CD56: a useful tool for the diagnosis of small cell lung carcinomas on biopsies with extensive crush artefact

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Background/Aims: The diagnosis of small cell lung carcinoma (SCLC) on bronchial biopsy is often problematical as a result of intense crush artefact. Several antibodies are now available to help in the diagnosis of SCLC and their value was assessed in this clinical situation.

Methods/Results: Twenty cases of SCLC and 10 control cases (one non-Hodgkin lymphoma, three non-small cell carcinomas, one follicular reactive hyperplasia, and five chronic non-specific inflammations) with extensive crush artefact were stained using antibodies to CD56, MNF116, thyroid transcription factor 1 (TTF-1), and CD45. All SCLCs showed strong positive staining for CD56 in 75–100% of recognisable tumour cells, even in areas where there was extensive crush artefact. Eighteen of 20 cases were positive for TTF-1 and 16 of 20 were positive for MNF116 in the tumour cells, but both of these antibodies showed little or no staining in areas of crush artefact. Control cases comprising lymphoid cells were positive for CD45 in areas of crush artefact, but all cases of SCLC were negative.

Conclusion: CD56, along with markers for cytokeratins—TTF-1, and CD45—are useful in the diagnosis of SCLC in biopsies with extensive crush artefact and can help confirm the diagnosis in cases where features are equivocal.
RESULTS

Clinical features
There were 14 male patients, aged from 52 to 81 years (mean, 67.36), and six female patients, aged from 58 to 86 years (mean, 70.2).

There were three lymph node biopsies, 16 bronchial biopsies, and one mediastinoscopy.

Immunohistochemistry
All SCLCs were strongly positive for CD56. Anti-CD56 showed a strong pattern of cytoplasmic staining in 75–100% of tumour cells, even in areas of crush artefact (figs 1, 2).

Eighteen of 20 cases were moderately to weakly positive for TTF-1 within the nuclei (fig 3), but staining was often more heterogeneous and focal than for CD56, ranging from 25% to 50% of tumour cells. Areas of crush artefact were typically negative. Sixteen of 20 cases were also moderately or weakly positive for MNF116 (fig 1B); variation of staining was seen, as for TTF-1, with crushed areas often being negative. All cases were negative for CD45. Both seromucous glands and nerve bundles in biopsies also expressed CD56, whereas surface epithelium in bronchial biopsies was negative.

In the control group, CD45 was positive in lymphoid aggregates, whereas in one case atypical cells stained for CD45 and further immunohistochemistry confirmed a non-Hodgkin B cell lymphoma. Three cases of non-small cell carcinoma were positive for MNF116, but only weakly positive for CD56, indicating that these were large cell neuroendocrine carcinomas, whereas TTF-1 was positive in one case.

DISCUSSION

The diagnosis of SCLC is most often made on small biopsies and cytological specimens. Practising pathologists may not be familiar with all its morphological guises. Frequent artefacts and difficulties in interpretation may arise from inadequate fixation, suboptimal processing, “bubbling”, crushing, squeezing, dyscohesion, and necrosis, making the diagnosis of SCLC and its distinction from other malignancies, particularly lymphoma, very difficult.

“Haematoxylin and eosin stained slides need to be interpreted along with the immunostaining to come to a firm diagnosis of small cell lung carcinoma”

Neural cell adhesion molecules are specifically expressed by neural, peripheral neuroectodermal, and neuroendocrine tissues and tumours. They belong to the immunoglobulin family of cell surface adhesion proteins involved in direct cell–cell adhesion.15–17 CD56 or neural cell adhesion molecule is also found in natural killer cells, natural killer-like T cells, myocytes, and seromucous glands.18
In our study, we tested the use of CD56 neural cell adhesion molecule as a diagnostic aid for the immunohistochemical diagnosis of SCLC. CD56 showed a strongly diffuse cytoplasmic staining in all SCLC in our series, even in badly crushed biopsy specimens. CD56 showed a uniform strong staining pattern in SCLC, whereas crushed areas were often negative for TTF-1 and MNF116. However, it is important to realise that CD56 is found in seromucous glands, nerve bundles, non-small cell carcinoma, and some lymphomas, so haematoxylin and eosin stained slides need to be interpreted along with the immunostaining to come to a firm diagnosis of SCLC. Areas of preserved morphology are still needed to be confidant of the diagnosis of small cell carcinoma.

MNF116 stains all carcinomas in the lung, but is usefully combined with CD56 and TTF-1 for distinguishing SCLC from non-Hodgkin lymphoma. Non-small cell carcinomas with CD56 staining indicate a neuroendocrine phenotype.

The use of TTF-1 in SCLC has been studied extensively, and has been used to distinguish SCLC from non-pulmonary small cell carcinomas, especially in combination with cytokeratins. In our study TTF-1 showed moderate positivity in most cases, and was a useful adjunct to CD56 in the diagnosis of SCLC.

In conclusion, we found that antibodies to CD56, MNF116, and TTF-1 made up a useful panel of immunohistochemical markers for the diagnosis of SCLC in extensively crushed biopsy specimens. This panel is extremely useful combined with histology and should be applied in difficult bronchial biopsies with crush artefact in every day practice.

**Take home messages**

- Immunohistochemistry for CD56, thyroid transcription factor 1, and CD45 is useful in the diagnosis of small cell lung carcinoma in biopsies with extensive crush artefact.
- Combined with histology, these antibodies can help confirm the diagnosis in cases where features are equivocal.

**References**


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