Utility of cytopathology in diagnosis and molecular testing of lung cancer

We read with interest the editorial by Booton et al on advances in the treatment and diagnosis of non-small cell lung cancer. Recently published best practice guidelines for pathology recommend the provision of as precise a diagnosis as possible, with optimisation of specimen use. We advocate the utility of cytopathology in this regard and share our experience of the diagnostic potential and the range of ancillary tests possible on respiratory-related cytology specimens.

During a 20-month period (1 September 2009 to 30 April 2011), 227 patients were diagnosed with lung cancer at our centre, 162 of whom (264 samples) had malignant cytology from a range of exfoliative (bronchial brushings, washings and lavages; pleural fluid) and fine needle aspiration samples, the latter encompassing transbronchial and transesophageal ultrasound guided fine needle aspiration of mediastinal lymph nodes and lung. Patients had one to four samples each. Morphological diagnosis of keratinising squamous cell carcinoma could be made with confidence without the need for immunocytochemistry, and in experienced hands, cytological appearances of small cell carcinoma are also characteristic. Subtyping of other carcinomas was undertaken by means of immunocytochemistry performed on agar cell blocks, material permitting (table 1). A morphological diagnosis of keratinising squamous cell carcinoma could be made with confidence without the need for immunocytochemistry, and in experienced hands, cytological appearances of small cell carcinoma are also characteristic. Subtyping of other carcinomas was undertaken by means of immunocytochemistry performed on agar cell blocks, material permitting (table 1).

A morphological diagnosis of non-small cell carcinoma not otherwise specified, due to insufficient material for immunotyping, may still be clinically useful depending on other clinical and staging information. If required, extra material can be requested for further subtyping.

Epidermal growth factor receptor mutation testing was requested in 36 cases, with mutations identified in six patients. Three tests failed due to insufficient DNA. In some cases where testing was not possible due to insufficient sample, direct communication with the treating clinician was undertaken to request more material, for example, pleural fluid. Testing for ALK-EMIL4 fusion was performed in one case.

The strategic use and triage of cytological material enable the maximum diagnostic and therapeutic information to be obtained. This may entail using all of the material in a sample for ancillary tests without producing traditional diagnostic slides, when the diagnosis has already been established in preceding samples. Close collaboration with...
clinicians, radiologists and oncologists, both on a day-to-day basis and at respiratory multidisciplinary team meetings, has led to the recognition of the value of diagnoses made on cytology samples, enabling therapeutic intervention based on cytological diagnosis alone, as many cases have no or inconclusive histology samples. However, this relies on high quality cytology preparations and accomplished cytopathologists. In our opinion, these samples are best procured and reported in large expert centres.

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REFERENCES

Table 1  Number of patients diagnosed with different lung cancer tumour types based on the method of diagnosis (excluding 18 cases where pleural fluid samples contained adenocarcinoma that may have originated from the lung or other primary sites)

<table>
<thead>
<tr>
<th>Tumour type</th>
<th>Morphological diagnosis only</th>
<th>Diagnosis based on ICC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squamous cell carcinoma</td>
<td>46</td>
<td>7</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>12</td>
<td>42</td>
</tr>
<tr>
<td>Adenosquamous carcinoma</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Non-small cell carcinoma NOS</td>
<td>15</td>
<td>4</td>
</tr>
<tr>
<td>Small cell carcinoma</td>
<td>8</td>
<td>6</td>
</tr>
</tbody>
</table>

ICC, immunocytochemistry; NOS, not otherwise specified.

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