Pathology Case of the Month

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Clinical History

This 84-year-old woman was referred to BUMCP radiology for biopsy of a 2 cm left upper lobe lung nodule.

The nodule had increased in size from 1.4 cm on 1/10/22.

She has a history of breast cancer, resected and treated, initially diagnosed out of state in 2021.

Recently, she moved to the Phoenix area, followed by a local oncologist.
Percutaneous CT guided core biopsies of the lung nodule were obtained.

Representative HE images follow in the next slides.

What is your differential diagnosis?

What ancillary tests would you order (IHC, FISH, etc)?

What other information is pertinent to working up this case?
Core biopsy histology
Core biopsy histology
Core biopsy histology
Core biopsy histology
Core biopsy histology
Differential Diagnosis

spindle cell carcinoma of pulmonary or metastatic origin (most likely, many sites, GU, GYN, breast, less likely GI)

solitary fibrous tumor: unusual location unless arising from fissure; histology not typical unless ”dedifferentiated”; sarcomatoid mesothelioma- unlikely for similar reasons

leiomyosarcoma: histology not typical; very rare primary

synovial sarcoma: location not typical; the uniform spindle cell short fascicular growth of monophasic or biphasic tumors is not present; high grade variants more often ”round cell”
Differential Diagnosis

Metastatic melanoma: histology not entirely characteristic of spindle cell or desmoplastic variants, but must always consider melanoma in the differential

Vascular neoplasm/ angiosarcoma: not particularly vasoformative or hemorrhagic by histology

Metastatic or primary pulmonary sarcoma; diagnosis of exclusion; latter includes intimal sarcoma of pulm. artery

malignant inflammatory myofibroblastic tumor
Immunohistochemistry

spindle cell carcinoma: panCK, CK5, p40, p63

Solitary fibrous tumor: STAT6

Sarcomatoid mesothelioma: calretinin, CK, WT1, BAP1 loss

Smooth muscle neoplasm: desmin

Melanoma: SOX-10, S100, Melan A

Synovial sarcoma: CK, TLE1, SS18 IHC and/or FISH

Malignant IMT: sma, ALK (clones ALK1 or ALK D5F3)

Additional: TTF1, GATA3, mammaglobin, ER
desmin
CD31

Tumor cells negative
Vascular endothelium and histiocytes positive
STAT6
TTF-1
GATA3

mammoglobin
PDL1
CPS 60%
Metastatic spindle cell/ sarcomatoid/ metaplastic carcinoma of breast origin (with minor squamous component)

PanCK/ CK5/ p40 expression support the diagnosis

Lack of expression of other markers except TLE1

Per additional history and outside path report obtained from the patient’s oncologist, the patient was treated for TNBC of metaplastic spindle cell type in the fall of 2021 (stage pT4c pN2).

Treated by mastectomy and chemotherapy.
Comprehensive tumor profiling: Caris Life Sciences:

Reiterated the triple negative phenotype and high PD-L1 expression

TMB: low (not always predictive of PD-L1 status)
MSI: stable

Mutations:
PIK3CA (not eligible for FDA approved drug, as tumor is ER negative)
MUTYH and TERT mutations also detected
High-grade conventional ductal type most common

Metaplastic types:

Matrix producing (chondro/ osteosarcoma)

Squamous cell carcinoma

High-grade spindle cell/ sarcomatoid

Low grade adenosqamous type (better prognosis)

Low grade fibromatosis-like (better prognosis)
Spindle cell/ sarcomatoid Carcinoma of the breast

Metaplastic carcinomas: 0.1 to 1% of all breast cancers.

Subtype of triple negative breast cancer:

Use multiple keratins, including CK5 and p63/p40

Triple negative; mammaglobin/ GCDFP negative

Reduced or absent expression of GATA 3

Calretinin(38-54%) and SOX-10 (60%) often expressed in TNBC

TRSP1 recently reported as expressed in nearly all conventional IDC and 86-95% of TNBC sub-types
TLE1 expression reported in a wide variety of tumor types; specificity is limited

Obtaining history and prior pathology, even if outside your institution/laboratory is critical: Do not rely solely on the oncologist/treating physician to provide it.

Panel of IHC markers and correlation with morphology, tumor location and imaging is paramount in assessment

Metaplastic breast ca:
Genetics: PI3K and MAPK pathway, ARID1A, KMT2C, TERT

Treatment: PD-L1+: eligible for immunotherapy
Sacituzumab govitecan (TRODELVY): Trop-2 directed ab-topoisomerise inhibitor drug conjugate (adv or metastatic, 2\textsuperscript{nd} / 3\textsuperscript{rd} line)
Additional examples of TNBC

Basal TNBC

p40
Mixed metaplastic and signet ring ca

CK5/6
Metastatic TNBC

calretinin
References

WHO Classification of Breast Tumors, 5th edition.

