

Borderline early squamous cell lung cancer



The strategy regarding centrally located early squamous cell cancer (SCC) and its precursor lesions currently relies on sensitive diagnostic tools, such as autofluorescence bronchoscopy (AFB), high-resolution computed tomography (HRCT) and positron emission tomography with 18 fluorodeoxyglucose (FDG-PET) [1, 2].

Inclusion criteria for bronchoscopic treatment with curative intent include: HRCT occult lesions, $\leq 1 \text{ cm}^2$ with visible proximal and distal margins on AFB, and node (N)0 metastases (M)0 findings on FDG-PET scan [1]. Bronchoscopic staging is inaccurate if the distal border is invisible, as possible invasion distal to the segmental bronchi cannot be ruled out.

Task 1 and 2

Two cases are presented here that demonstrate some limitations that can arise from the use of non- and minimally invasive diagnostic tools for staging of SCC and its precursor lesions. Read through and critically assess the case presentations, and suggest things that could have been done differently.

Case 1

A 72-year-old male was referred for staging of radiologically occult SCC, diagnosed by sputum cytology. The patient presented with progressive cough and occasional haemoptysis. He had stopped smoking 40 years previously and had a 15 pack-year smoking history.

AFB demonstrated multiple suspicious lesions in the tracheobronchial mucosa. The region of RB6 was clearly abnormal, with a surface area of $< 1 \text{ cm}^2$, and the distal margin was clearly visible. Histological examination showed microinvasive SCC. No abnormalities were seen on HRCT. The FDG-PET scan was positive for primary tumour and with suspicion for N2+3 involvement (4R and 5; figure 1). Mediastinoscopy and anterior mediastinotomy

were performed, but the corresponding nodes showed only anthracosis.

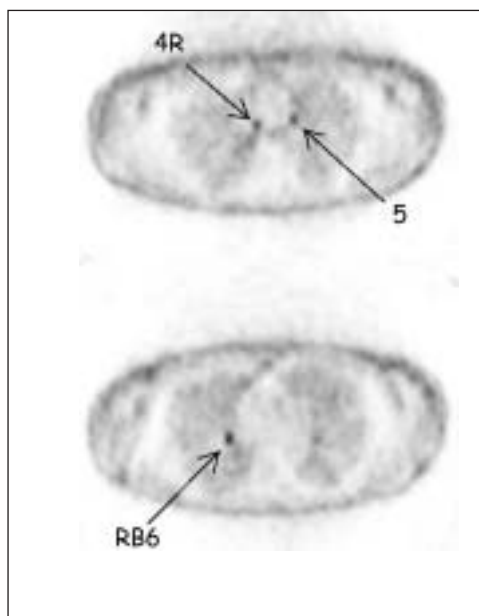


Figure 1

Positron emission tomography with 18 fluorodeoxyglucose scan of transaxial 5-mm images of case 1, showing activity of the primary microinvasive squamous cell cancer in the right superior basal lobe carina (RB6) region, and positive 4R (N2) and 5 (N3) mediastinal lymph nodes.

Bronchoscopic electrocautery of the RB6 was performed based on the inclusion criteria. On repeat AFB, the mucosal lesion was seen to spread to the subsegmental RB6 region with an invisible distal border. Biopsy specimens showed severe dysplasia. Repeat HRCT showed bronchial wall thickening of this particular segment, and FDG-PET scan remained tumour positive.

The transition to more extended AFB criteria with regard to surface area and distal border led to the decision to perform a bilobectomy. The resection specimen showed an extensive field of severe dysplasia to the level of the subsegmental bronchi without an invasive component of SCC.

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Answer 1

In case 1, the strict inclusion AFB criteria, repeat HRCT and FDG-PET scan findings led to over-diagnosis and overtreatment. However, in retrospect, as inaccurate staging of the lesion's distal border precludes local curative treatment by any bronchoscopic method, more invasive diagnostic and therapeutic procedures would still have been required.

Case 2

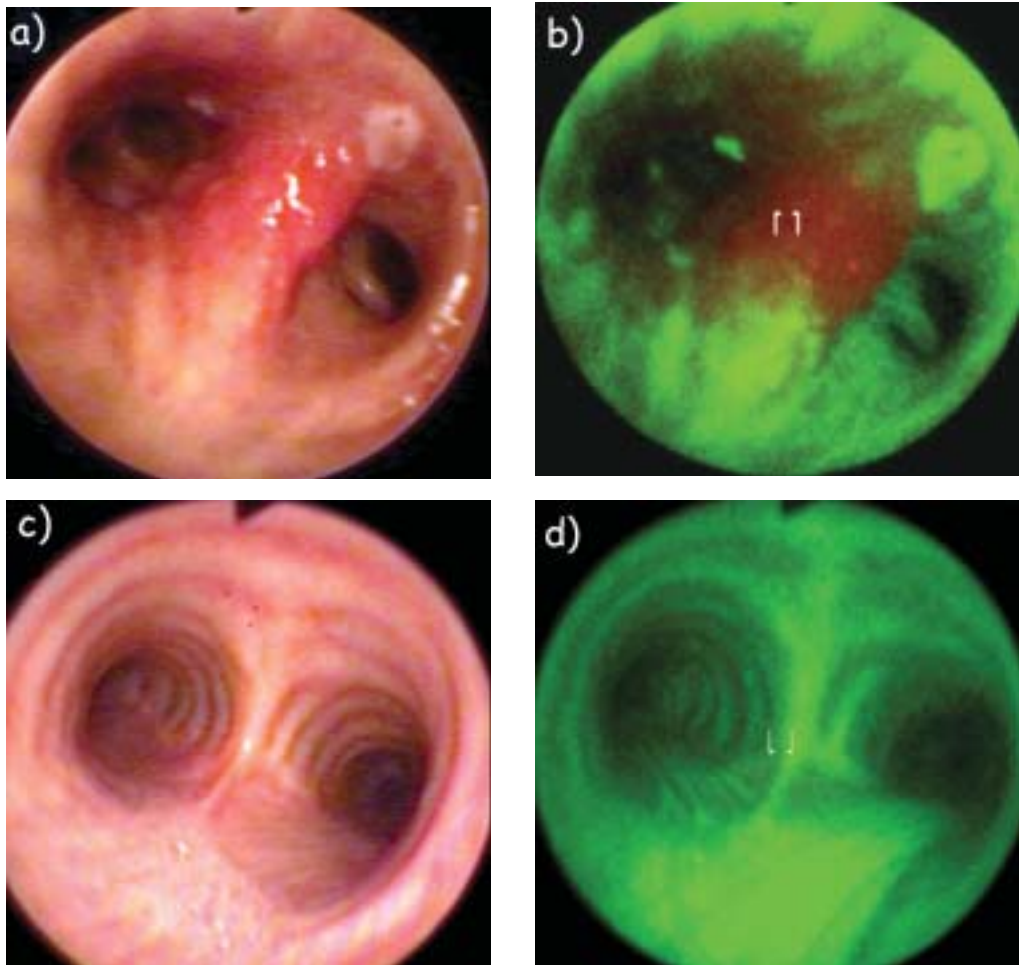
A 54-year-old female underwent repeat bronchoscopies because of dysplasia in the left main bronchus prior to referral. She smoked heavily and had a 67-pack-year smoking history. Her brother died of lung cancer 2 years prior to referral. She was referred because of progressive mucosal redness of the left main bronchus (LMB) region, after which AFB was performed. Extensive and irregular mucosal redness was found in the LMB region towards the left upper lobe segmental bronchi

with an invisible distal margin (fig. 2: a and b). Repeat biopsies during follow-up showed gradual progression from dysplasia to carcinoma *in situ* in the 2-year period. The carinal RB6 region was also AFB suspicious, but histology was normal. HRCT examination showed no abnormalities. FDG-PET scan showed no activity of the LMB region, but was positive for the RB6 region.

As microinvasive SCC cannot be ruled out distal of the segmental bronchi in the left upper lobe, a left pneumonectomy was performed. Three microinvasive SCC fields, measuring 0.18, 0.19 and 0.36 mm, and extensive severe dysplasia of the left main bronchus mucosa were found microscopically. Surgical resection was radical. Within 4 months, RB6 mucosa, which was considered "false-positive" on FDG-PET and AFB, progressed to SCC. Photodynamic therapy (PDT) combined with external irradiation did not achieve a complete response, and the patient died of fatal haemorrhage due to radiation necrosis. Autopsy revealed viable tumour tissue with necrotic fistulisation to the right lower pulmonary vein.

Figure 2

Bronchoscopic (a) and autofluorescence bronchoscopic (b) images of case 2, showing extensive mucosal involvement of severe dysplasia and carcinoma *in situ* in the left carina region towards the left upper lobe, accompanied by images of a normal field (c, d) in the main carina for comparison.



Answer 2

In case 2, the presence of microinvasive SCC beyond the distal segments in the left upper lobe was correctly identified after performing more invasive diagnostic end-therapeutic procedures. However, even in retrospect, the optimal management of a "false-positive" AFB and FDG-PET lesion in the RB6 carina remains uncertain due to limited knowledge of the natural history of SCC (*in situ*) and its precursor lesions. As demonstrated, it is impossible to predict the malignant potential of these lesions based on histopathological classification alone.

Discussion

For early-detected central SCC, sensitive diagnostic tools are currently used for accurate staging. The cure rate of early-stage SCC, either bronchoscopically or by surgical resection, is 70–100%. However, the limitations of non- and minimally invasive techniques for staging can lead to insecurities with regard to the actual tumour stage. This is of primary importance, as accurate staging is a prerequisite for choosing the most appropriate treatment strategy. The two cases reported here are clear examples of how sensitive diagnostic and staging methods can lead to controversial issues.

The ability to detect mucosal changes early, and the feasibility of non- and minimal invasive staging and treatment methods, such as AFB, HRCT and FDG-PET, in combination with the curative potential of bronchoscopic treatment (e.g. electrocautery and PDT), make the clinical strategy regarding patients with early SCC complex [3].

Despite increased sensitivity, bronchoscopic staging is limited to central mucosal lesions. The size of the fiberoptic bronchoscope and the smaller segmental bronchial tubes do not allow accurate sampling to exclude the presence of microinvasive SCC in the distal segments [4]. Inaccurate staging regarding the lesion's distal border precludes local treatment with curative intent by any bronchoscopic method [1]. Therefore, invasive diagnostic and therapeutic procedures are required in such cases and, even in retrospect, the management would have been similar as already discussed.

The limitation of bronchoscopic staging for accurate assessment of lesions extending beyond the (sub-) segmental bronchi needs to be recog-

nised, as it cannot definitely exclude microinvasive cancer, especially with positive FDG-PET images.

However, due to field cancerisation, with the inherent high risk of developing subsequent lung cancer primaries [5], less invasive interventional procedures are warranted to preserve healthy lung tissue and quality of life. Surgical resection for occult SCC might be considered relatively wasteful, hence, the use of bronchoscopic treatment, such as PDT or electrocautery, which has clearly been shown to be cost-effective [6].

Limited knowledge about the natural history of SCC and the gold standard of histological classification has raised questions about the potential value of dynamic staging methods, such as AFB and FDG-PET scans, for the initial findings of "false-positive" cases [7, 8]. Due to lack of knowledge about malignant potential and probability of progression or regression of these lesions, the optimal treatment approach has not yet been established.

The increased sensitivity of current diagnostic tools is a double-edged sword, leading both to redundant medical procedures and correctly identifying the individual risk prior to advanced disease stage; however, overdiagnosis and overtreatment remain controversial issues [9].

References

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