Primary Lung Carcinosarcoma with Malignant Peripheral Nerve Sheath Tumour; A Cytological and Histological Description of a Rare and Unusual Entity

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Clinical Presentation
A 78 year old male, an ex-heavy smoker, with a background history of low grade adenocarcinoma of the caecum and recent weight loss presented with a right lower lobe lung nodule. The nodule was found to be increasing in size on CT chest imaging, showed moderately intense FDG activity, and was thought to represent an isolated metastasis from the colorectal carcinoma.

Cytological Findings
The patient underwent Endobronchial ultrasound (EBUS)-guided fine needle aspiration (FNA) of the right lower lobe lung lesion. This resulted in moderately cellular smears with a population of spindle cells of variable nuclear size with irregular nuclear contours and fine chromatin pattern, in a background of benign bronchial cells and blood. The majority of the spindle cells were entrapped in loose stromal fragments. The cell block demonstrated lesional material comprising spindle cells embedded in loose myxoid stroma. A broad immunohistochemical panel was performed with tumour cells showing positive expression for CD99, CD56 and focal CD117, NF, GFAP, EMA, B-catenin, Desmin, Actin, SOX10, PR or p40. The H3K27 proliferative index was estimated at 20 to 30%. Overall the tumour cells in the cell block showed a non-specific immunohistochemical staining pattern.

Figure 1: EBUS guided FNA - (A) H&E smear showing spindled cells with nuclear atypia in a background of benign bronchial cells (10X), (B) Cell block showing spindled cells embedded in loose myxoid stroma (10X), (C) Cell block showing spindled cells embedded in loose myxoid stroma (20X), (D) Cell block showing spindled cells embedded in loose myxoid stroma (10X), (E) Cell block with spindled cells showing loss of nuclear H3K27 tri-methylation (20X)

Discussion
Overall the cytological features were not typical of a colorectal metastasis or primary lung carcinoma, and the case was reported as indeterminate spindle cell lesion. A broad differential diagnosis of mesenchymal tumours was considered, including the following:

- Leiomyoma/Leiomyosarcoma
- Spindle cell melanoma
- Solitary fibrous tumour
- Gastrointestinal stromal tumour
- Inflammatory myofibroblastic tumour
- Neuroendocrine tumour
- Synovial sarcoma
- Rhabdomyosarcoma

On cytology alone the spindle cell lesion could not be further subclassified. Excision of the lesion was required for a definitive diagnosis, hence the patient underwent a right lower lobe lobectomy. On histological assessment, the majority of the tumour exhibited a sarcomatous appearance comprising HPF regions of malignant spindle cells in a vaguely myxoid background accompanied by necrosis and marked mitotic activity (40/10HPF). A minor carcinomatous component was also identified, showing mixed squamous and glandular differentiation with an in-situ carcinoma component. On immunohistochemistry, the sarcomatous component showed focal positive immunostaining for S100 and complete loss of nuclear H3K27 tri-methylation. H3K27me3 immunohistochemistry is useful as a diagnostic marker of Malignant Peripheral Nerve Sheath Tumour (MPNST), and given its utility in the resection specimen, the stain was retrospectively applied to the cytology cell block which showed concordant loss of expression in the spindle cells, supporting a diagnosis of MPNST. The minor carcinoma component showed positive staining for squamous markers p40 and CK5, with focal staining for glandular markers TTF1 and Napsin–A, in keeping with a carcinomatous component of adenocarcinoma. An extended FISH analysis was performed and no genetic defects were identified. The final diagnosis on the resection was Carcinosarcoma (95% MPNST, 5% adenocarcinoma).

Carcinosarcomas are malignant biphasic neoplasms composed of malignant epithelial and mesenchymal components1, and are notably rare tumours in the lung, accounting for less than 0.01% of all lung cancers2. Typically squamous cell carcinoma is the most common epithelial component, whilst reported sarcomatous elements include Rhabdomyosarcoma, Angiosarcoma, Chondrosarcoma, Osteosarcoma and Liposarcoma3. A primary lung MPNST is a rare but described entity; however the presence of MPNST forming the sarcomatous component of a primary lung carcinosarcoma is exceedingly rare and remains unreported in current literature.

References