

# Urinary Bladder Metastasis Originating from Lung Adenocarcinoma

## A Case Definitively Diagnosed by Immunohistochemistry

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Received May 2010  
Accepted June 2010

**Keywords:** urinary bladder, adenocarcinoma of lung, neoplasm metastasis, immunohistochemistry

### INTRODUCTION

Primary adenocarcinomas of the urinary bladder, including urachal carcinoma, account for approximately 0.5% to 2% of all the primary bladder epithelial malignancies.<sup>(1)</sup> However, secondary involvement of the bladder by metastatic spread or direct extension from adenocarcinomas arising in other organs can also occur. The morphological and histopathological similarities can sometimes blur the distinctions between primary and secondary lesions, especially in biopsy specimens.<sup>(2)</sup>

The immunohistochemistry of thyroid transcription factor 1 (TTF-1) is useful for determining primary sites of metastatic adenocarcinoma. Thyroid transcription factor 1 is expressed in most primary and metastatic sites of the lung adenocarcinomas. By contrast, expressions of TTF-1 in adenocarcinomas other than lung adenocarcinomas and their metastatic sites are rare.<sup>(3)</sup> Primary bladder adenocarcinomas expressing TTF-1 have not been reported.

Recently, the immunohistochemical panel of TTF-1/cytokeratin 7 (CK7)/cytokeratin 20 (CK20) is generally and reliably used for establishing a lung adenocarcinoma origin of distant sources of metastases, where the primary adenocarcinomas can arise.<sup>(4)</sup> However, to the best of our knowledge, differentiation between the bladder and lung adenocarcinomas using this panel has not been reported so far.

### CASE REPORT

A 78-year-old man underwent video-assisted thoracoscopic surgery (VATS)

lobectomy in July 2006 for early-stage lung cancer (Figure 1). Histopathological examination showed a mixed subtype adenocarcinoma staged as IA, pT1N0M0. Subsequently, his disease relapsed locally and metastasized to hilar lymph nodes. He was administered induction chemotherapy consisting of carboplatin and docetaxel, followed by gemcitabine and vinorelbine, and the molecular-targeted agent (erlotinib).

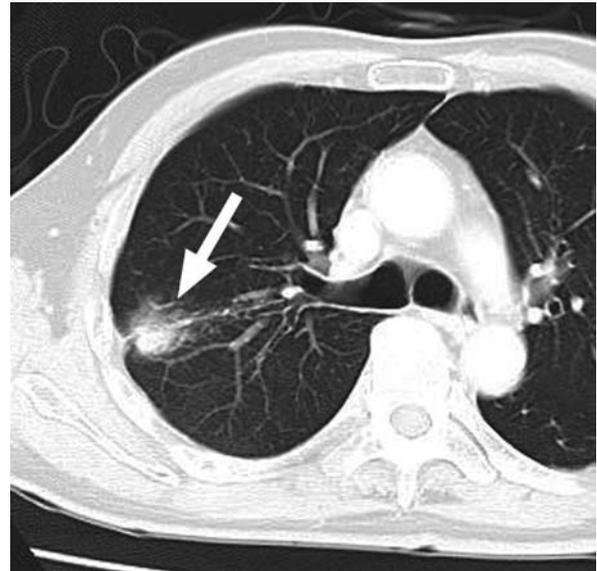
In May 2008, the patient was referred to the department of urology for assessment of gross hematuria. Intravenous urography revealed a vesical stone 22 mm in diameter that was suspected to be the cause of the patient's urinary symptoms. A vesicolithotripsy was subsequently performed. During the operation, a 3-mm diameter papillary tumor on the right lateral wall of the bladder was incidentally observed (Figure 2). Hence, we also performed a cold cup biopsy of the bladder tumor.

The tumor was histopathologically diagnosed as an adenocarcinoma located beneath the intact urothelial epithelium without the bladder muscle invasion. Immunohistochemical examination demonstrated tumor cells positive for TTF-1 and CK7 and negative for CK20 (Figure 3). Because of the clinical history and the identical immunohistochemical expression pattern in the lung and bladder adenocarcinomas, the bladder tumor was diagnosed as a metastasis of the lung adenocarcinoma.

After the cold cup biopsy, no recurrence of the bladder tumor was detected by ultrasonography. However, the primary lung cancer progressed, and the patient died five months after the cold cup biopsy.

## DISCUSSION

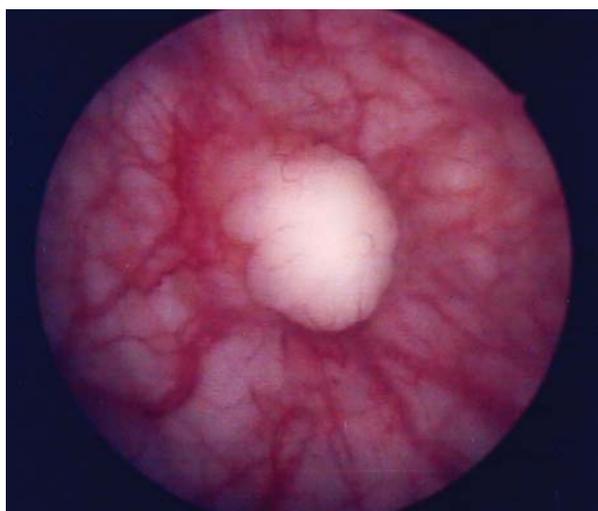
Lung cancer is the most frequently occurring form of cancer in the world, and lung adenocarcinoma is the most common cell type representing approximately 50% of all lung cancer cases.<sup>(5)</sup> Whereas lung cancer is a common form of cancer,



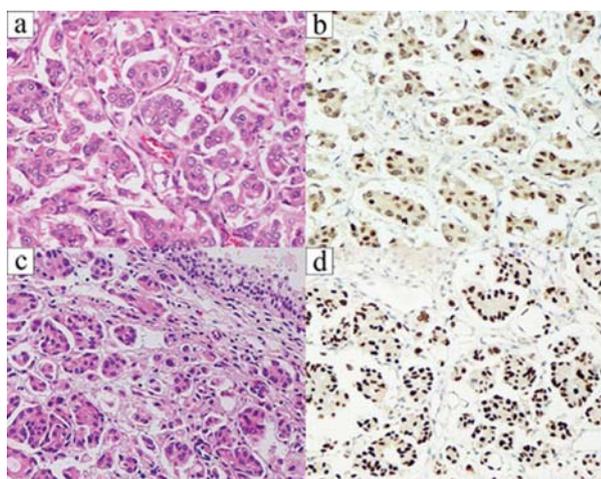
**Figure 1.** Computed tomography scan of the chest performed prior to lobectomy revealed a primary lung adenocarcinoma with a cross section of 20 × 12 mm in the upper lobe of the right lung (arrow).

bladder metastasis from the lung cancer, particularly from lung adenocarcinoma, is uncommon. In a computed tomography-based study examining 72 patients with metastatic non-small cell lung cancer, no urinary tract metastases were detected.<sup>(6)</sup> In an autopsy-based study of 148 patients with distant metastases of lung cancer, only one (0.7%) case of bladder metastasis was detected, in which the cell type was unknown.<sup>(7)</sup> In a study of 282 secondary neoplasms in the bladder, representing 2.3% of all malignant bladder tumors, eight (2.8%) cases originated from lung cancer (four, squamous cell carcinomas; one, adenocarcinoma; and one, small cell carcinoma).<sup>(2)</sup> However, lung adenocarcinoma-originated tumor was found in only one (0.4%) of the 282 patients, and the process for diagnosis was not mentioned in this study. In individual case reports, only one Spanish article has described bladder metastasis of lung adenocarcinoma.<sup>(8)</sup>

In the absence of immunohistochemistry, a pathological differential diagnosis of primary or secondary bladder adenocarcinomas is difficult. The similar features of primary lung and secondary bladder adenocarcinomas complicate the ability



**Figure 2.** Gross appearance of the urinary bladder tumor during the cold cup biopsy.



**Figure 3.** Histopathological findings. (a, b) Primary lung adenocarcinoma. Immunohistochemically positive for thyroid transcription factor 1 (TTF-1) (a: Hematoxylin and Eosin,  $\times 100$ ; b: TTF-1,  $\times 100$ ). (c, d) Metastatic site in the urinary bladder. The adenocarcinoma is visible under an intact urothelial epithelium with Hematoxylin and Eosin staining. (c: Hematoxylin and Eosin,  $\times 100$ ; d: TTF-1,  $\times 100$ ).

to differentiate between these two lesion types, especially in biopsy specimens.<sup>(2)</sup> In the present case, clinical history and immunohistochemical staining for TTF-1, CK7, and CK20 confirmed the diagnosis of bladder metastasis originating from the previous lung adenocarcinoma. The intact urothelial epithelium overlying the bladder tumor, which suggests that a tumor is a secondary lesion, also contributed to the differential diagnosis.<sup>(2)</sup>

In the present case, lung adenocarcinoma had already relapsed and the distinctive diagnosis of the bladder tumor of the pulmonary origin regrettably did not affect subsequent survival. However, considering the high prevalence of lung adenocarcinomas and the knowledge that bladder adenocarcinomas represent 0.5% to 2% of all primary bladder epithelial malignancies, urologists and thoracic surgeons will potentially encounter patients with both bladder adenocarcinomas and likely localized lung adenocarcinomas. For such patients, differential diagnoses for determining whether the bladder adenocarcinoma is primary or metastatic are essential to treat them optimally. Therefore, the immunohistochemical panel of TTF1/CK7/CK20, which is considered as a suitable method for distinguishing between primary and secondary bladder adenocarcinomas, is clinically significant.

### CONFLICT OF INTEREST

None declared.

### REFERENCES

1. Thomas DG, Ward AM, Williams JL. A study of 52 cases of adenocarcinoma of the bladder. *Br J Urol.* 1971;43:4-15.
2. Bates AW, Baithun SI. Secondary neoplasms of the bladder are histological mimics of nontransitional cell primary tumours: clinicopathological and histological features of 282 cases. *Histopathology.* 2000;36:32-40.
3. Lau SK, Luthringer DJ, Eisen RN. Thyroid transcription factor-1: a review. *Appl Immunohistochem Mol Morphol.* 2002;10:97-102.
4. Oien KA. Pathologic evaluation of unknown primary cancer. *Semin Oncol.* 2009;36:8-37.
5. Ginsberg MS, Grewal RK, Heelan RT. Lung cancer. *Radiol Clin North Am.* 2007;45:21-43.
6. Quint LE, Tummala S, Brisson LJ, et al. Distribution of distant metastases from newly diagnosed non-small cell lung cancer. *Ann Thorac Surg.* 1996;62:246-50.
7. Abrams HL, Spiro R, Goldstein N. Metastases in carcinoma; analysis of 1000 autopsied cases. *Cancer.* 1950;3:74-85.
8. Martin-Marquina Aspiunza A, Diez-Caballero Alonso F, Rodriguez-Rubio Cortadellas FI, et al. [Bladder metastasis of lung adenocarcinoma]. *Actas Urol Esp.* 1997;21:406-8.