NGS and FNA Cytology: Their Significance in the Diagnosis and Treatment of Metastatic Non-Small Cell Lung Carcinoma (NSCLC)

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Clinical Presentation
• December 2018, 47 year old female presented to the emergency department with shortness of breath, fatigue and left leg oedema
• A chest x-ray was performed, revealing a rounded 2.2 x 2.2cm opacity in the right middle lobe
• The mass identified was not previously seen on a comparison chest x-ray nine months prior, after the patient was admitted to the emergency department following a bicycle accident
• A Positron Emission Tomography (PET) scan identified many FDG-avid mediastinal lymph nodes and an avid right supraclavicular lymph node.

Histological Investigation
Specimen:
• Two 18g core biopsies of the supraclavicular lymph node were performed under ultrasound guidance concurrently, with FNA collection.
• H&E Sections evaluated
• IHC Sections for confirmatory diagnosis

Tissue retrieved from cytology preparations
• Cores of tissue infiltrated by a moderately differentiated adenocarcinoma

Histology Results
• Metastatic adenocarcinoma consistent with a lung primary

NGS Results
• Tissue retrieved from cytology preparations
• NGS performed using the Ion PGM™ platform, which accommodates analysis of small specimens, requiring only 10ng of DNA
• A clinically relevant mutation was detected in Exon 21 of EGFR gene
• The L858R mutation results in an amino acid substitution at position 858 in EGFR, from a leucine (L) to an arginine (R)
• This mutation is known to confer increased sensitivity to EGFR-tyrosine kinase inhibitors (TKI’s)

Discussion
• Cytopathology has a significant role to play in the era of molecular pathology, specimens are collected by minimally invasive means, and can be prepared and assessed in a shorter time frame, in comparison to surgical histology specimens
• In this case, a morphological diagnosis and a mutational profile of the metastatic tumour was performed on a subcutaneous FNA of lymph node
• A clinically relevant sensitising mutation was detected in the EGFR gene using NGS, allowing the patient to begin targeted treatment, avoiding conventional cytotoxic chemotherapy
• NGS results can then be used to guide decisions on the appropriate treatment plans for patients, whose response to targeted therapies may change throughout the course of their treatment