


Spindle Cell Lesion of Thoracic Pathology - A Journey From Biopsy To Resection Specimen

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Disclosure of Relevant Financial Relationships

No relevant financial relationships

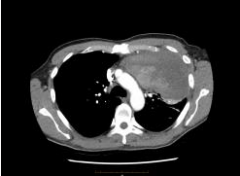
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Clinical Information

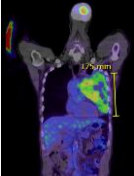
78M presented with 4 weeks of dyspnoea on exertion, 7 kg weight loss, central chest pain

ECOG 0 prembid
Smoker 1 cig / day
Manual labourer

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CT Chest Angiography (To exclude PE)
Large necrotic mass (17 x 12 x 10 cm) involving most of the lingula



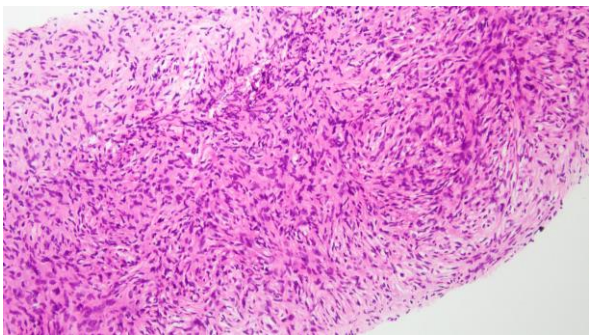
PET scan
Large left lingular mass, extending to left hilum; abutting mediastinum. Heterogeneous FDG activity suggestive of a necrotic malignancy

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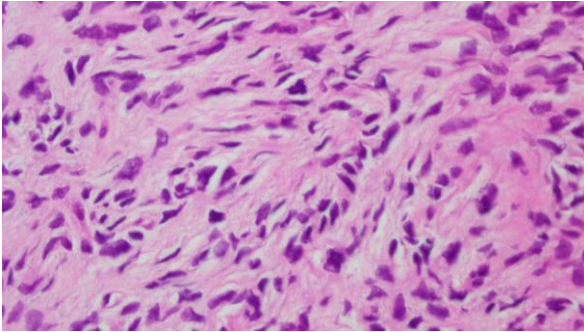
'Core biopsy, left upper lobe'



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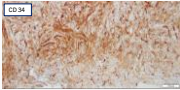
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Immunohistochemistry

Negative	Positive
AE1/AE3, CK8/18, CK7	CD34, CD99 and BCL2. TLE-1 (patchy)
EMA, Calretinin	
STAT-6	FISH: NO evidence of SS18 rearrangement
D2-40	
S100, SOX-10	
Pan TRK	
Smooth muscle actin	



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Diagnosis

Left upper lobe core biopsy:
High grade sarcoma not otherwise specified

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Patient's progress

Chemotherapy:

- 4 cycles Doxorubicin/ifosfamide/MESNA
- Complicated by sepsis requiring ICU admission.

Re-assessment/progress PET (2 months after commencing treatment)

- Small reduction in overall size
- More significant reduction in PET-avid volume (>520cc to 235cc)

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Genomic findings

Panel	Purity	MSI Status	TMB
T50500	73%	MS Stable (1.6% unstable sites)	3.9 Mut/Mb

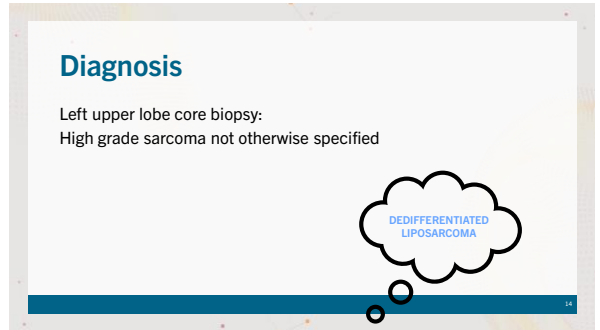
The following mutations were detected in the tumour:

Mutation	VAF / CopyNo	Notes
CDK4 amplification	92 copies	Amplification of oncogene CDK4.
FRS2 amplification	53 copies	Amplification of oncogene FRS2
MDM2 amplification	210 copies	Amplification of oncogene MDM2.
ATRX loss	0 copies	Biallelic loss of tumour suppressor ATRX.
CDKN2A loss	0 copies	Biallelic loss of tumour suppressor CDKN2A.
CDKN2A loss	0 copies	Biallelic loss of tumour suppressor CDKN2A.

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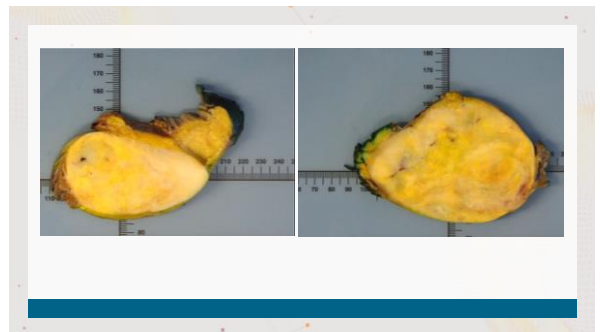
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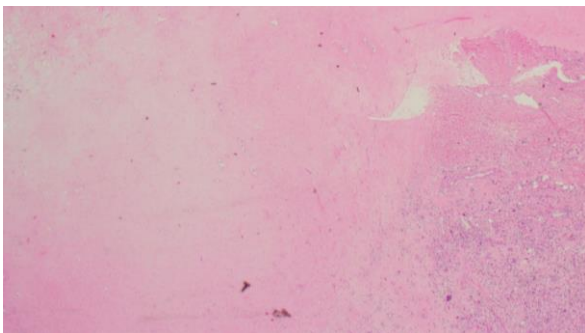
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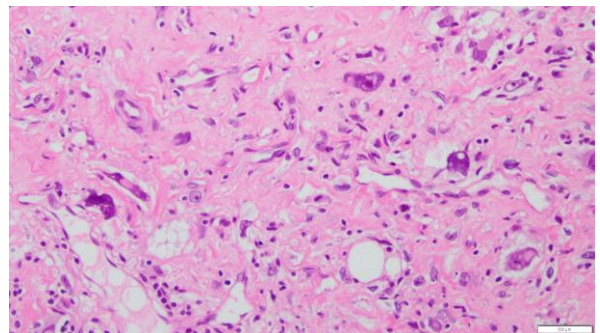
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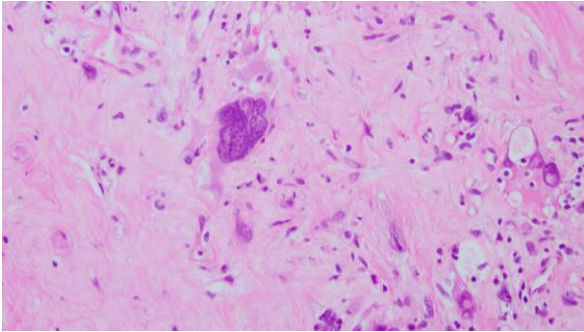
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DIAGNOSIS

LEFT CHEST TUMOUR:

**DEDIFFERENTIATED LIPOSARCOMA
WITH PARTIAL TREATMENT RESPONSE**

Focal background well-differentiated component also present

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Mediastinal liposarcoma

- Primary mediastinal liposarcomas are rare, <1% of all mediastinal tumors¹
- Histologic examination revealed that most of the cases were well differentiated liposarcomas (10/24), followed by dedifferentiated liposarcomas (8/24), pleomorphic liposarcomas (4/24), and myxoid liposarcomas (2/24)¹
- DDLPS = WDLPS + nonlipogenic spindle cell sarcoma²
- DDLPS & ALT/WDLPS: amplification of *MDM2* and *CDK4* (12q14-q15)

Hahn et al. Am J Surg Pathol 2007;31:1868-1874
Tibay et al. Journal of Anapath Case Reports (2023) 17:372

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Radiology: Cardiothoracic Imaging

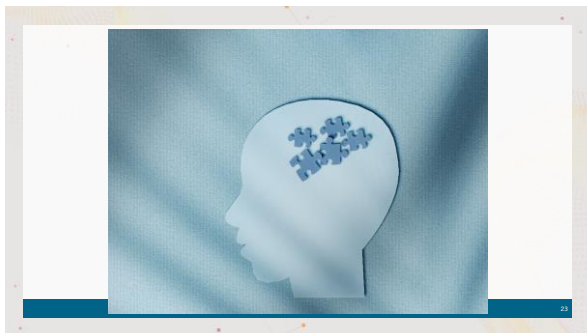
Imaging and Clinical Findings in a Series of Six Cases of Rare Primary Mediastinal Liposarcoma

Gardak S, Wang BS • David Bin, MD • Jane Y. Chen, MD • Raymond Thomas, MD • Meera J. Vora, MD • Susan K. Hebb, MD, PhD

A large 11.2 × 7-cm anterior mediastinal mass. Percentage of soft tissue is estimated to be 10%. As the mass is made up of both fat and connective tissue, other portions of the mass are approximately 0 HU, hyperattenuating to fat and slightly hypodense to muscle.

Radiology: Cardiothoracic Imaging 2022;42(2):e10259

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Analysis of *MDM2* Amplification: Next-Generation Sequencing of Patients With Diverse Malignancies

Kato et al. JCO Precis Oncol. © 2018 by American Society of Clinical Oncology

***MDM2* amplification occurred in 3.5% of patients (n: 102,878)**

- Liposarcoma (63%)
- Gallbladder adenocarcinoma (11%)
- Sarcoma (10%)
- Urothelial carcinoma (10%)
- Lung carcinoma (9%)

The most common co-alterations

- *CDK4* (43.6%)
- *FRS2* (40.8%)
- *TP53*
- *CDKN2A*
- *EGFR*

DOI: <https://doi.org/10.1200/JCO.17.00235>

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Spindle cell tumours with MDM2 amp

- Dedifferentiated liposarcoma
- Melanoma (may be dedifferentiated/undifferentiated)*
 - Clinical history
 - IHC for melanocyte markers + BRAF +/- additional molecular
- Lung adenocarcinoma (sarcomatoid)

May not be possible to reach final diagnosis on core biopsy



*Dedifferentiated melanoma with MDM2 gene amplification mimicking dedifferentiated liposarcoma <https://doi.org/10.1038/s41688-021-0129-0>

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Discussion: Spindle cell tumours of the 'lung'

- Diagnostic challenge, especially if:
 - Small biopsy
 - Misleading history ('lung' vs 'mediastinal' vs 'pleural')
 - Non-specific radiological features
 - No well-differentiated/characteristic histological component
 - Non-specific IHC profile
- Molecular testing as an adjunct

Sarcomatoid carcinoma, Mesothelioma, Solitary fibrous tumour, Melanoma Leiomyoma, Synovial sarcoma, Liposarcoma

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Take-home points

- Primary mediastinal sarcoma = rare
- Requires multidisciplinary approach in small core biopsy
 - Clinical and radiological correlation essential
- Molecular testing = important adjunct
 - May require excision specimen for final integrated diagnosis

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THANK YOU



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