



Lung Cancer Diagnostics and Prognostics - Tissue Is an Issue

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Editorial

There has been burgeoning of knowledge brought about by the introduction of molecular and immuno markers in the evolution of various types of lung cancer and management. Classification of lung cancer into two categories i.e., small cell and non-small cell carcinoma is no more acceptable to the oncologists and other Multi-Disciplinary Team (MDT) members dealing with this cancer. This has prompted us to use immuno histochemical markers for further classification of non-small cell carcinomas in situations where histology is not showing classic features of an adenocarcinoma (gland formation, mucin secretion) or squamous cell carcinoma (keratin pearl formation, intercellular bridges). Markers commonly used are TTF1 and Napsin A for an adenocarcinoma. Commonly used markers for squamous cell carcinoma are P63 and CK5/6. If morphology is suggestive of neuroendocrine differentiation markers such as CD56, Chromogranin and synaptophysin are added. List of markers is expanded when histology and markers mentioned earlier fail to sub-classify a lung cancer. Possibilities for a diagnosis on a biopsy from a lung mass include metastatic tumours, mesothelioma, melanoma, lymphoma, sarcoma etc. There are huge implications for a wrong diagnosis as patient will be referred to a wrong MDT and dealt by incorrect surgical procedure, given incorrect chemotherapy/radiotherapy and may have a completely different outcome.

If this was not enough, we are now faced with an added burden of providing tissue sample for molecular testing especially in primary pulmonary adenocarcinoma. This is to facilitate targeted therapies for non-small cell lung cancers following the discovery of a number of targetable driver mutations such as Epidermal Growth Factor Receptor (EGFR), Anaplastic Lymphoma Kinase (ALK-EML translocation) and c-Ros Oncogene 1 (ROS1) rearrangement [1]. These molecular markers require a number of different testing platforms such as Polymerase Chain Reaction (PCR) for EGFR testing, FISH/immuno histochemistry for ALK-EML translocation and ROS1 sgene rearrangements in non- small cell carcinomas.

Some non-small cell lung cancers acquire resistance to Tyrosine Kinase Inhibitors (TKI) due to a number of resistant mutations, commonest being T790 mutation in Exon 20. Around 20% of patients who relapse on TKIs can also show amplification of the MET gene [2]. This testing also requires tissue sample.

List is getting even bigger with passing time. Adenocarcinomas of lung will also require testing for HER2, BRAF, PIK3CA, AKT1, MAP 2KI, NRAS, RET & KRAS. Similarly Squamous cell carcinomas will require testing for FGFR 1Amp, EGFR vIII, EGFR and DDR [3].

Immune modulators active against tumours expressing the PD-L1 protein require precise analysis of the tumour. PD-L1 testing in non-small cell lung cancer is another test that is required to deliver immunotherapy for patients with good performance status (PSO/1), tumours being negative for EGFR mutation and ALK-EML translocation. Whilst molecular markers mentioned above are subjected to reflex testing on all TTF1 positive adenocarcinomas and non-small cell carcinoma, PD-L1 testing requires a decision of the MDT as it is not only the type of cancer but also the stage and performance status of the patient that is taken into consideration for this testing. Only locally advanced or metastatic non-small cell carcinoma are eligible for treatment with agents like Pembrolizumab. This test requires a minimum of 100 tumour cells for a valid result and to start immunotherapy.

There is competing demand on tissue for diagnostic evaluation and molecular profiling of a patient's tumour to help with the biomarker driven treatment. Tissue obtained from patients with lung cancer varies tremendously depending upon the site of the biopsy, size of needle used, expertise of the clinician, and associated disease such as emphysema with risk of pneumothorax, etc. There is

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move towards converting cytology samples into histology by the use of cell blocks and clots in most laboratories with aim of cutting sections for immuno histochemistry and molecular testing. However, there are times when very few cells are available for histological evaluation and further testing. There are logistic issues of having testing platforms at multiple sites, cost implication of testing, manpower required for the extra activity generated from sending samples away, dealing with queries from clinicians/patients and governance around all this activity. There is also mounting pressure from the trusts/MDTs for a quick turnaround time due a very narrow window to meet national cancer targets and avoid penalties.

This requires alternative strategy. Liquid biopsy is being proposed as a solution [4]. Circulating tumour DNA is a potential surrogate for the entire genome. The use of blood samples from cancer patients could be a useful resource for the analysis of mutations and secondary mutations responsible for resistance to treatment. This requires expertise to extract high quality DNA from circulating tumour cells present in the plasma along with financial resources and technical expertise.

Next Generation Sequencing (NGS) is likely to replace traditional capillary-based single gene sequencing by a first generation technique (Sanger sequencing). NGS will be able to reveal mutations in low percentage and to screen the mutational status of different tissue/liquid samples including biopsies, cytology samples and circulating plasma DNA [5].

Lung cancer is at the forefront of innovation and all these developments are going to benefit lung cancer patients. However, there are cost implications associated with these exciting developments.

References

1. Selinger CI, Li BT, Pavlakis N, Links M, Gill AJ, Lee A, et al. Screening for ROS1 gene rearrangements in non-small cell lung cancers using immuno histochemistry with FISH confirmation is an effective method to identify this rare target. *Histopathology*. 2017;70(3):402-11.
2. Kerr KM. Personalized medicine for lung cancer: new challenges for pathology. *Histopathology*. 2012;60(4):531-46.
3. Li T, Kung HJ, Mack PC, Gandara DR. Genotyping and genomic profiling of non-small cell lung cancer: implications for current and future therapies. *J Clin Oncol*. 2013;31(8):1039-49.
4. Heitzer E, Ulz P, Geigl GB. Circulating tumour DNA as a liquid biopsy for cancer. *Clin Chem*. 2015;61(1):112-23.
5. Coco S, Truini A, Vanni I, Dal Bello MG, Alama A, Rijavec E, et al. Next generation sequencing in non-small cell lung cancer: new avenues towards the personalized medicine. *Curr Drug Targets*. 2015;16(1):47-59.