SAR Journal of Medical Case Reports

Abbreviated Key Title: *SAR J Med Case Rep*
Home page: https://sarpublication.com/journal/sarjmcr/home
DOI: https://doi.org/10.36346/sarjmcr.2026.v07i06.001

ISSN 2707-7780 (P)
ISSN 2709-6947 (O)

Case Report

The Jellyfish Sign: A Novel Radiological Clue to Lung Malignancy in a Peripheral Pulmonary Nodule

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Article History: | Received: 06.09.2026 | Accepted: 31.10.2026 | Published: 03.11.2026 |

Abstract: ***Background*:** Accurate characterization of peripheral pulmonary nodules is essential for differentiating benign lesions from malignancy and identifying features associated with tumour invasion. The Jellyfish sign is a recognized computed tomography (CT) morphological feature associated with visceral pleural invasion (VPI) in selected patients with lung cancer. Multiple pleural tags extending towards different pleural surfaces represent a related imaging feature that may also predict VPI. ***Case Presentation*:** A 50-year-old male farmer presented with intermittent right-sided chest pain of three months' duration. The pain was initially dull and aching but subsequently became pleuritic. He had a history of pulmonary tuberculosis involving the right lung approximately 10 years earlier, for which he had completed treatment and achieved clinical cure. He had no history of smoking, tobacco consumption, or other addictions. There was no history of fever, cough, or weight loss. Clinical examination revealed no cyanosis, clubbing, or peripheral oedema. Respiratory examination demonstrated normal vesicular breath sounds without adventitious sounds. Haematological investigations, viral markers, liver function tests, and renal function tests were within normal limits. Initial chest radiography was unremarkable. High-resolution computed tomography (HRCT) demonstrated a 2.8-cm peripheral pulmonary nodule in the anterior segment of the right upper lobe, with pleural tags extending towards both the costal pleura and the major fissure. CT-guided percutaneous biopsy was uneventful, and three specimens were obtained for histopathological examination and immunohistochemistry (IHC). The diagnosis of primary pulmonary adenocarcinoma was established. Molecular evaluation demonstrated an epidermal growth factor receptor (*EGFR*)-positive tumour, with negative ALK and ROS1 results. Histopathological assessment confirmed visceral pleural invasion. Positron emission tomography–computed tomography (PET-CT) demonstrated no evidence of mediastinal lymph node or distant metastases. The tumour was clinically classified as cT2aN0M0 (Stage IB), and intraoperative mediastinal lymph node sampling was performed for pathological staging. ***Conclusion*:** This case highlights the importance of detailed assessment of pleural-tag patterns in peripheral pulmonary nodules. The Jellyfish sign and multiple tags directed towards different pleural surfaces may provide useful information about the relationship between a tumour and the pleura, particularly the possibility of VPI. However, imaging findings cannot independently establish histological invasion or replace comprehensive staging. Histopathological confirmation and molecular characterization remain essential for appropriate management.

Keywords: Jellyfish Sign, Lung Adenocarcinoma, Visceral Pleural Invasion, Pleural Tags, HRCT Thorax, EGFR Mutation, Peripheral Pulmonary Nodule, Case Report.

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INTRODUCTION

Lung cancer remains a major cause of cancer-related morbidity and mortality worldwide. Early diagnosis of localized disease is important because it may permit curative-intent treatment. However, distinguishing malignant pulmonary nodules from benign inflammatory, infective, and fibrotic lesions remains a frequent diagnostic challenge.

The evaluation of pulmonary nodules involves assessment of lesion size, attenuation, margins, internal

architecture, growth pattern, and relationship to adjacent anatomical structures. Features such as spiculation, pleural retraction, and architectural distortion may increase suspicion of malignancy, although none is independently diagnostic in every patient [1–3].

In tuberculosis-endemic regions, previous pulmonary tuberculosis may complicate radiological interpretation because residual fibrosis, granulomatous nodules, and pleural abnormalities can resemble other pulmonary pathologies. A previous history of tuberculosis should therefore not lead to automatic attribution of a new pulmonary lesion to post-infectious change.

Pleural tags are linear opacities extending between a pulmonary lesion and an adjacent pleural surface. Their configuration and distribution may provide information about tumour–pleural relationships.

The Jellyfish sign has been described in thoracic radiology literature as a CT feature associated with VPI in selected patients with small, pleural-attached non-small-cell lung cancers (NSCLC). A retrospective study published in *Radiology* in 2024 found that the Jellyfish sign independently predicted VPI in pleural-attached nodules, whereas multiple tags directed towards different pleural surfaces independently predicted VPI in pleural-tag nodules [4, 5].

We report a case of EGFR-positive primary pulmonary adenocarcinoma in a 50-year-old nonsmoking male farmer with a remote history of treated pulmonary tuberculosis. HRCT demonstrated a 2.8-cm peripheral right upper lobe nodule with pleural tags extending towards the costal pleura and major fissure. Histopathological evaluation confirmed adenocarcinoma with VPI. This case illustrates the potential clinical relevance of pleural-tag morphology and the importance of integrating imaging with tissue diagnosis, molecular characterization, and pathological staging.

CASE PRESENTATION

Patient Information and Clinical History: A 50-year-old male farmer presented with intermittent right-sided chest pain of three months' duration. The pain was initially dull and aching but subsequently assumed a pleuritic character. His medical history was significant for pulmonary tuberculosis involving the right lung approximately 10 years earlier. He had completed the prescribed antitubercular treatment and had reportedly achieved clinical cure. The patient had no history of smoking, tobacco consumption, or other addictions. There was no history of fever, cough, or weight loss. His occupational history was significant for agricultural work. Details regarding potential exposure to pesticides, crop dust, biomass smoke, or other agricultural inhalants were not available.

Clinical Examination: General examination revealed no cyanosis, clubbing, or peripheral oedema. Respiratory system examination demonstrated normal vesicular breath sounds without wheezing, crackles, or other adventitious sounds. No additional abnormal examination findings were reported.

Laboratory Investigations: Haematological investigations, viral markers, liver function tests, and renal function tests were within normal limits. No significant abnormalities were reported in the available laboratory investigations.

Initial Radiological Evaluation: The initial chest radiograph was reported as normal, without an obvious focal pulmonary opacity. Because the patient's chest pain persisted and the radiograph did not explain his symptoms, HRCT of the thorax was performed.

HRCT Thorax Findings

HRCT demonstrated a 2.8-cm peripheral pulmonary nodule in the anterior segment of the right upper lobe. Detailed assessment revealed linear pleural tags extending from the lesion towards two anatomically distinct structures:

- The adjacent costal pleura.
- The major fissure.

The central nodular component and associated pleura-directed extensions produced a configuration resembling the body and tentacles of a jellyfish. [Image 1 and Image 2]

The presence of pleural tags directed towards both the costal pleura and the major fissure was a notable morphological feature. The lesion was initially considered potentially benign, but its indeterminate nature warranted further investigation.

The exact CT attenuation, margin characteristics, extent of pleural contact, and presence or absence of associated lymphadenopathy should be documented from the original images.

CT-Guided Percutaneous Biopsy

CT-guided percutaneous biopsy was performed to establish the diagnosis. The procedure was uneventful, with no procedure-related air leak or other immediate complication reported. Three biopsy specimens were collected and submitted for histopathological examination and IHC.

Histopathology and Molecular Characterization

Histopathological examination and IHC established the diagnosis of primary pulmonary adenocarcinoma, tumor cells are positive for CK7, TTF-1, and Napsin A, and negative for CK20. Molecular evaluation demonstrated an *EGFR*-positive tumour, with negative ALK and ROS1 results. [Image 3]

The specific *EGFR* variant and the methodology used for ALK and ROS1 testing were not provided. These details should be incorporated into the final manuscript if available because they influence therapeutic decision-making.

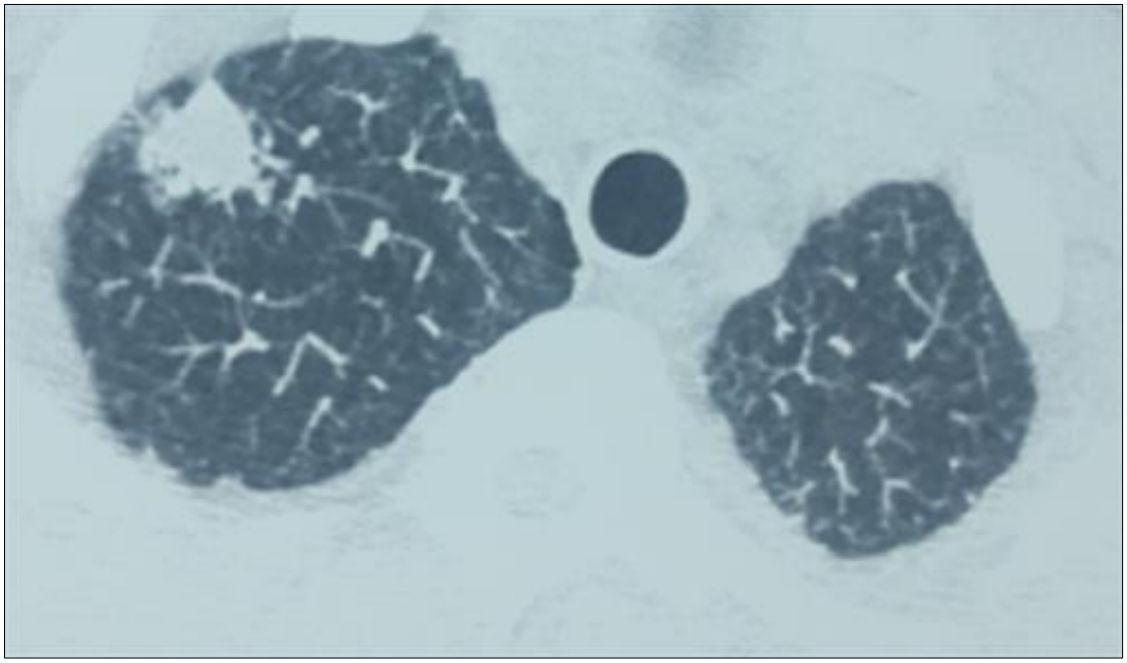


Image 1: Right upper lobe anterior segment peripheral pulmonary nodule of 2.8 cm size

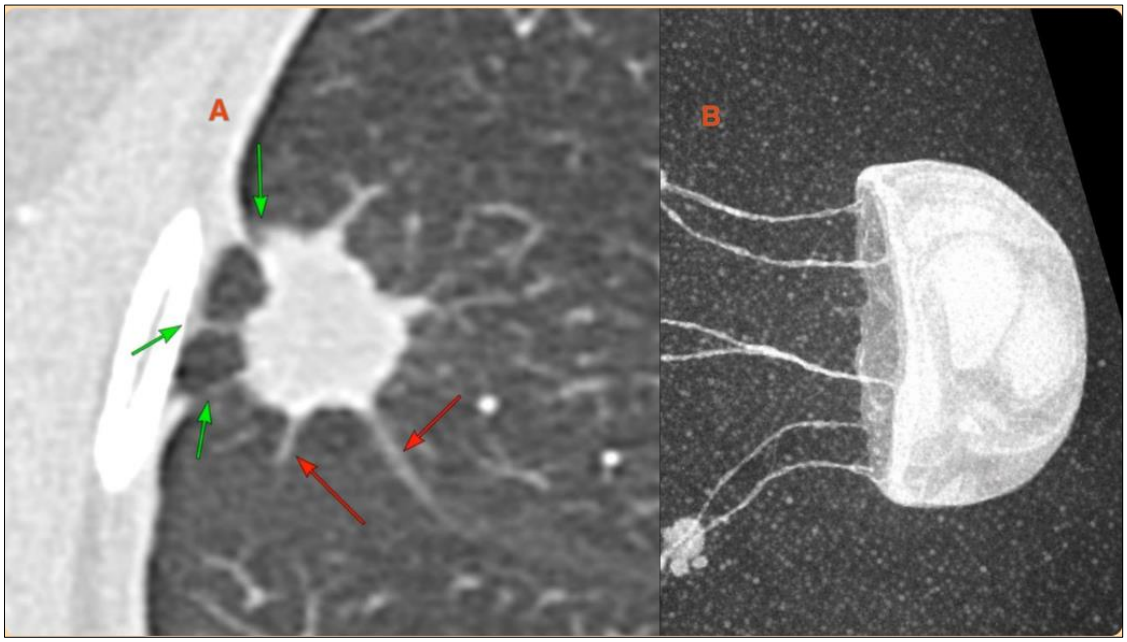


Image 2: Pleural tags in green arrow with visceral pleural invasion and red tags with visceral pleural plus major fissure involvement [section A]. Jellyfish image with tentacles in section B.

Visceral Pleural Invasion

Histopathological assessment confirmed visceral pleural invasion. This finding is clinically important because VPI affects the T category of a lung tumour and may influence prognostic assessment and subsequent management. Although the HRCT demonstrated pleural tags directed towards the costal pleura and major fissure, the radiological appearance alone could not establish VPI. The definitive diagnosis depended on histopathological assessment. [Image 2]

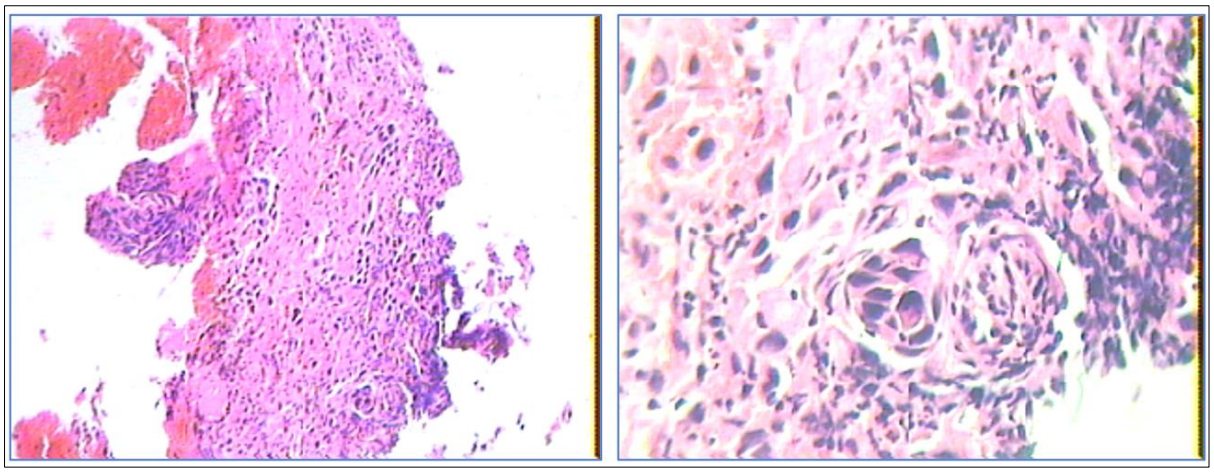


Image 3: Histopathology showing non-small cell carcinoma

PET-CT and Tumour Staging:

PET-CT demonstrated no evidence of mediastinal lymph node involvement or distant metastatic disease.

Based on the 2.8-cm tumour with VPI and the absence of radiologically evident nodal or distant metastases, the lesion was clinically classified as cT2aN0M0 (Stage IB).

Intraoperative mediastinal lymph node sampling was performed for pathological staging.

The final pathological classification depends on the definitive surgical specimen and the pathological assessment of the sampled regional lymph nodes. If the primary tumour is confirmed as pT2a and all regional lymph nodes are negative, the final designation would be pT2aN0M0 (Stage IB).

The pathological T category and final stage should be confirmed using the TNM edition adopted by the treating institution and target journal. Visceral pleural invasion remains a T2 feature for a tumour of this size in the current staging system [6].

Multidisciplinary Management Plan:

The patient was evaluated by the oncology and thoracic surgery teams.

Given the apparently localized disease, surgical management was planned, considering local resection or anatomical segmental resection according to the multidisciplinary assessment.

The treatment plan also included oncological follow-up and consideration of EGFR-targeted therapy, taking into account the molecular findings and definitive pathological stage.

The final operative procedure, pathological lymph node status, specific *EGFR* variant, and subsequent treatment decisions should be documented when available.

Follow-up information regarding completion of surgery, initiation of targeted therapy, and clinical outcome was not available at the time of preparation of this report.

DISCUSSION

1. Diagnostic Challenge of a Peripheral Pulmonary Nodule

This case illustrates the difficulty of distinguishing malignant pulmonary lesions from benign post-infectious changes, particularly in a patient with a remote history of pulmonary tuberculosis.

Pulmonary tuberculosis may result in residual fibrosis, granulomatous nodules, pleural thickening, and architectural distortion. Such changes may complicate the interpretation of subsequent thoracic imaging.

However, previous tuberculosis does not exclude a new primary lung malignancy. New or persistent pulmonary lesions should be evaluated according to their current clinical and radiological characteristics rather than attributed automatically to previous infection.

In this patient, the right upper lobe lesion was not apparent on initial chest radiography but was identified on HRCT. Subsequent biopsy established primary pulmonary adenocarcinoma.

The case reinforces the importance of tissue diagnosis when imaging findings remain indeterminate.

2. Significance of a Normal Chest Radiograph

The initial chest radiograph was reported as normal despite the presence of a 2.8-cm peripheral pulmonary lesion on HRCT.

Lesion visibility on chest radiography depends on its location, density, margins, and superimposition by

ribs, vessels, and other thoracic structures. CT provides superior spatial resolution and allows more precise evaluation of pulmonary lesions and their relationship to adjacent anatomical structures [1, 2].

This case emphasizes that a normal chest radiograph does not exclude pulmonary malignancy when symptoms persist or the clinical presentation remains unexplained.

3. The Jellyfish Sign: Definition and Morphological Characteristics

The Jellyfish sign is a recognized CT morphological feature described in the assessment of small, pleural-attached lung cancers.

In the published literature, the classic sign is characterized by multiple linear septations extending between a pleural-attached nodule and the costal pleura on adjacent CT sections. The linear extensions resemble the tentacles of a jellyfish.

Sun and colleagues investigated CT predictors of VPI in 379 patients with subpleural NSCLC measuring 30 mm or less. Their study distinguished pleural-attached nodules from pleural-tag nodules. The Jellyfish sign was associated with VPI in pleural-attached nodules, whereas multiple tags extending towards different pleural surfaces were independently associated with VPI in pleural-tag nodules [4].

This distinction is important when interpreting the present case.

The lesion demonstrated tags extending towards both the costal pleura and the major fissure. This configuration is consistent with a multidirectional pleural-tag pattern. Whether the lesion also meets the formal definition of the classic Jellyfish sign requires review of the original HRCT images, particularly whether multiple linear septations are visible between a pleural-attached nodule and the costal pleura on adjacent sections.

The sign should therefore be discussed as a recognized radiological feature, while the multiple pleural tags in this case should be described separately rather than assuming that the two patterns are identical.

4. Clinical Importance of the Jellyfish Sign

The principal clinical significance of the Jellyfish sign is its potential to provide information about the relationship between a peripheral lung tumour and the visceral pleura, particularly the possibility of VPI.

VPI is an important pathological feature because it influences the T category and may affect prognosis and treatment planning.

In the 2024 *Radiology* study by Sun and colleagues, VPI was more frequent in pleural-attached solid nodules than in pleural-tag solid nodules: 31% versus 16%, respectively.

For pleural-attached nodules, the Jellyfish sign was independently associated with VPI, with an odds ratio of 21.60. For pleural-tag nodules, the presence of multiple tags directed towards different pleural surfaces independently predicted VPI, with an odds ratio of 9.30 [4].

These findings suggest that the number, distribution, and configuration of pleural extensions may provide information beyond the presence of a single pleural tag.

However, these results should be interpreted within their study population. The investigation assessed VPI among patients with established NSCLC; it did not establish the Jellyfish sign as a stand-alone diagnostic test for distinguishing malignant from benign pulmonary nodules.

Accordingly, the sign should be considered a potentially useful CT feature for evaluating tumour–pleural relationships rather than a substitute for histopathology.

5. Significance of Multiple Pleural Tags towards Different Surfaces

The presence of pleural tags directed towards both the costal pleura and major fissure is an important feature of this case.

The costal pleura lines the inner surface of the chest wall, while the major fissure separates the upper and lower lobes of the right lung.

Multiple tags extending towards different pleural surfaces may reflect a complex relationship between the lesion and the surrounding lung architecture. In the study by Sun and colleagues, this pattern was independently associated with VPI in pleural-tag nodules [4].

The finding is particularly relevant here because VPI was subsequently confirmed histopathologically.

Nevertheless, the association does not establish that the pleural tags directly represent tumour invasion. A tag may reflect fibrosis, architectural distortion, or traction, and a fissure-directed extension does not independently establish direct invasion of the fissure or adjacent lobe.

In this patient, the imaging pattern provided a potentially informative preoperative clue, whereas histopathology established the definitive presence of VPI.

6. Pathological Basis of Pleural Tags and VPI

Pleural tags may arise from fibrosis, architectural distortion, or traction associated with a pulmonary lesion. In malignant tumours, tumour-associated desmoplastic reactions and fibrosis may contribute to the development of linear extensions towards the pleura.

However, similar appearances can occur in benign inflammatory and fibrotic conditions.

VPI is a histopathological diagnosis involving the visceral pleural layers. It should not be inferred solely from the presence of pleural tags or the Jellyfish sign on CT.

In this case, histopathological confirmation of VPI provides important radiological–pathological correlation. However, the available information does not establish the exact mechanism responsible for the observed pleural tags.

7. EGFR-Positive Pulmonary Adenocarcinoma in a Nonsmoker

Pulmonary adenocarcinoma is an important consideration in patients with peripheral pulmonary nodules, including individuals without a smoking history.

Although smoking is a major risk factor for lung cancer, its absence does not exclude malignancy. Histopathology and appropriate IHC are essential for confirming the diagnosis and distinguishing primary pulmonary adenocarcinoma from other malignancies when necessary [7, 8].

Molecular testing further characterizes lung adenocarcinoma and may identify alterations that guide targeted treatment.

In this case, molecular evaluation demonstrated an *EGFR*-positive tumour, with negative ALK and ROS1 results. The specific *EGFR* variant should be reported because therapeutic indications depend on the molecular alteration and disease setting.

8. Implications for Staging and Management

The demonstration of VPI in a 2.8-cm pulmonary adenocarcinoma is clinically important because VPI places a tumour of this size in the T2a category.

PET-CT showed no evidence of mediastinal lymph node or distant metastases. The lesion was therefore clinically classified as cT2aN0M0 (Stage IB), and intraoperative mediastinal lymph node sampling was undertaken for pathological staging.

The final pathological stage depends on the resected tumour and regional lymph node findings.

The oncology and thoracic surgery teams planned surgical management, with consideration of resection and subsequent oncological follow-up. The role of adjuvant EGFR-targeted therapy should be determined by the exact *EGFR* variant, definitive pathological stage, applicable treatment guidance, and multidisciplinary assessment. An *EGFR*-positive result alone does not establish the precise postoperative treatment plan [6-9].

9. Role of CT-Guided Biopsy

CT-guided percutaneous biopsy is an established technique for obtaining tissue from appropriately selected peripheral pulmonary lesions.

Potential complications include pneumothorax and pulmonary haemorrhage. The risks depend on lesion location, needle trajectory, and patient characteristics [10].

In this patient, the procedure was uneventful, with no procedure-related air leak or other immediate complication reported. Three biopsy specimens were obtained for histopathological examination and IHC.

The biopsy established primary pulmonary adenocarcinoma, allowing subsequent molecular characterization, staging, and multidisciplinary planning.

10. Future Research and Clinical Implications

This case highlights the importance of detailed assessment of pleural-tag morphology in patients with peripheral pulmonary nodules.

The Jellyfish sign has a recognized role in the literature as a potential predictor of VPI in selected pleural-attached lung cancers. Multiple tags extending towards different pleural surfaces represent a related but distinct CT feature that may also be associated with VPI.

Future studies could investigate the reproducibility of these features and their relationship with histopathologically confirmed VPI in larger, multicentre cohorts.

Standardized imaging definitions, blinded radiological assessment, and correlation with surgical pathology would help determine their clinical utility.

The present case provides a useful example of a peripheral lung adenocarcinoma with multidirectional pleural tags and confirmed VPI. It reinforces the value of integrating detailed CT interpretation with histopathology, molecular testing, and comprehensive staging.

Learning Points

1. A normal chest radiograph does not exclude pulmonary malignancy. Persistent symptoms may warrant further imaging.

2. Previous tuberculosis should not lead to diagnostic anchoring. A new pulmonary lesion requires independent assessment.
3. The Jellyfish sign is a recognized CT feature associated with VPI in selected pleural-attached lung cancers. It is not a stand-alone marker of malignancy.
4. The classic Jellyfish sign and multiple tags directed towards different pleural surfaces are distinct imaging patterns. The original CT images should be reviewed to determine the most accurate terminology.
5. Pleural tags may provide clues to tumour–pleural relationships but do not independently establish VPI. Histopathological confirmation is required.
6. VPI has important staging implications. In a 2.8-cm lung adenocarcinoma, confirmed VPI supports a T2a classification.
7. Molecular characterization contributes to treatment planning. The exact *EGFR* variant should be documented when available.
8. Multidisciplinary management is essential. Surgical and systemic treatment decisions should incorporate the definitive pathological stage, nodal findings, molecular results, and patient-specific factors.

CONCLUSION

This case describes a 50-year-old nonsmoking male farmer with a 2.8-cm peripheral adenocarcinoma in the anterior segment of the right upper lobe. Despite a normal initial chest radiograph and the absence of constitutional or respiratory symptoms, HRCT demonstrated pleural tags extending towards both the costal pleura and the major fissure.

Histopathological evaluation confirmed primary pulmonary adenocarcinoma with visceral pleural invasion. Molecular testing demonstrated an *EGFR*-positive tumour, with negative ALK and ROS1 results. PET-CT showed no evidence of mediastinal lymph node or distant metastases. The tumour was clinically classified as cT2aN0M0 (Stage IB), and intraoperative mediastinal lymph node sampling was performed for pathological staging.

The case emphasizes the importance of carefully assessing pleural-tag patterns and their relationship to adjacent pleural surfaces. The Jellyfish sign is a recognized imaging feature associated with VPI in selected lung cancers, while multiple tags directed towards different pleural surfaces represent a related but distinct finding.

The central clinical message is that pleural-tag morphology may provide valuable preoperative information about tumour–pleural relationships, but definitive diagnosis and staging must rely on histopathological assessment and comprehensive clinical evaluation.

Abbreviations:

ALK, anaplastic lymphoma kinase; CT, computed tomography; EGFR, epidermal growth factor receptor; HRCT, high-resolution computed tomography; IHC, immunohistochemistry; M0, absence of distant metastasis; N0, absence of regional lymph node metastasis; NSCLC, non-small-cell lung cancer; PET-CT, positron emission tomography–computed tomography; ROS1, ROS proto-oncogene 1, receptor tyrosine kinase; TNM, tumour, node, and metastasis; VPI, visceral pleural invasion.

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