



Alveolar Squamous Cell Metaplasia: Preneoplastic Lesion?

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To the Editor,

We have read with great interest the report of Song *et al.*¹ on lung squamous cell carcinomas (SCC) developing in the context of usual interstitial pneumonia. Squamous dysplastic foci were detected at the tumor periphery. However, such lesions are rarely mentioned in the medical literature, possibly because most tumors are already at an advanced stage when resected.

We would like to draw attention on microscopic lesions of the same morphological spectrum, those of squamous cell metaplasia (SCM) of the alveolar lining that we have recently identified in a zone of mild alveolar fibrosis on a lung resection specimen for a 2.3-cm large adenocarcinoma. The lesions consisted of several foci of nonkeratinizing SCM developing/in continuity with the unilayered alveolar lining (Fig. 1). When multicellular and pluristratified, the SCM lesions protruded in the underlying fibrous tissue of the alveolar wall. The zone of mild interstitial fibrosis with approximately 10 SCM foci measured 2.5–3 mm and was detected in normal lung parenchyma, at distance from the tumor. There were no well-defined honeycomb-type lesions in the resected lung. In the SCM foci, p63 was positive in basal and suprabasal cells and negative in superficial cells. There were no major cellular atypia, dyskeratosis, or keratin foci. Rare alveolar cells also showed nuclear p63 expression as well as several rounded buds (cystic or not), some reminiscent of thyroid solid cell nests. Thyroid transcription factor 1 and cytokeratin 5/6 (CK5/6) were positive throughout the whole thickness of SCM foci (Fig. 1). Pneumocyte bi-/multinucleation was also seen as well as lympho-

cytic foci, one of them at contact to a SCM focus.

Here, we report SCM of the alveolar unilayered epithelium. Multicellular, stratified SCM foci were detected on the hematoxylin and eosin stained slide while only paucicellular foci were detected on the immunohistochemistry slides for p63 or CK5/6. The precise origin of these lesions is difficult to identify, p63⁺CK5⁺ cells being reported in alveolar regeneration of chronic pulmonary fibrosis, diffuse alveolar damage, acute/usual interstitial pneumonia or influenza infection.²⁻⁶ In the present case, the presence of lymphocytic foci may suggest a viral origin. However, given the fact that SCCs may also develop in the peripheral lung tissue, a putative preneoplastic potential can be proposed for alveolar SCM.⁷

In conclusion, SCM may develop from the unilayered alveolar lining. The presence of several SCM foci may constitute a preneoplastic background for peripheral squamous cell carcinomas or squamous-type component in adenocarcinomas.

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Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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REFERENCES

1. Song DH, Choi IH, Ha SY, *et al.* Usual interstitial pneumonia with

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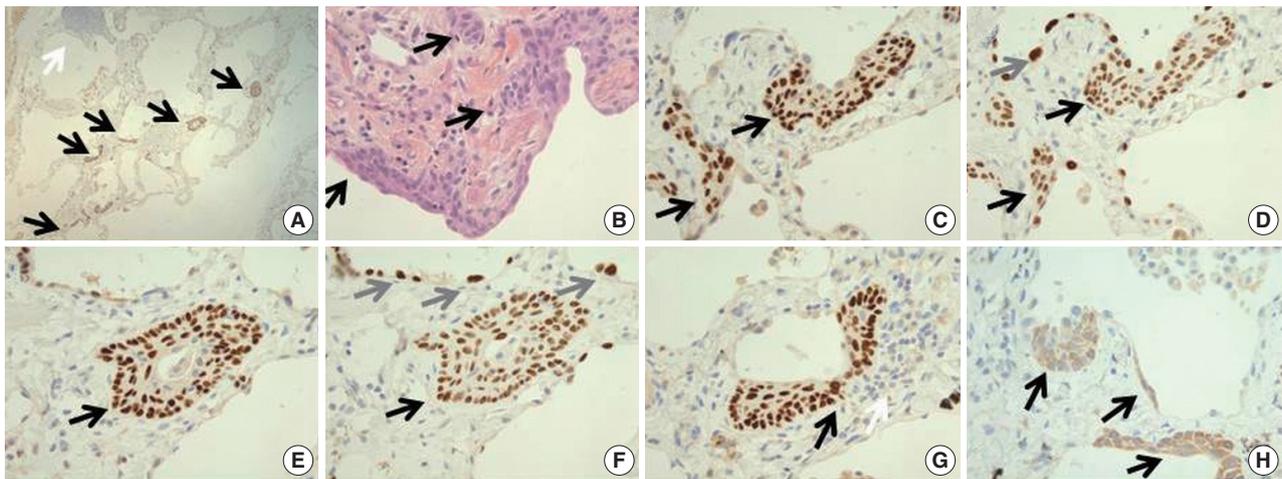


Fig. 1. (A) The lung parenchyma shows a zone of multiple (approximately 10) p63-positive squamous cell metaplasia (SCM) foci (black arrows for SCM foci, white arrow for lymphocytic focus). (B) On the hematoxylin and eosin stained slide, the lesions consist in a multilayered epithelium composed of basal cuboidal cells, suprabasal cells and superficial spindle-appearing cells (black arrows). (C) The basal and suprabasal cells are immunoreactive for p63 while superficial cells are negative (black arrows for p63⁺ cells). (D) Thyroid transcription factor 1 is expressed by the cells throughout the entire thickness of the lesion, in both p63⁺ and p63⁻ cells (black arrows for SCM foci, gray arrow for atypical pneumocyte nuclei). (E, F) A cystic cellular bud (reminiscent of thyroid solid cell nests) is detected in an alveolar septum (black arrows for the SCM bud, gray arrows for binucleated pneumocytes). (G) One of the SCM foci develop at close contact to the lymphocytic infiltrate (p63 immunohistochemistry, black arrow for the SCM focus, white arrow for the lymphocytic infiltrate). To note would be the presence of a binucleation with immunoreactivity to p63 in the SCM focus. (H) Cytokeratin 5/6 is expressed in spindle-appearing cells lining the alveoli and in the SCM foci (black arrows for cyokeratin 5/6⁺ cells).

- lung cancer: clinicopathological analysis of 43 cases. *Korean J Pathol* 2014; 48: 10-6.
- Meyer EC, Liebow AA. Relationship of interstitial pneumonia honeycombing and atypical epithelial proliferation to cancer of the lung. *Cancer* 1965; 18: 322-51.
 - Rosai J. Rosai and Ackerman's surgical pathology. 10th ed. Philadelphia: Elsevier Mosby, 2011.
 - Chilosi M, Poletti V, Murer B, *et al.* Abnormal re-epithelialization and lung remodeling in idiopathic pulmonary fibrosis: the role of deltaN-p63. *Lab Invest* 2002; 82: 1335-45.
 - Zuo W, Zhang T, Wu DZ, *et al.* p63(+)Krt5(+) distal airway stem cells are essential for lung regeneration. *Nature* 2015; 517: 616-20.
 - Kato E, Takayanagi N, Takaku Y, *et al.* Incidence and predictive factors of lung cancer in patients with idiopathic pulmonary fibrosis. *ERJ Open Res* 2018; 4: 00111-2016.
 - Krimsky W, Mugañlinskaya N, Sarkar S, *et al.* The changing anatomic position of squamous cell carcinoma of the lung: a new conundrum. *J Community Hosp Intern Med Perspect* 2016; 6: 33299.