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LETTER TO THE EDITOR

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Bronchioloalveolar carcinoma with nodular ("morule-like") features

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Sir,

In the recent World Health Organization (WHO) classification of lung and pleural tumours [4], bronchioloalveolar carcinoma (BAC) was considered a variant of pulmonary adenocarcinoma characterised by an exclusive growth upon the wall of pre-existing alveoli ("lepidic growth"), without stromal infiltration. When these strict criteria are applied, BAC becomes a rare neoplasm. Traditionally, it is subdivided into two types: mucinous and non-mucinous, the latter being composed of type-II pneumocytes and/or Clara cells [1, 2]. We describe a non-mucinous BAC with peculiar foci of nodular growth, an apparently unreported finding in such a tumour.

The patient was a 51-year-old woman, non-smoker, presenting with dry cough and malaise. A chest X-ray revealed a diffuse opacity in the lower lobe of the left lung, which did not resolve with antibiotic therapy. A total body computed tomography (CT) scan was negative for extrapulmonary lesions. An explorative thoracotomy was performed, followed by a left pneumonectomy. Two years after surgery, the patient presented with multiple opacities in the controlateral lung, not biopsied and clinically interpreted as neoplastic recurrences. Chemotherapy was therefore administered, but the patient died of disease progression 6 years after surgery. No autopsy was performed.

Macroscopically, the lower lobe and the lingula showed an ill-defined area of parenchymal consolidation, 10 cm in diameter. Histologically, most of the lesion was composed of moderately atypical columnar cells, with overlapping nuclei, abundant eosinophilic cytoplasm and frequent apical snouting, growing along the alveolar wall (Fig. 1). In the material examined (ten blocks from the tumour), the underlying pulmonary architecture was always preserved, and no foci of stromal infiltration were present. Occasionally, multiple small intra-alveolar neoplastic nodules were observed, composed of cells morphologically identical to those lining the alveoli (Fig. 1). The nodules had a squamoid appearance, bearing some resemblance to the morules seen in endometrioid adenocarcinoma of the uterus or in well-differentiated foetal adenocarcinomas of the lung [3]: however, no obvious squamous differentiation was seen. The other lung parenchyma, the bronchial margin and the hilar lymph nodes were unremarkable.

Immunohistochemically, cytokeratin AE1/AE3, cytokeratin 7 and thyroid transcription factor (TTF)-1 were strongly expressed in the lepidic and in the nodular component of the tumour (Fig. 1), whereas chromogranin and synaptophysin were negative. Collagen IV and laminin confirmed the endo-alveolar location of the nodules (Fig. 1).

This lesion fulfils the morphologic criteria for non-mucinous BAC, being composed of neoplastic cells with an exclusive "lepidic" growth, in the absence of stromal invasion [4]. The peculiar feature of our case consists in the multiple foci of nodular growth, a finding which, to the best of our knowledge, has not been previously described in BAC. In our opinion, these foci should be considered non-invasive, based on the absence of both architectural complexity and stromal desmoplasia. It seems likely that this phenomenon represents just a

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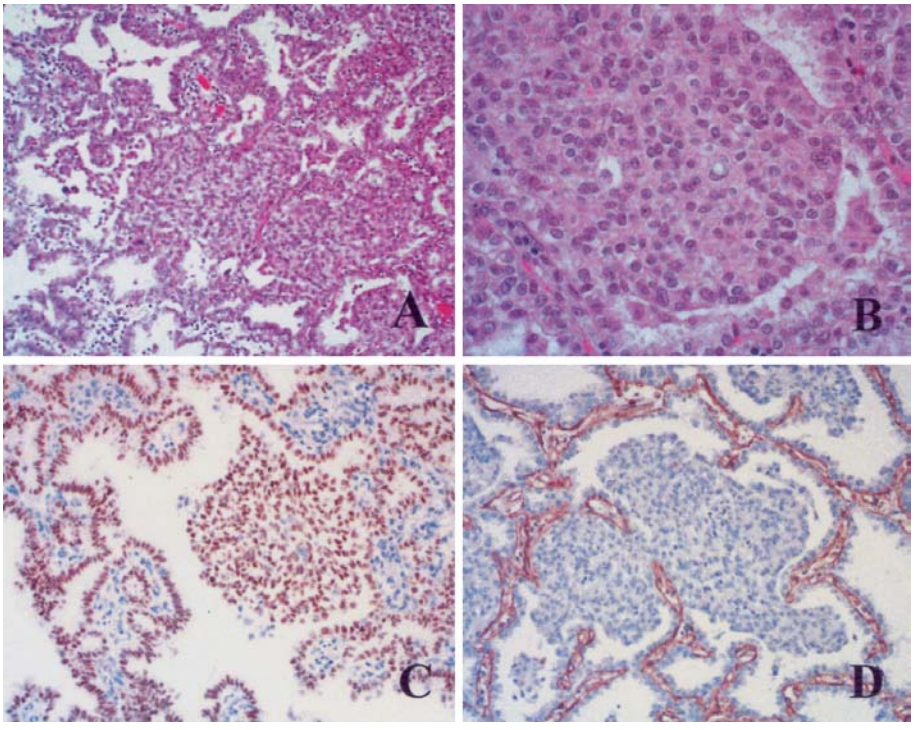

Fig. 1 **A** The tumour has the classical features of non-mucinous bronchioloalveolar carcinoma. Focally, small nodules are present (haematoxylin and eosin, ×100), **B** at high magnification, the nodular areas have a squamoid, "morule-like" appearance. The cells forming the nodules are identical to those growing along the alveolar wall (haematoxylin and eosin, ×400), **C** the neoplastic cells are immunoreactive for TTF-1, both in the nodular and in the lepidic component (avidin biotin peroxidase complex, ×200) **D** collagen IV confirms the endoalveolar location of the nodules (avidin biotin peroxidase complex, ×400)

morphologic curiosity, to be differentiated from a real infiltration and still consistent with a diagnosis of BAC.

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