



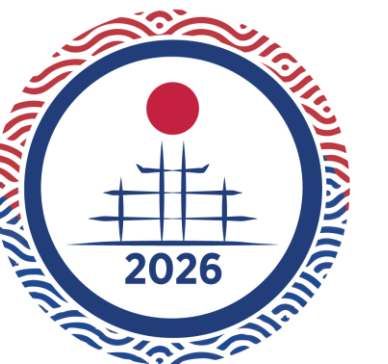
P#3459: Pleural Extra-skeletal Ewing Sarcoma With Adamantinoma-Like Features: A Report of Three Cases

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INTRODUCTION

A rare Ewing sarcoma variant with epithelial mimicry — a recognised diagnostic pitfall, confirmed only by EWSR1 rearrangement.

- Adamantinoma-like Ewing sarcoma (ALES) is a rare, distinctive variant within the Ewing sarcoma family of tumours, first described by Van Haelst et al. (1975) and genomically confirmed by Bridge et al. (1999). It shows dual neuroectodermal and epithelial differentiation.
- ~5% of Ewing sarcomas arise in the head & neck (sinonasal tract, salivary glands), where up to 20% show epithelial differentiation. Involvement of other sites — pleura, viscera — is exceptionally rare.

Why This Series

- 3 patients with histopathological and molecular markers confirmed ALES managed at our centre.
- Illustrates the spectrum of presentation and the diagnostic pathway required to reach this rare diagnosis
- .
- Highlights sites/settings where ALES is not yet widely recognized.

CASE ASCERTAINMENT

- Design:** Retrospective case series.
- Setting:** Department of TB & Respiratory Diseases, NITRD, New Delhi — a national tertiary referral centre for respiratory and thoracic disease.
- Case Selection:** All patients with histopathologically and molecularly confirmed ALES (EWSR1 rearrangement on FISH) evaluated at our centre were included.
- Diagnostic Workup:** Clinical & radiological evaluation (CECT / WB PET-CT) → image-guided tissue biopsy → histopathology (H&E) → immunohistochemistry panel (CD99, FLI-1, Vimentin, PanCK, Ki-67 ± p40) → confirmatory FISH for EWSR1 rearrangement.
- Data Collected:** Demographics, presenting complaints, imaging findings, histopathology, IHC/molecular results, treatment received, and outcome/follow-up status for each case.
- Ethics:** Written informed consent obtained; patient identifiers removed from all images and text.

DISCUSSION AND CONCLUSION

Discussion

- ALES diagnosis rests on a morphology + IHC + molecular triad. Its epithelial mimicry (cytokeratin, p40 positivity) is a well-documented pitfall, risking misdiagnosis as carcinoma, mesothelioma, or another small round cell tumour.
- In TB-endemic settings, overlapping respiratory symptoms can add a further layer of diagnostic delay — as in Case 1, where empirical anti-tubercular therapy preceded diagnosis.
- Demonstrating EWSR1 rearrangement (FISH or sequencing) is mandatory for a confident diagnosis and is what ultimately distinguishes ALES from its histological mimics.
- Treatment follows extraskeletal Ewing sarcoma protocols (VDC/IE-based chemotherapy ± local therapy), which differ substantially from carcinoma-directed regimens — underscoring why accurate diagnosis changes management.
- All three patients were female (31–43 years) with intrathoracic/pleuropulmonary disease at presentation — an unusual site distribution for ALES, which is classically head & neck. In Cases 1 and 2, the first biopsy was non-diagnostic or equivocal (inconclusive thoracoscopic HPE; 'lymphoid proliferation, reactive/neoplastic' on trucut), and only a repeat sample with a fuller IHC panel reached the diagnosis — underscoring how easily ALES is missed on an initial, limited workup. Case 2 also illustrates overlap with mesothelioma (BAP-1 loss), while Case 3's IHC (CD99/FLI-1/Vimentin-positive, PanCK-negative) was a more 'conventional' Ewing/PNET profile without the epithelial markers that define the adamantinoma-like pattern — worth the authors revisiting on morphology before final classification.

Conclusion

- ALES is a rare, under-recognized entity outside the head & neck; clinical suspicion should extend to unusual sites, including the pleura and other viscera.
- High index of suspicion plus mandatory EWSR1 molecular confirmation is essential to avoid misdiagnosis and ensure Ewing-protocol-appropriate treatment.
- Across this series, an initial non-diagnostic or equivocal biopsy was the norm rather than the exception — clinicians and pathologists evaluating pleuropulmonary small round cell lesions in young adults should keep ALES on the differential and pursue a full IHC panel (± EWSR1 studies) before settling on a reactive or purely epithelial diagnosis.

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Artificial Intelligence (AI) Use Disclaimer

AI Tool(s) Used: Claude (Anthropic) assisted with literature synthesis and drafting/formatting of this poster's content. All data, interpretation, and conclusions were reviewed and approved by the authors.

CASE PRESENTATIONS

Three patients with confirmed Adamantinoma-like Ewing Sarcoma, illustrating the diagnostic spectrum of this rare entity.

CASE 1

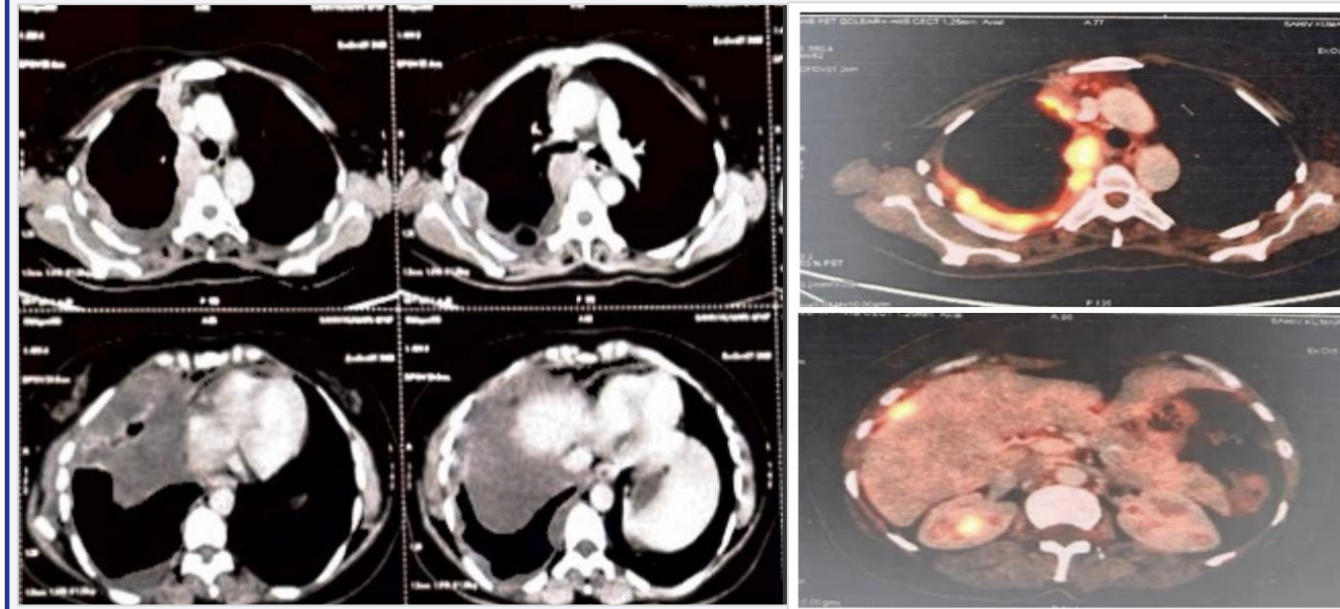
43F — Pleural

DEMOGRAPHICS & PRESENTATION

- A 43-year-old female presented with complaints of dyspnea, low-grade fever and right-sided chest pain for 3 months.
- Examination showed decreased breath sounds and decreased chest wall movements on right side. Chest X Ray showed right hemithorax opacification with collapse of the underlying lung parenchyma.
- USG guided tap, s/o low ADA, exudative pleural effusion with cell block negative for malignancy.

IMAGING

- CXR: right hemithorax opacification with underlying lung collapse. CECT: right pleural effusion with pleural thickening. WB PET-CT: metabolically active costal/mediastinal pleura, right lower lobe nodule, and liver metastasis (M1).

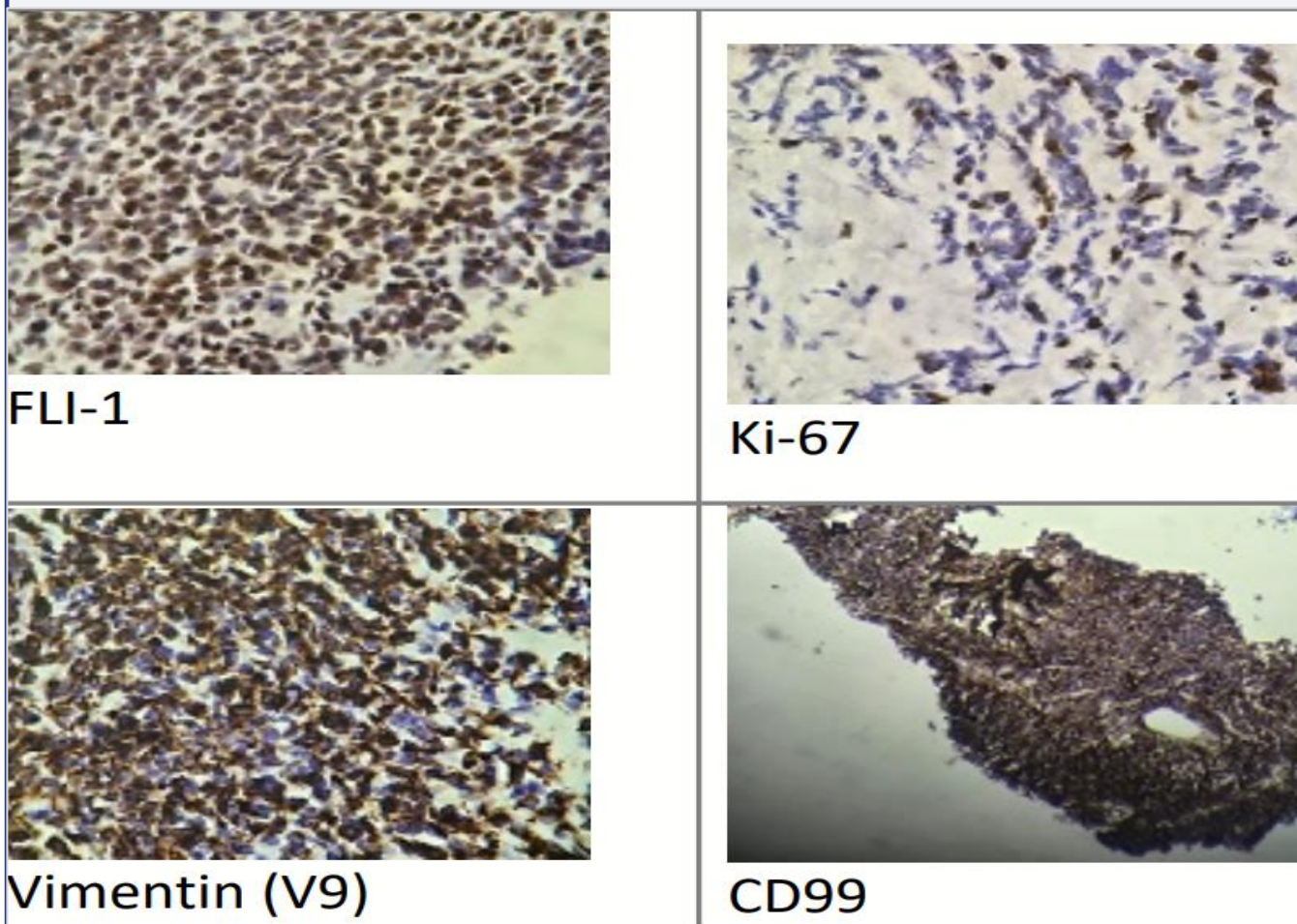


HISTOPATHOLOGY

Thoracocentesis: exudative effusion, low ADA, cell block negative. Medical thoracoscopy: sludged parietal pleural nodules (initial HPE inconclusive). USG-guided biopsy — H&E: round-oval cells in sheets, vacuolated/clear cytoplasm, vesicular nuclei, no necrosis.

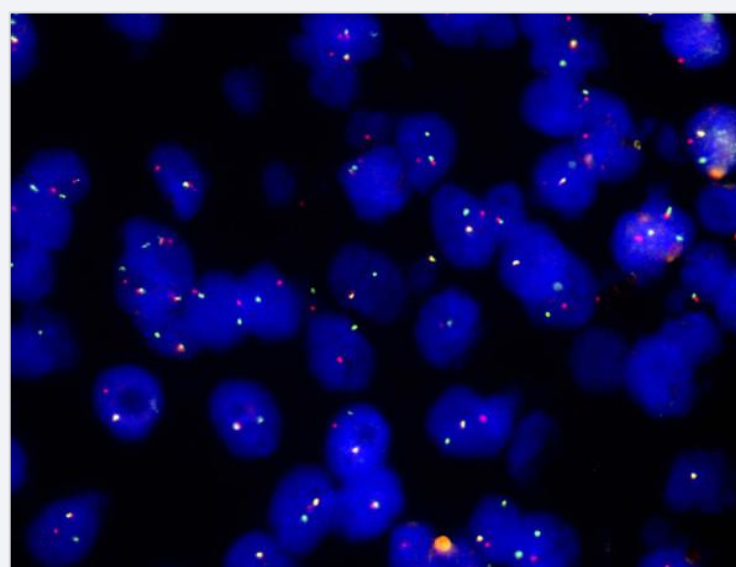
IHC & MOLECULAR

CD99+, FLI-1+, Vimentin+, PanCK+ (patchy — epithelial mimicry), high Ki-67. FISH: EWSR1 rearrangement positive (split signals, >30% cells).



MOLECULAR ANALYSIS

FISH for EWSR1 gene rearrangement
Split signals in >30% of tumour cells
Consistent with EWSR1 gene rearrangement



TREATMENT & OUTCOME

- Person diseased is on standard therapy for Soft tissue sarcoma as per ASCO and NCCN Guidelines with VDC-IE regimen (Vincristine, Doxorubicin, Cyclophosphamide) per extraskeletal Ewing sarcoma protocol.
- She has completed 4 cycles of both VDC and IE and is currently clinically stable and is on followup. Our institutional protocol is to get a repeat PET-CT at 6 weeks.

PATIENT PERSPECTIVES

I was initially stressed due to my diagnosis, specially when I was told that this is not a common tumor that occurs in the lung. But now, my tumor is responding and that gives me hope.

(Note: This is translated from patient' mother tongue Hindi)

CASE 2

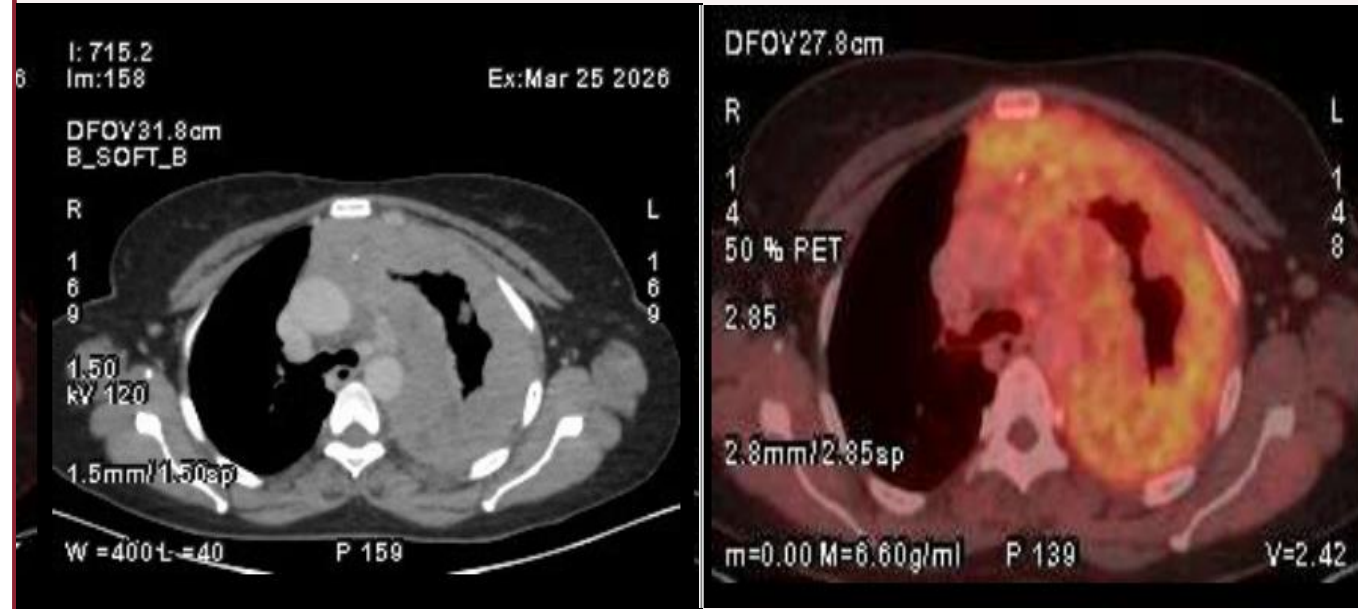
37F — Pleural

DEMOGRAPHICS & PRESENTATION

- 37-year-old female. Progressive breathlessness and left-sided chest pain for 2 months, with dry cough and low-grade evening fever.
- Examination: decreased air entry and chest wall movement, left side; stony-dull percussion note over the lower left hemithorax.
- Chest X Ray showed linear complete collapse of the eft hemithorax opacification with collapse of the underlying lung parenchyma

IMAGING

- WB PET-CT: FDG-avid irregular, heterogeneously enhancing confluent pleural nodular/mass lesions along the left costal, mediastinal and diaphragmatic pleura (max thickness 5cm, SUVmax 4.7), compressing the left main bronchus with subsegmental atelectasis; FDG-avid prevascular/AP-window/bilateral hilar nodes (SUVmax 2.9); mild pericardial effusion.

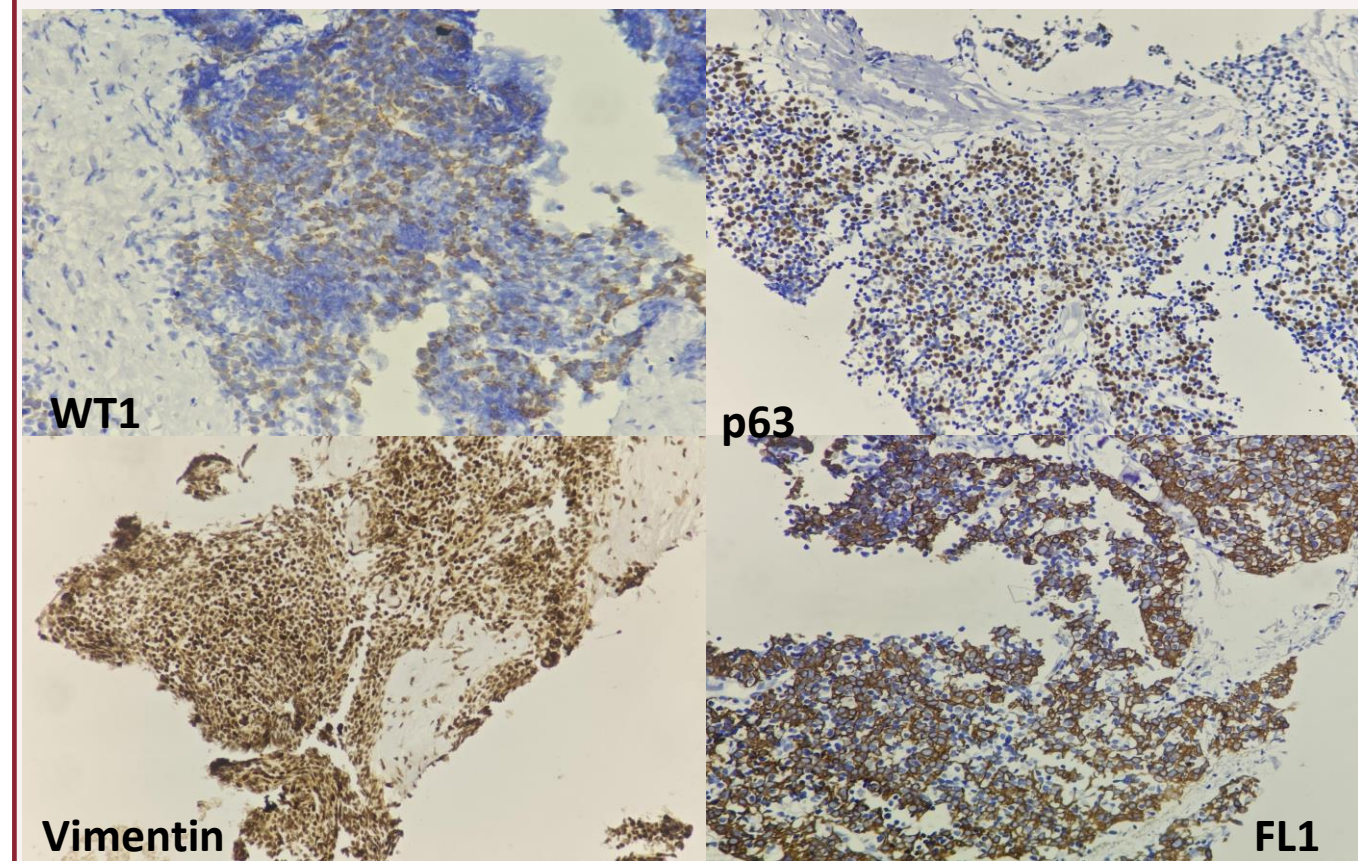


HISTOPATHOLOGY

Trucut Biopsy: round-to-oval smaller lymphoid cells (CD3+, LCA+) admixed with larger small round cells.

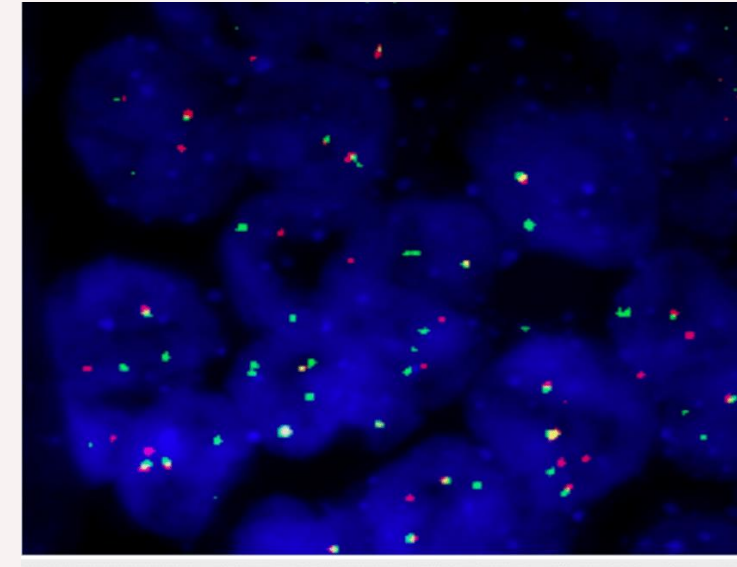
IHC & MOLECULAR

Larger cell population: p63+, FLI-1+, PanCK+, CK5/6+, with loss of BAP-1; negative for p40, Ber-Ep4, WT-1, TTF-1. Mesothelioma was a close differential (BAP-1 loss), but diffuse FLI-1 positivity and cell morphology favoured ALES.



MOLECULAR ANALYSIS

FISH for EWSR1 gene rearrangement
Split signals in >50% of tumour cells
Consistent with EWSR1 gene rearrangement



TREATMENT & OUTCOME

- The person affected under went a biopsy and full panel of investigations.
- During her course in the hospital, she succumbed to a hospital acquired infection.
- No cancer specific therapy could be administered to this person prior to this event.

PATIENT PERSPECTIVES

The relatives of the person deceased refused to give a comment on the perspectives

CASE 3

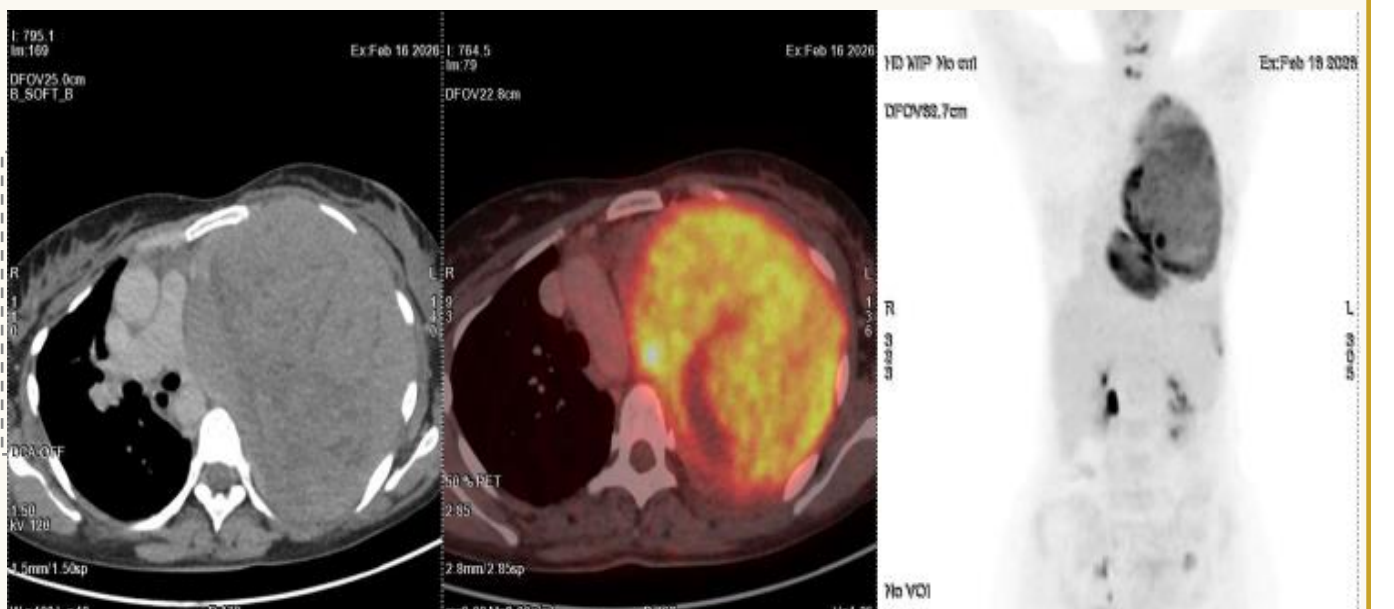
31F — Left Lung/Pleura

DEMOGRAPHICS & PRESENTATION

- 31-year-old female. Left-sided chest pain and progressively worsening breathlessness for 6 weeks, with occasional dry cough; no haemoptysis.
- Examination: markedly diminished breath sounds over the entire left hemithorax, with mediastinal shift to the left.
- Chest X Ray showed left hemithorax opacification with collapse of the underlying lung parenchyma

IMAGING

- WB PET-CT: large FDG-avid, heterogeneously enhancing, partly necrotic soft-tissue mass in the left hemithorax involving upper & lower lobes, 11.5×11.5×19.7cm (SUVmax 12.9), abutting mediastinal/costal pleura and encasing the left main bronchus and pulmonary veins; complete left lung collapse; moderate left pleural effusion with FDG-avid pleural thickening (SUVmax 5.8).

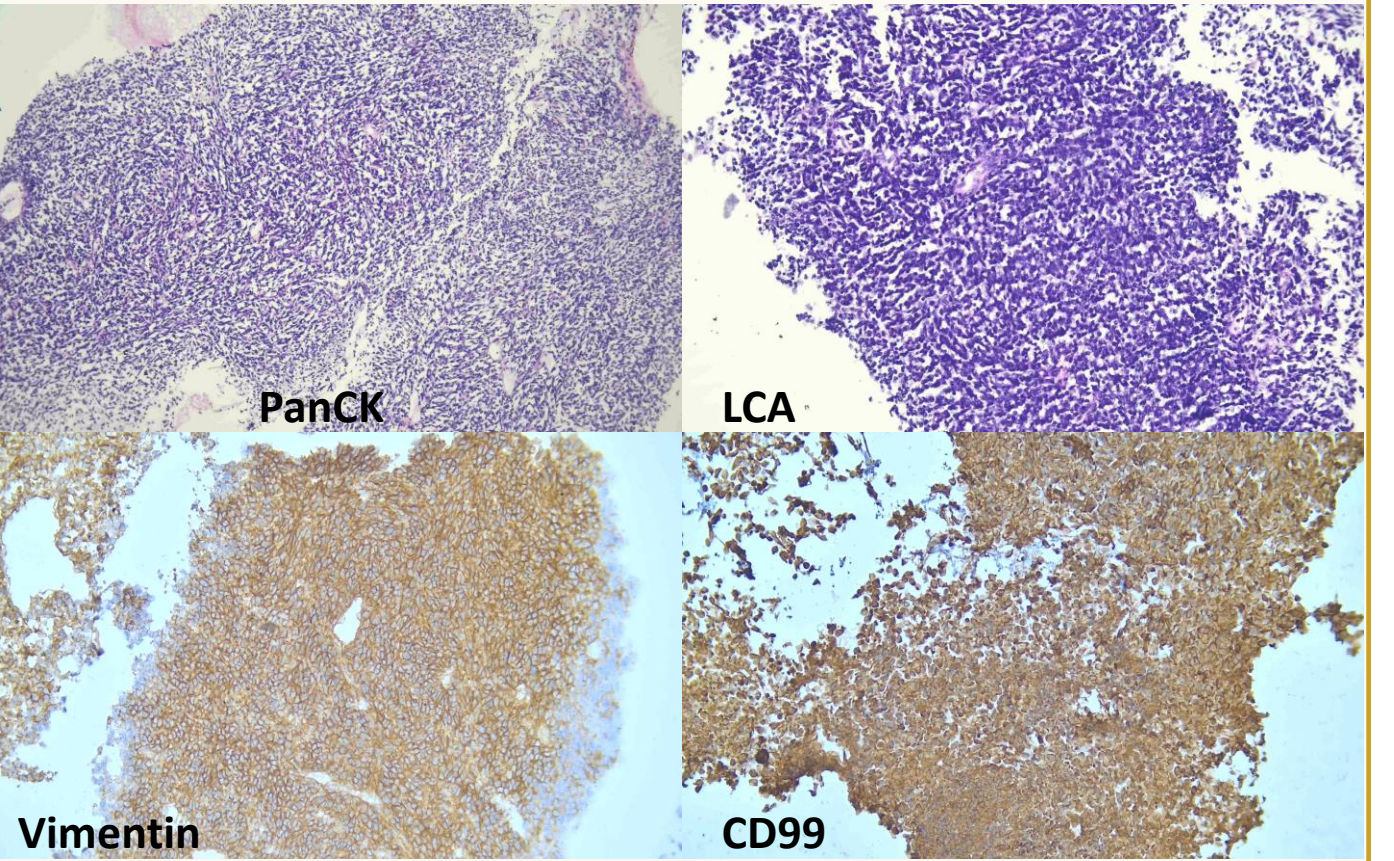


HISTOPATHOLOGY

USG-guided transthoracic biopsy: sheets of round-to-oval cells with monomorphic nuclei, focal rosettes — reported as 'small round cell tumour, ?PNET'. IHC panel recommended for confirmation.

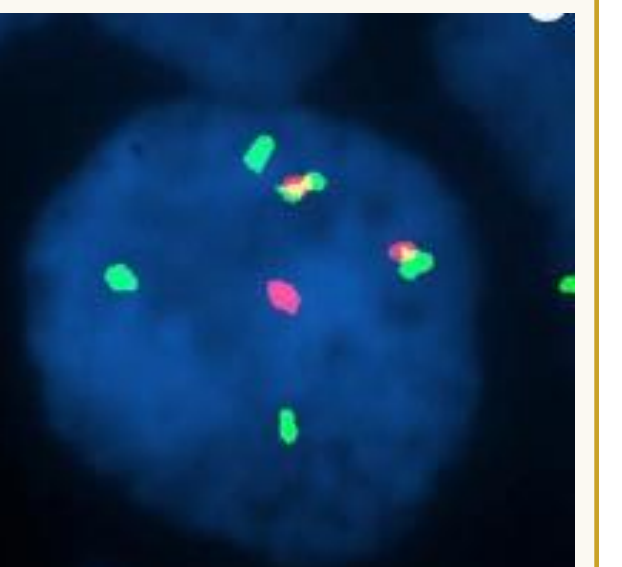
IHC & MOLECULAR

Diffuse positive for Vimentin, FLI-1, CD99; negative for PanCK, Synaptophysin, LCA. Final diagnosis: consistent with Ewing sarcoma.



MOLECULAR ANALYSIS

FISH for EWSR1 gene rearrangement
Split signals in >70% of tumour cells
Consistent with EWSR1 gene rearrangement



TREATMENT & OUTCOME

- This person with above mentioned disease had a post biopsy exacerbation leading to type 2 respiratory failure. Following which she was intubated and put on a respirator.
- Multiple weaning attempts were given but failed.
- She eventually underwent a tracheostomy. As of now, she has received 1 cycle of VDC with reduced dose. She is on follow-up

PATIENT PERSPECTIVES

I feel hopeless due to this disease all the time. Furthermore, to complicate the already existing tumor, I had to be put on a ventilator and have a tube put in my throat which is hampering with both daily activities and also cosmetically affecting me. I feel ashamed to see or talk to other people in this manner. (Note: This is translated from patient' mother tongue Hindi)