Human Pathology: Case Reports xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Human Pathology: Case Reports

journal homepage: http://www.humanpathologycasereports.com

Case Report

Late-onset solitary metastasis of urothelial bladder carcinoma mimicking primary lung adenocarcinoma with a lepidic component

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ARTICLE INFO

Article history:
Received 27 May 2016
Received in revised form 26 August 2016
Accepted 31 August 2016
Available online xxxx

ABSTRACT

1. Introduction

Pulmonary oligometastases are often resected for therapeutic purposes [1]. The differential diagnosis between primary and secondary malignancies in the lung is generally straightforward, with the exception of squamous cell carcinomas, which may be confused with head and neck metastases [2], and rare multicentric primary lung tumors that mimic metastatic disease [3].

A single case of delayed metastasis secondary to ureteral urothelial carcinoma has been reported [4]. We report a similar case of urothelial carcinoma of the bladder that mimicked a primary tumor, with the confounding presence of adjacent adenocarcinoma-in situ. To our knowledge this is the first such reported case.

2. Case report

A 61 year-old male with a significant smoking history is found on CT imaging to have a 1.4 × 1.0 cm lobular mass in the left upper lobe suspicious for primary lung neoplasm. The patient underwent surgery for a primary lung tumor, including wedge resection followed by completion lobectomy and mediastinal lymph node dissection.

Five years prior, he had undergone adjuvant chemotherapy and radical cystoprostatectomy for high grade invasive urothelial carcinoma, stage pT3b pN0. Lymphovascular invasion was present. Margins were uninvolved, and the cancer was considered cured.

On gross examination, the wedge resection specimen (7.9 × 3.2 × 1.4 cm) showed a firm heterogeneous tan-brown nodule measuring 1.5 cm in greatest dimension and grossly abutting the pleura. An intraoperative frozen section was performed and diagnosed as poorly differentiated carcinoma, favor urothelial. Postoperative pathologic examination revealed the mass to be a poorly differentiated carcinoma (blue insert in Fig. 1) with an adjacent 2 mm focus of adenocarcinoma in situ (red insert in Fig. 1). While the 2 mm lesion is small enough to meet criteria for the diagnosis of atypical adenomatous hyperplasia, the atypia and nuclear pleomorphism of the cells in the 2 mm lesion were more consistent with the morphology of adenocarcinoma in situ. The poorly differentiated carcinoma was negative for TTF-1, napsin, CK7, p40, p63, and uroplakin, while expressing positivity for GATA-3. The 2 mm focus of adenocarcinoma in situ was positive for TTF-1 and CK7, and negative for GATA-3 (Figs. 2 and 3).

3. Discussion

Pulmonary metastasis is seen in 20% of patients with recurrent urothelial carcinoma of the bladder [5]. Approximately 80%–90% are diagnosed in the first 3 years after diagnosis of the primary tumor. The majority occur at the time of cystectomy or in the first 24 months, at a median interval of 16 months [6,7]. Risk factors for systemic recurrence include a pathologic stage of pT3 or pT4, and the presence of positive margins and lymph node metastases [6].

The final diagnosis of the poorly differentiated carcinoma was largely based on GATA-3 positivity. Reports have shown GATA-3 to be a highly sensitive (>80%) marker of urothelial carcinomas, however, rare poorly differentiated adenocarcinomas of the lung have demonstrated GATA-3 positivity in 40–60% of cells [8].

Only 25% of metastatic urothelial carcinomas occur as single lung nodules [9]. Because of their infrequent presentation as single lesions, urothelial carcinomas represent only 1% of surgically resected pulmonary oligometastases of all primary sites [10]. However, the lung is the most common site for oligometastases arising from the bladder

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http://dx.doi.org/10.1016/j.ehpc.2016.08.008

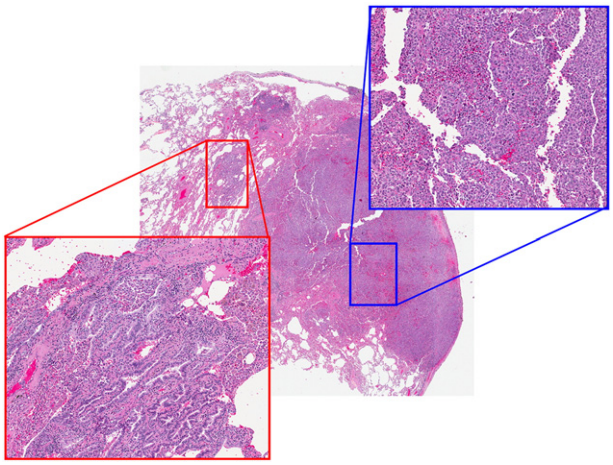

Fig. 1. Metastatic urothelial carcinoma adjacent to lung adenocarcinoma in situ (Hematoxylin and eosin stain).

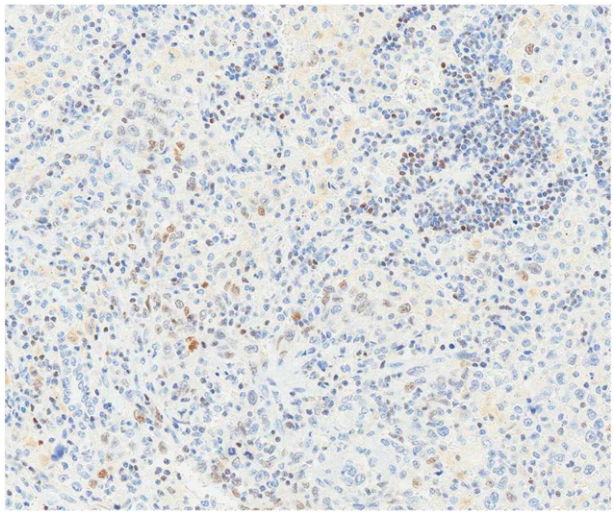

Fig. 3. Left: Positive GATA-3 immunostaining in both carcinoma cells (left) and adjacent tumor infiltrating lymphocytes (right).

urothelium [9]. Late onset pulmonary metastases are exceptionally rare, and have been reported for urothelial carcinomas of the upper urothelial tract as single case reports [4].

In this report, we describe the evaluation of a patient with a distant history of bladder carcinoma with a new lung mass, ultimately consistent with metastatic growth of urothelial carcinoma, coexisting with an adjacent incidental microscopic focus of primary lung adenocarcinoma in situ. Since metastatic bladder cancer was initially not strongly considered in the differential diagnosis, the presence of the minute focus of pulmonary adenocarcinoma in situ could lead to erroneously diagnosing the entire lesion as primary lung adenocarcinoma. This case raises two issues of practical and academic significance: (a) the importance of immunohistochemistry in the diagnosis of lung tumors, and (b) the possibility of concurrent neoplasms of different origins in adjacent/collision sites. The latter possibility has been previously reported in lung tumors [11]. Poorly differentiated carcinomas of the lung can also be an especial challenge to diagnose on frozen section regarding the distinction between primary and metastatic lesions, and findings in such cases should be communicated to the surgeon to convey the limitations of frozen section evaluation [12]. A high index of suspicion for pulmonary metastatic involvement should therefore be maintained, even in the presence of adjacent pulmonary carcinoma in situ.

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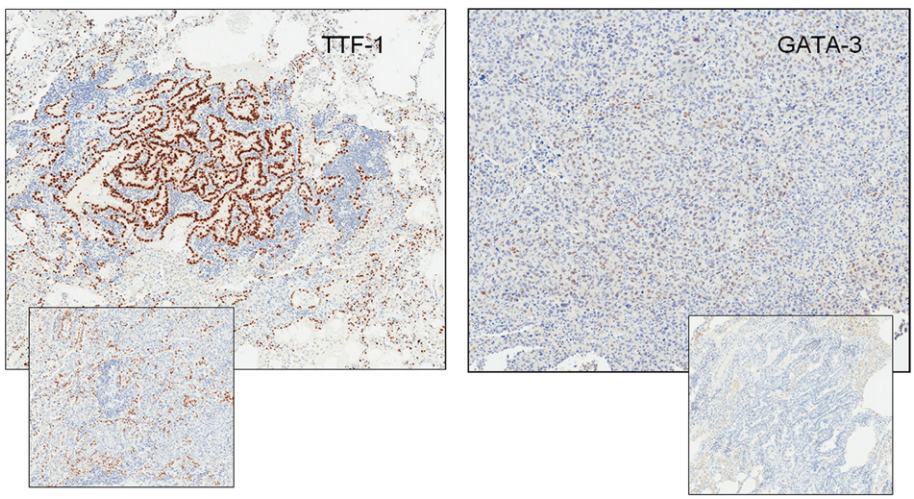

Fig. 2. Left: Positive TTF-1 immunostaining in lung adenocarcinoma in situ (Insert: TTF-1 negative metastatic urothelial carcinoma; entrapped benign lung is showing positivity); Right: Positive GATA-3 in metastatic urothelial carcinoma (Insert: GATA-3 negative lung adenocarcinoma in situ).

Please cite this article as: S. Shyu, et al., Late-onset solitary metastasis of urothelial bladder c..., Human Path Case Reports (2016), http://dx.doi.org/10.1016/j.ehpc.2016.08.008

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