigation (including conducting experiments, and collecting clinical data and specimens), and wrote the original draft. HP performed data curation and formal analysis (application of statistical, computational and other quantitative techniques to analyze and interpret study data). JC participated in conceptualization, supervision, and review and editing of the manuscript. JYC, HP and JC confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

This study was approved by the Institutional Review Board (IRB) of The Catholic University of Korea (Seoul, Korea; IRB no. 2025-1442-0001). The study was performed in accordance with the principles of the Declaration of Helsinki.

Patient consent for publication

Written informed consent was obtained from the patient for publication of the case details and accompanying images.

Competing interests

The authors declare that they have no competing interests.

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