TITLE:
Lung metastasis of ta bladder cancer: a case report and literature review.

AUTHOR(S):
Sano, Takeshi; Hamada, Shinshichi; Haitani, Takao; Nakashima, Masakazu; Kajita, Yoichiro; Shichiri, Yasumasa

CITATION:
Sano, Takeshi ...[et al]. Lung metastasis of ta bladder cancer: a case report and literature review.. Korean journal of urology 2013, 54(4): 271-273

ISSUE DATE:
2013-04

URL:
http://hdl.handle.net/2433/173766

RIGHT:
© The Korean Urological Association, 2013.; This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/3.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.
Case Report

Lung Metastasis of Ta Bladder Cancer: A Case Report and Literature Review

Takeshi Sano, Shinshichi Hamada, Takao Haitani, Masakazu Nakashima, Yoichiro Kajita, Yasumasa Shichiri

Departments of Urology and Pathology, Otsu Municipal Hospital, Otsu, Department of Urology, Kyoto University Graduate School of Medicine, Kyoto, Japan

A 66-year-old man with a history of multiple transurethral resections for recurrent bladder tumors, staged as Ta according to the International Union Against Cancer staging guidelines, presented with a complaint of dry cough. A round nodule with a diameter of 7.5 cm was detected in the lung by chest computed tomography, and a video-assisted thoracoscopic lobectomy was performed. Pulmonary metastasis of recurrent bladder cancer was diagnosed by immunohistochemistry staining for the urothelium-specific protein uroplakin Ia. Subsequently, 2 cycles of systemic chemotherapy were administered. Two and a half years after treatment, no recurrence of pulmonary lesions has been detected. A combination of complete resection of pulmonary lesions and systemic chemotherapy may result in a good prognosis for patients with non-muscle-invasive bladder cancer.

Keywords: Indirect fluorescent antibody technique; Solitary pulmonary nodule; Urinary bladder neoplasms

INTRODUCTION

Nonmuscle-invasive bladder cancer seldom shows distant metastasis. In addition, it is extremely rare for bladder cancer staged as Ta under the International Union Against Cancer guidelines to result in distant metastasis. We present the case of a patient with a distant pulmonary metastasis of Ta bladder cancer; the patient did not have a history of muscle-invasive disease. We review the literature concerning non-muscle-invasive bladder cancer with distant metastasis and discuss management and treatment outcomes.

CASE REPORT

A 66-year-old man had been diagnosed with Ta bladder cancer 6 years before he complained of dry cough in July 2009. He had a history of recurrent non-muscle-invasive bladder tumors and had therefore undergone 7 transurethral resections (TURs) and had received intravesical chemotherapies (8 cycles of weekly mitomycin-C after the 4th TUR and 5 cycles of biweekly pirarubicin after the 5th TUR). All tumors were <1 cm, well pedunculated, and papillary. The number of tumors ranged from 1 to 6 in each respective TUR. The pathological findings of all TURs indicated the presence of urothelial carcinoma (stage Ta without carcinoma in situ, grade 1 or 2) without lymphatic or vascular invasion. The last TUR in January 2009 showed the same findings as the previous TURs, i.e., there were 3 tiny papillary tumors located at the right lateral wall, at the posterior wall, and adjacent to the left ureteral orifice, and pathological examination indicated results similar to those of the previous TURs. Chest radiography at 6 months after the last TUR detected a round nodule (diameter, 7.5 cm) in the right lower lung. We carefully rechecked the chest radiograph obtained in April 2008, which showed a small nodule (diameter, 1 cm) in the same area. These observations suggest that the lung metastasis had occurred more than 1 year previously. The initial diagnosis based on the computed tomography findings was primary lung can-
FIG. 1. A computed tomography scan showing a large mass in the upper lobe of the right lung.

FIG. 2. Uroplakin Ia (UP-Ia) staining in bladder urothelial carcinoma and lung metastasis (×200; bar=200 μm). (A) Bladder urothelial carcinoma shows diffuse cytoplasmic staining and umbrella cells show strong immunoreaction for UP-Ia. (B) Moderate positive immunostaining in lung metastasis.

For nonmuscle-invasive bladder cancer, the probability of recurrence at 5 years ranges from 31% to 78% [3], whereas the risk of distant metastasis is extremely low. Matthew et al. [4] reviewed cases of more than 1,000 patients treated for bladder cancer, regardless of the stage, and identified 9 patients with superficial urothelial carcinoma and distant metastatic disease (including 3 patients with stage pTa disease). Three patients underwent radical cystectomy, and muscle invasion was not identified on pathologic examination [4]. Because vessels are absent in the bladder mucosa, it is thought that Ta bladder cancer does not have the potential for lymphatic or hematogenous metastasis. Several iatrogenic mechanisms of metastasis in clinically diagnosed Ta cancer have been postulated: microscopic invasion by an understaged tumor, intravascular dissemination of tumor cells during transurethral resection, and degeneration of the basal membrane caused by intravesicular therapy [5].

It is often difficult to definitively diagnose pulmonary metastasis of bladder cancer. Histopathologic features of non-keratinized squamous-cell carcinoma of the lung are similar to those of urothelial carcinoma. Uroplakins (UPs) are urothelium-specific proteins and have 4 subtypes: Ia, Ib, II, and III. Kageyama et al. [1] reported that UP-Ia has higher sensitivity for urothelial carcinoma than UPs II and III. They investigated the expression of UP-Ia in primary and metastatic urothelial carcinoma. Among primary and
Lung Metastasis of Ta Bladder Cancer

TABLE 1. Summary of the literature reporting patients with lung metastasis of nonmuscle-invasive bladder cancer

| Reference                          | Age/gender | T category | Histologic grade | Time to metastasis (mo) | Outcome       |
|------------------------------------|------------|------------|------------------|-------------------------|---------------|
| Seymour et al., 1972 [7]           | 33/M       | T<2        | Grade 2          | 190                     | 11 mo NED     |
| Matthews et al., 1984 [4]          | 48/F       | Ta         | Grade 1          | 100                     | Not available |
| Matthews et al., 1984 [4]          | 73/M       | T1         | Grade 2          | 25                      | DOD at 1 mo   |
| Matthews et al., 1984 [4]          | 77/M       | T1         | Grade 2          | 12                      | Not available |
| Koh, et al., 1994 [8]              | 42/M       | T1         | Grade 2          | 108                     | NED           |
| Dougherty et al., 2009 [9]         | 78/M       | Ta         | Low grade*       | 120                     | More than 24 mo NED |
| Dougherty et al., 2009 [9]         | 61/M       | Ta         | Low grade*       | 48                      | 36 mo NED     |
| Present case                       | 66/M       | Ta         | Low grade*       | 72                      | 6 mo NED      |

NED, no evidence of disease; DOD, died of disease.

Tumor grade was evaluated using 1973 World Health Organization (WHO) grading. *Low grade was evaluated using 2004 WHO grading.

metastatic lesions, the detection rate of UP-Ia was 96.8% and 72.2%, respectively. UP-Ia can be a promising marker for identifying urothelial carcinoma.

To the best of our knowledge, 15 cases of non-muscle-invasive bladder cancer with distant metastasis have been reported in the English literature. Metastatic sites include the lungs, liver, bones, ovaries, and brain. Furthermore, 7 cases of lung metastasis have been reported (Table 1). All patients with bone metastasis (including 2 with stage pTa disease) died shortly after diagnosis [4], and 1 patient with solitary brain metastasis died less than 3 months after brain surgery [6]. On the other hand, as indicated in Table 1, the outcomes in most patients with lung metastasis were good, except for 1 patient (stage Ta, grade 2) who died 1 month after diagnosis [4]. Other studies have demonstrated a good prognosis in 3 patients with Ta bladder cancer and lung metastasis after a combination of lobectomy and neoadjuvant or adjuvant chemotherapy [7-9]. Death due to pulmonary metastasis of Ta bladder cancer has not been reported, because the malignant potential of the metastatic lesions is low, and metastatic lesions can be completely resected with ease. Although the effects of adjuvant chemotherapy remain undetermined, some authors have reported that adjuvant chemotherapy may contribute to the removal of systemically circulating cancer cells.

A combination of complete resection of the lung lesions and systemic chemotherapy may lead to good prognosis for patients with non-muscle-invasive bladder cancer.

CONFLICTS OF INTEREST
The authors have nothing to disclose.

ACKNOWLEDGMENTS
The authors would like to express their gratitude to Dr. Susumu Kageyama, Department of Urology, Shiga University of Medical Science, for his support in supplying anti uroplakin Ia antibody and data evaluation.

REFERENCES

1. Kageyama S, Yoshiki T, Isuno T, Tanaka T, Kim CJ, Yuasa T, et al. High expression of human Uroplakin Ia in urinary bladder transitional cell carcinoma. Jpn J Cancer Res 2002;93:523-31.
2. von der Maase H, Hansen SW, Roberts JT, Dogliotti L, Oliver T, Moore MJ, et al. Gemcitabine and cisplatin versus methotrexate, vinblastine, doxorubicin, and cisplatin in advanced metastatic bladder cancer: results of a large, randomized, multinational, multicenter, phase III study. J Clin Oncol 2000;18:3068-77.
3. Sylvester RJ, van der Meijden AP, Oosterlinck W, Witjes JA, Bouffion C, Denis L, et al. Predicting recurrence and progression in individual patients with stage Ta T1 bladder cancer using EORTC risk tables: a combined analysis of 2596 patients from seven EORTC trials. Eur Urol 2006;49:466-77.
4. Matthews PN, Madden M, Bidgood KA, Fisher C. The clinicopathological features of metastatic superficial papillary bladder cancer. J Urol 1984;132:904-6.
5. Kakohi Y, Nishio Y, Hashimura T, Takeuchi H, Yoshida O. Clinicopathological analysis on invasion and metastasis in superficial bladder cancer. Hinyokika Kiyo 1992;38:783-8.
6. Zennami K, Yamada Y, Nakamura K, Aoki S, Taki T, Honda N. Solitary brain metastasis from pT1, G3 bladder cancer. Int J Urol 2008;15:96-8.
7. Seymour JE, Malin JM Jr, Pierce JM Jr. Late metastases of a superficial transitional cell carcinoma of the bladder: report of a case. J Urol 1972;108:277-8.
8. Koh KB, Rogowski K, Smith PH. Cavitating pulmonary metastases from superficial transitional cell carcinoma of urinary bladder: case report. Scand J Urol Nephrol 1994;28:201-2.
9. Dougherty DW, Gonsorik VK, Harper LE, Trussell JC, Drabick JJ. Superficial bladder cancer metastatic to the lungs: Two case reports and review of the literature. Urology 2009;73:210.e3-5.