AN APPROACH TO THE DIAGNOSIS OF RARE LUNG TUMOURS

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Any primary tumour arising in the lung apart from carcinomas and carcinoids falls under the umbrella term of a 'rare lung tumour'. This therefore includes other epithelial tumours, mesenchymal tumours, lymphomas, and even teratomas and melanomas. Their classification has been updated in the 2015 WHO classification, with the last decade seeing greater understanding of cellular origin, such as sclerosing haemangioma being definitively identified as a low-grade epithelial neoplasm. New tumours with specific genetic abnormalities have also been identified (e.g., pulmonary myxoid sarcoma with EWSR1-CREB1 translocation), and lymphangioleiomyomatosis and Langerhans cell histiocytosis are now also classified as neoplasms.

It is useful therefore to have a uniform approach to a potential 'rare' neoplasm. I first apply the 2015 WHO classification, then correlate this with morphological (e.g., clear cell, spindle cell etc.) differential diagnoses and the known immunohistochemical profile to see whether the proposed diagnosis is consistent with these data. I then review the case again in relation to whether the presentation of the tumour is appropriate for my proposed diagnosis (benign/low-grade versus malignant cytology, tumour location, solid/cystic, local/diffuse) and finally review once more in the context of whether tumour might be a secondary process or even a reactive process.

HUNTING FOR THE SIGNATURES OF CANCER BY PLASMA DNA SEQUENCING

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Liquid biopsy refers to the analysis of DNA released by tumours into the circulation of patients for the detection, prognostication, selection of therapeutic targets or monitoring of malignancies. For example, regulatory approval has been granted for the detection of epidermal growth factor receptor mutations in plasma of patients with non-small cell lung cancers as a means to stratify therapy. However, the key challenge in the diagnostics of cancer is about its early detection. Given that cancers are highly heterogeneous, our group has been developing whole genome approaches to detect the signatures of cancer via a liquid biopsy. The rationale is to extract as much of the molecular information as possible from a plasma sample to catch a glimpse of the possible presence of cancer. Genome-wide approaches to detect tumour-associated copy number aberrations, molecular size profile, DNA methylation signatures and transcriptomic features from circulating nucleic acids have been developed. We have further developed an approach to pinpoint the anatomical location of malignancy, naming to determine a tissue map non-invasively. In summary, many

facets of molecular information could be extracted from a liquid biopsy.

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AN APPROACH TO THE DIAGNOSIS OF INTERSTITIAL PNEUMONIAS IN ADULTS AND CHILDREN

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In adults with an idiopathic interstitial pneumonia (IIP), an updated classification system was published in 2013. Although definitions for the seven histological patterns remain essentially unchanged, there has been substantial progress in our understanding. In relation to usual interstitial pneumonia (UIP), updated management recommendations were published in 2011, with the most significant change recommending varying degrees of confidence in diagnosis. A pattern of UIP is also being increasingly recognised in patients with chronic hypersensitivity pneumonitis. Idiopathic non-specific interstitial pneumonia is now better defined as a specific clinico-pathological entity, with the majority cases proving to have secondary associations/causes after multidisciplinary review. Respiratory bronchiolitis–interstitial lung disease is now commonly diagnosed without surgical biopsy, and acute exacerbation of IIPs is now well defined. A group of rare entities, including pleuroparenchymal fibroelastosis and rare histological patterns, is also introduced. There have also been advances in the undertaking of biopsies with most institutions sampling at least two sites, ideally using preoperative targeting. These histological patterns are also recognised in children, although classification is more complex and includes entities specific to a younger age group (e.g., neuroendocrine hyperplasia of infancy, pulmonary interstitial glycogenosis). Surfactant protein gene mutations are also being increasingly identified.

B-CELLS BEHAVING BADLY I: A BETTER BASIS TO BEHOLD BELLIGERENCE IN SMALL B-CELL LYMPHOMAS

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Small B-cell lymphomas and leukaemias (SBCLs) are a clinically, morphologically, immunophenotypically and genetically heterogeneous group of neoplasms that include chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL), mantle cell lymphoma (MCL), follicular lymphoma (FL), lymphoplasmacytic lymphoma (LPL), marginal zone lymphoma (MZL) and hairy cell leukaemia (HCL). The pathogenesis of some of these lymphoid malignancies is characterised by distinct translocations, for example t(11;14) and t(14;18), respectively, in most cases of MCL and FL. By contrast, other entities are associated with a variety of non-specific and non-diagnostic but nevertheless recurrent and prognostically pertinent numeric