

# Urinary bladder metastasis from lung adenocarcinoma: A rare cause of hematuria

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## Abstract

We presented an unusual case of hematuria caused by a solitary bladder metastasis from lung adenocarcinoma. A confident diagnosis of secondary adenocarcinoma of the bladder was made by clinical suspicion based on patient's past history, careful examination of tumor morphology, and a directed panel (cytokeratin [CK] 7/CK20/thyroid transcription factor 1) of immunohistochemistry. We sought, through sharing our experience in the investigative and diagnostic process, to contribute to the better understanding of this unusual cause of hematuria.

**Key Words:** Adenocarcinoma, bladder metastasis, hematuria

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## INTRODUCTION

Primary adenocarcinoma of the urinary bladder is uncommon, it accounted for 0.5-2% of all primary epithelial malignancies arising from the bladder.<sup>[1]</sup> Secondary neoplasm of the bladder is a rarity, comprising 2.3% of all malignant bladder tumors.<sup>[2]</sup> Secondary adenocarcinoma of the bladder is even rarer, consisting of only 1.9% of all malignant bladder tumors in a review evaluating 6,289 cases of bladder tumors.<sup>[2]</sup> Due to its paucity and limited clinical experience, a finding of adenocarcinoma of the bladder entailed a diagnostic challenge in most patients.

We herein report an unusual case of hematuria, caused by a solitary bladder metastasis from lung adenocarcinoma. A confident diagnosis of secondary adenocarcinoma of the bladder was made based on patient's past medical history,

histological morphology of an intact transitional epithelium, and a directed panel of immunohistochemistry. We sought, through sharing our experience in the investigative and diagnostic process, to contribute to the better understanding of this unusual cause of hematuria.

## CASE REPORT

### Presenting history

A 53-year-old man had history of adenocarcinoma of the lung with liver metastases. He was found to have brain metastasis when he presented with intra-cranial bleeding, which necessitated an excision of the solitary brain metastasis.

He presented with hematuria 1 year after the initial diagnosis of his lung cancer. Initial investigations with plain radiographs and mid-stream urine sampling were unrevealing.

### Urine cytology

His urine cytology demonstrated suspicious cells with marked variation of nuclear size, irregularity of nuclear outline, and abnormal chromatin pattern [Figure 1].

### Imaging

He underwent a computed tomographic urography, which revealed a 2.7 cm contrast-enhancing posterior bladder wall

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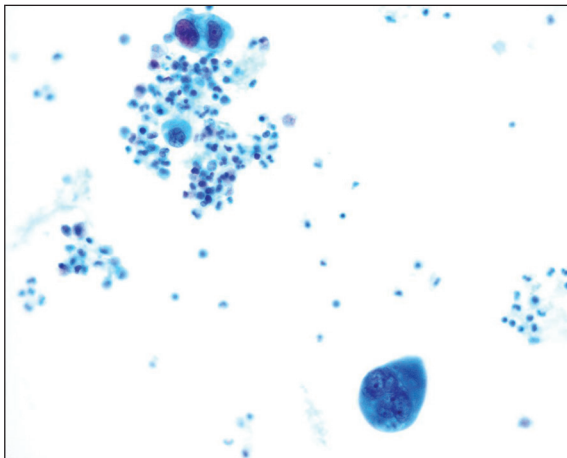
mass with transmural involvement. The urogram phase revealed its fungative morphology [Figure 2].

**Flexible cystoscopy and transurethral resection**

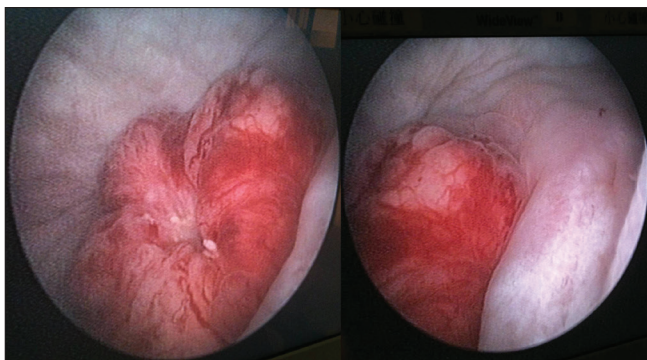
Our patient underwent a flexible cystoscopy, which revealed a 3 cm sessile vascular growth with rugged edges and a central crater at the left lateral wall. The surrounding mucosa appeared distorted and elevated, which was suggestive of a growth beneath the intact bladder mucosa [Figure 3]. Biopsy of the tumor mass revealed adenocarcinoma, favored lung primary. A transurethral resection of bladder tumor was performed to alleviate his hematuria.

**Histological appearance**

Figure 4 shows the histological appearance of the brain metastasis. The tumor demonstrated true papillae with fibrovascular cores, features which were diagnostic of adenocarcinoma. The tumor was also diffusely and strongly positive for thyroid transcription factor 1 (TTF1) (mouse monoclonal, 1:100, Dako Denmark), a marker which was positive in majority of primary lung adenocarcinoma.<sup>[3]</sup>



**Figure 1:** Suspicious urine cytology: Papanicolaou stain, x600



**Figure 3:** Left: Sessile vascular tumor. Right: Distorted and elevated surrounding mucosa

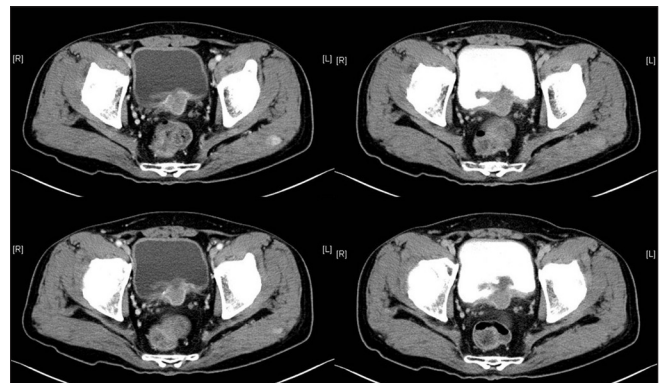
Figure 5 shows the histological appearance of the bladder tumor. The tumor was morphologically reminiscent of the brain metastasis. The overlying transitional cell epithelium was intact and benign, whereas the underlying detrusor muscle was extensively infiltrated by the tumor. A directed panel of immunohistochemistry (Figure 6) revealed the tumor cells showed a cytokeratin 7 (CK7) (mouse anti-human, 1:300, Dako Denmark) positive, CK20 (mouse anti-human, 1:100, Dako Denmark) negative and TTF1 positive phenotype, which was most compatible with adenocarcinoma of lung primary.<sup>[3]</sup> It was of note that the residual transitional epithelium retained its CK20 positive property.

**Patient outcome**

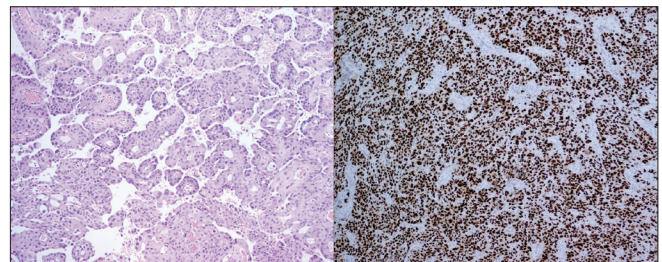
Our patient had external-beam radiotherapy for his scalp metastasis but decided not for further systemic therapy for his lung cancer. There was no recurrence of gross hematuria as reported by the patient up to the time when this article was prepared (3 months post-transurethral resection). Our transurethral resection achieved its palliative role for the patient.

**DISCUSSION**

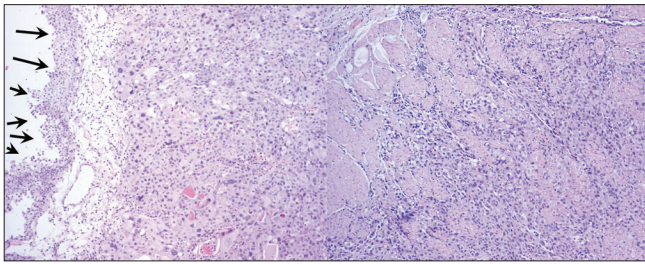
According to the Hong Kong Cancer Registry, lung cancer ranked first in both incidence rate (62.6/100,000 persons) and cancer-specific mortality in 2009. From year 1990 onwards,



**Figure 2:** Computed tomography urogram. Left: Contrast phase. Right: Urogram phase



**Figure 4:** Brain metastasis. Left: Features diagnostic of adenocarcinoma. Right: Thyroid transcription factor 1 positivity



**Figure 5:** Bladder tumor. Left: Mucosal involvement by tumor with an intact overlying transitional cell epithelium (arrows). Right: Detrusor muscle infiltration

adenocarcinoma was the commonest cell type among all lung carcinoma in Hong Kong. Despite its prevalence, bladder metastasis from lung primary was a rarity. According to a large autopsy study, bladder metastasis was observed in 0.16% of all cases of lung cancer with metastasis.<sup>[4]</sup>

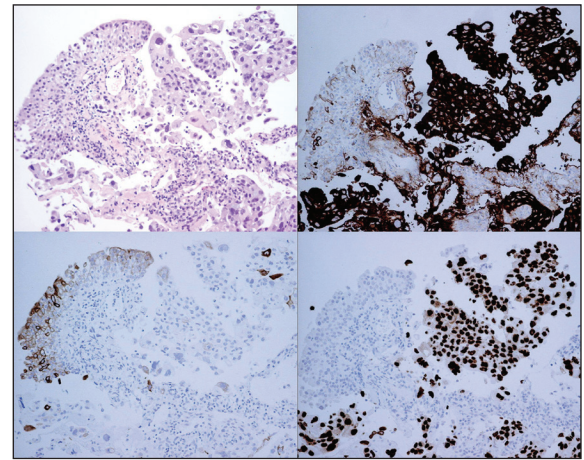
Adenocarcinoma of the urinary bladder was an uncommon encounter. Primary adenocarcinoma accounted for 0.5-2% of all primary bladder malignancy;<sup>[1]</sup> clinical experience on secondary adenocarcinoma from lung origin came no better than a handful of case reports.<sup>[5-9]</sup> Due to the rarity of both conditions, a finding of adenocarcinoma of the urinary bladder often entailed a diagnostic challenge.

The definitive diagnosis of our patient was less of a challenge due to his obvious background of lung cancer. In general, however, the establishment of an accurate diagnosis depended on three important factors: clinical suspicion based on patient's past history, careful examination of tumor morphology, and a directed panel of immunohistochemistry.

A thorough enquiry on patient's past medical condition was fundamental in arriving an accurate diagnosis. It helped clinicians to form proper clinical suspicion and spared the pathologists from making futile ventures in the quest for primary site.

Careful examination of the tumor morphology contributed to the correct prediction of the site of origin. For metastatic adenocarcinoma, morphology alone enabled prediction of the correct primary site as a single choice in 26% of cases.<sup>[10]</sup> Notwithstanding, lung adenocarcinoma had a range of appearances and was notoriously pleomorphic.

In terms of immunohistochemistry, CK7 and CK20 were the most widely used and reviewed markers for prediction of primary site in metastatic adenocarcinoma.<sup>[3]</sup> With its high sensitivity and 98% specificity (in the context of adenocarcinoma), the addition of TTF1 would confidently determine whether the adenocarcinoma was of lung origin.<sup>[3]</sup> In combination, a panel of CK7/CK20/TTF1 would



**Figure 6:** Immunohistochemistry of bladder tumor. Top left: Routine H and E stain. Top right: Cytokeratin 7 (CK7) +ve. Bottom right: CK20 -ve. Bottom left: Thyroid transcription factor 1 +ve

be reasonably sensitive and highly specific for inferring an adenocarcinoma of lung origin.<sup>[3]</sup>

The route of metastasis of bladder secondaries was probably hematogenous, this was evidenced by earlier case reports,<sup>[6,9]</sup> which showed submucosal tumor growth with intact mucosa. As the metastasis arose from submucosal layer, hematuria would only be appreciable when the mucosa was infiltrated. This contributed to its rarity in clinical encounter, in addition to the fact that it was rare in autopsy studies.<sup>[4]</sup>

Intra-vesical location of bladder secondaries was also evaluated in an autopsy study.<sup>[2]</sup> The commonest sites of involvement included anterior/lateral/posterior walls, trigone and bladder neck. Two case reports<sup>[7,9]</sup> revealed bladder metastasis from lung primary at the bladder trigone, causing upstream obstructions.

To the best of our knowledge, there were five published case reports from 1997 to 2012,<sup>[5-9]</sup> and our report would probably be the sixth in the literature. We summarized and compared the four case reports published in English and that of our patient [Table I]. The presence of bladder metastasis inevitably implied a wide-spread metastatic disease, the survival according to these case reports ranged from 5 to 9 months. Our transurethral resection achieved its palliative role to provide symptomatic relief for our patient.

We sought, through sharing our experience in the investigative and diagnostic process, to contribute to the better understanding of this unusual cause of hematuria.

## CONCLUSION

We presented an unusual case of hematuria caused by a solitary bladder metastasis from lung adenocarcinoma. A confident

**Table 1: Case reports of bladder metastasis from lung adenocarcinoma**

Case reports	Presenting symptom	Cystoscopic appearance	Treatment	Outcome
Lan <i>et al.</i> <sup>[6]</sup> (Taiwan)	Acute renal failure with bilateral hydronephroses	Persistent mucosal fold on a distended bladder	Palliative chemotherapy with gemcitabine and cisplatin	Died 8 months after diagnosis
Karatas <i>et al.</i> <sup>[7]</sup> (Turkey)	Acute renal failure with bilateral hydronephroses	Solid lesions on bladder wall	Palliative chemotherapy with gemcitabine and carboplatin	Died 9 months after diagnosis
Shirakawa <i>et al.</i> <sup>[8]</sup> (Japan)	Gross hematuria	3 mm papillary growth at right lateral wall	Cystoscopic biopsy	No recurrence of hematuria, died 5 months after diagnosis
Karle <i>et al.</i> <sup>[9]</sup> (USA)	Left hydronephrosis	Erythematous and bullous change of left ureteric orifice	Palliative chemotherapy with gemcitabine and carboplatin	Died 5 months after diagnosis
Our patient	Gross hematuria	3 cm sessile vascular growth with rugged edges and a central crater at left lateral wall	Transurethral resection	No recurrence of hematuria

diagnosis of secondary adenocarcinoma of the bladder was made by clinical suspicion based on patient's past history, careful examination of tumor morphology, and a directed panel (CK7/CK20/TTF1) of immunohistochemistry.

## 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. Oien KA. Pathologic evaluation of unknown primary cancer. *Semin Oncol* 2009;36:8-37.
4. Disibio G, French SW. Metastatic patterns of cancers: Results from a large autopsy study. *Arch Pathol Lab Med* 2008;132:931-9.
5. Martín-Marquina Aspiunza A, Díez-Caballero Alonso F, Rodríguez-Rubio Cortadellas FI, Díez Fernández L, Abad Vivas-Pérez JI, Rosell Costa D, *et al.* Bladder metastasis of lung adenocarcinoma. *Actas Urol Esp* 1997;21:406-8.
6. Lan SK, Lin YH, Tzai TS, Tsai YS. A rare instance of lung cancer metastasizing to the urinary bladder. *J Taiwan Urol Assoc* 2006;17:63-6.
7. Karatas OF, Bayrak R, Yildirim ME, Bayrak O, Cimentepe E, Unal D. Bladder metastasis of non-small cell lung cancer: An unusual cause of hematuria. *Int J Hematol Oncol* 2009;19:246-8.
8. Shirakawa H, Kozakai N, Sawafuji M, Sugiura H, Hara S. Urinary bladder metastasis originating from lung adenocarcinoma: A case definitively diagnosed by immunohistochemistry. *Urol J* 2012;9:530-2.
9. Karle W, Barazani Y, Tareen B. A rare case of metastatic lung cancer to the bladder. *Can Urol Assoc J* 2012;6:E147-9.
10. Sheahan K, O'Keane JC, Abramowitz A, Carlson JA, Burke B, Gottlieb LS, *et al.* Metastatic adenocarcinoma of an unknown primary site. A comparison of the relative contributions of morphology, minimal essential clinical data and CEA immunostaining status. *Am J Clin Pathol* 1993;99:729-35.

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