

## Primary Lung Adenocarcinoma With Enteric Morphology Associated With Primary Colon Adenocarcinoma<sup>☆</sup>



### *Adenocarcinoma primario de pulmón con morfología entérica asociado a un adenocarcinoma primario de colon*

To the Editor,

Primary lung adenocarcinoma with enteric morphology is an extremely rare variant of primary invasive adenocarcinoma. It is characterized by predominant colorectal-like components (>50%) and the tumor cells must be negative for all immunohistochemical enteric differentiation markers, such as CK20, CDX2, and mucin 2 (MUC2).<sup>1</sup>

We report an exceptional case of a lung adenocarcinoma with enteric morphology associated with a primary colon adenocarcinoma. To our knowledge, no similar case has been reported in the literature.

A 50-year-old man presented 2 months previously with severe anemia. Colonoscopy revealed moderately differentiated colon adenocarcinoma of the right colon with positive cytokeratine CK 7 and CK 20 and negative TTF-1 (thyroid transcription factor 1) on immunohistochemistry. Surgical resection of the digestive tumor, classified as T3N0M0, was performed through right colectomy and ileo-transverse side-to-side anastomosis. Simultaneously, in the lung, chest computed tomography revealed a 3.5 cm mass in the right lower lobe. Scan-guided biopsy showed a primitive lung adenocarcinoma with positive TTF-1 in the right lower lobe. The lung tumor was classified as T2N0M0. A lower right lobectomy with lymphadenectomy was performed successfully.

Morphologically, the lung tumor was described as whitish or gray-white with some focal areas of hemorrhage and necrosis. Histologically, prominent components of colorectal carcinoma-like glands with typical papillary structures were observed (Fig. 1a, b). On immunohistochemistry, anti-CK 7 and TTF-1 were positive. Anti-CK20 antibody, MUC2 and CDX2 were negative (Fig. 1c). Resected lymph nodes were negative for malignancy.

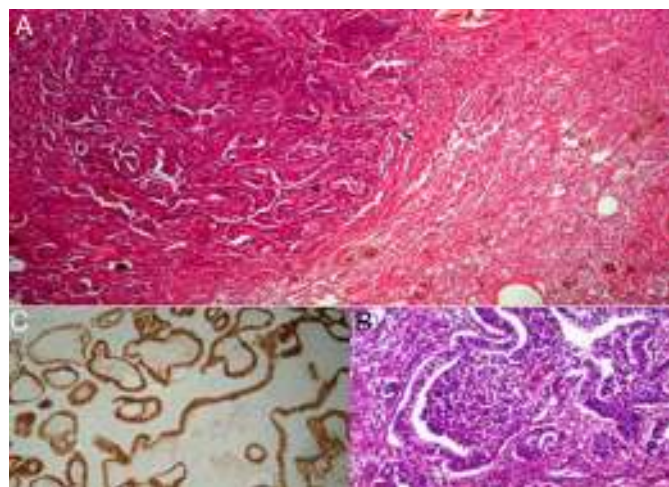
The patient did not receive adjuvant therapy and progress was uneventful until the ninth month, when he presented with isolated sternal metastasis from the surgically resected lung adenocarcinoma. Scheduled chemotherapy was reasonably well tolerated and toxicity was minimal. He continues to progress well after 6 months.

When lung tumor cells are negative for any intestinal protein markers, the entity is called “lung adenocarcinoma with enteric morphology”.

Other morphological types, including the lepidic pattern, can suggest a differential diagnosis of colon cancer.<sup>1,2</sup>

On immunohistochemistry, anti-CK7 is generally positive. TTF-1 is positive in 50% of cases. Enteric differentiation is confirmed by positivity of at least 1 of the following markers: CK20, CDX2 and MUC2. If these 3 markers are negative, morphology is considered enteric. Other markers such as villin can be useful. Therefore, no EGFR, K-Ras and ALK gene mutation has ever been reported, in contrast to colon adenocarcinoma and other subtypes of lung adenocarcinoma.<sup>3,4</sup>

In our particular case, the first challenge was to differentiate the primary lung adenocarcinoma with enteric morphology from



**Fig. 1.** (A) Adenocarcinomatous proliferation of lung parenchyma (Gx10). (B) Pathological view showing Lieberkuhnien glands (Gx20). (C) Pathological view showing positive anti-CK7 (Gx20).

colon adenocarcinoma metastasis. Meticulous, repeated examinations were performed and second opinions were obtained by the pathology team. The second challenge was the therapeutic strategy or the use of chemotherapy in the postoperative course.

This association causes problems for diagnosing lung adenocarcinoma with enteric morphology, especially in cases where the immunohistochemical study would be superimposed on that of pulmonary metastasis of colon adenocarcinoma, and offers opportunities for molecular diagnostics, such as EGFR mutation.

## References

- Hatanaka K, Tsuta K, Watanabe K, Sugino K, Uekusa T. Primary pulmonary adenocarcinoma with enteric differentiation resembling metastatic colorectal carcinoma: a report of the second case negative for cytokeratin 7. *Pathol Res Pract.* 2011;207:188–91.
- Lin D, Zhao Y, Li H, Xing X. Pulmonary enteric adenocarcinoma with villin brush border immunoreactivity: a case report and literature review. *J Thorac Dis.* 2013;5:E17–20.
- Zhang Y, Sun Y, Pan Y, Li C, Shen L, Li Y, et al. Frequency of driver mutations in lung adenocarcinoma from female never-smokers varies with histologic subtypes and age at diagnosis. *Clin Cancer Res.* 2012;18:1947–53.
- Sun PL, Seol H, Lee HJ, Yoo SB, Kim H, Xu X, et al. High incidence of EGFR mutations in Korean men smokers with no intratumoral heterogeneity of lung adenocarcinomas: correlation with histologic subtypes, EGFR/TTF-1 expressions, and clinical features. *J Thorac Oncol.* 2012;7:323–30.

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