

Urethral metastasis from esophageal cancer: symptoms of dysuria and cystoscopic diagnosis

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Abstract

Urethral malignant tumors are rare and can lead to stenosis, causing dysuria. We report a case of urethral metastasis secondary to esophageal cancer. At the time of diagnosis, a patient with esophageal squamous cell carcinoma presented with voiding difficulties, feeble stream, terminal dribbling and incomplete voiding. The urethral tumor was diagnosed using cystoscopy, and biopsy was thereafter performed. Histopathology of the urethral tumor microscopically resembled to that of esophageal cancer. On immunohistochemistry, the urothelium markers uroplakin 2 and GATA3 were negative in the carcinomatous component; however, GATA3 was detected on the lesion's surface. This case demonstrated that esophageal cancer metastasized to the urethra. Medical oncologists should consider this diagnosis in patients with cancer presenting with dysuria.

INTRODUCTION

More than 30% of patients with esophageal cancers are diagnosed with metastatic diseases [1]. The most common metastatic sites are the lymph nodes, liver, lungs, adrenals and bone. Urethral malignancies are rare, accounting for less than 1% of malignant tumors, and can cause urethral stenosis, which often occurs with dysuria [2]. Urethral metastasis commonly arises from prostate and bladder cancers [3]. No previous information was found in literature reporting on urethral metastases secondary to esophageal cancer. We report a case of urethral metastasis of esophageal cancer that was diagnosed via urethrocystoscopy in a patient complaining of dysuria.

CASE REPORT

A 61-year-old Japanese man presented with anorexia noted 2 months prior. The patient's medical history was unremarkable. He had been drinking three bottles of beer daily for over 40 years and smoking one to two packs of cigarettes daily for more than 45 years. The patient was diagnosed with esophageal carcinoma of the lower thoracic segment based on the upper gastrointestinal endoscopy findings. At the same time, endoscopy also exposed a superficial hypopharyngeal cancer as a synchronous malignancy. Endoscopic biopsy and histopathology revealed non-keratinizing squamous cell carcinoma. Computed tomography showed multiple pulmonary and liver masses and multiple enlarged lymph nodes. This included the right supraclavicular, mediastinal, paraaortic and right inguinal lymph nodes. Accordingly, he

was diagnosed with esophageal cancer with distant metastases (cT4aN4M1, stage IVB, according to the Union for International Cancer Control/American Joint Committee on Cancer staging classification system 8th edition).

At the time of esophageal cancer diagnosis, the patient also reported voiding difficulties, specifically, a poor stream, terminal dribbling and incomplete voiding. Routine urine tests revealed no traces of blood or protein remnants. The urine red blood cell count was 2.2/HPF and the white blood cell count was 2.6/HPF. Atypical cells were not detected on urine cytology. The patient was referred to a urologist, who performed a cystourethroscopy for a palpable penile lump. Cystourethroscopy revealed a smooth nodular, 5-mm mass in the penile urethra (Fig. 1). A transurethral biopsy was then performed. The bladder mucosa was smooth, and there were no notable abnormalities in the left and right urethral openings.

Microscopically, the urethral tumor showed abundant nuclear pleomorphism and was identified as a non-keratinizing squamous cell carcinoma. Its characteristics were similar to those of the esophageal tumor (Figs 2 and 3). Immunohistochemically, the tumor cells were positive for p40, indicating a squamous cell carcinoma (Fig. 2B). On immunohistochemistry, the urothelium markers, uroplakin 2 and GATA3 were negative in the carcinomatous component (Fig. 2C and D); however, GATA3 was detected on the surface of the lesion (Fig. 2E). Accordingly, the urethral tumor was diagnosed as a metastatic esophageal squamous cell carcinoma.

The patient underwent immediate radiotherapy and chemotherapy with 5-fluorouracil (5-FU) and cisplatin (CDDP) to achieve

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Figure 1. Cystourethroscopy revealed a 5-mm smooth nodular mass in the penile urethra.

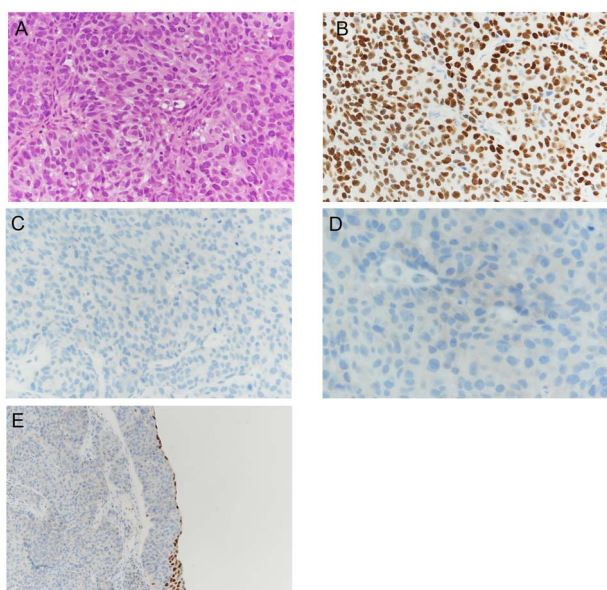


Figure 2. The urethral tumor showed moderately differentiated squamous cell carcinoma consistent with esophageal cancer (A); immunohistochemical section of urethral tumor was positive for (B) p40 and negative for (C) uroplakin 2 and (D) GATA3; GATA3 expression at the normal urothelium was observed (E).

local control. After concurrent chemoradiotherapy, the patient underwent chemotherapy with 5-FU and CDDP for metastatic disease. Following treatment, his dysuria was resolved, and he could urinate without discomfort. The follow-up period was ~3 months.

DISCUSSION

We have reported a case of urethral metastasis secondary to esophageal cancer. This case highlights two essential findings. First, esophageal cancer can metastasize to the urethra, resulting in voiding difficulties. Second, cystoscopy is a useful diagnostic tool for metastatic urethral tumors.

Esophageal cancer can metastasize to the urethra, and urethral metastatic tumors should be suspected in cancer patients

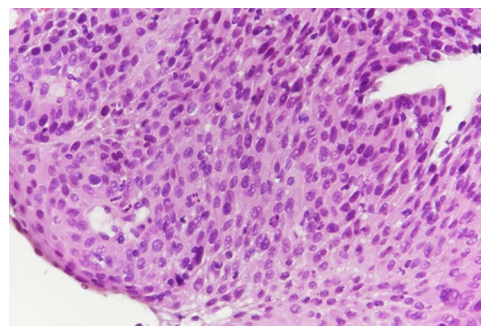


Figure 3. The esophageal tumor contained moderately to poorly differentiated squamous cell carcinoma.

presenting with dysuria. Metastatic tumors of the urethra occur more frequently than primary tumors [3]. Several reports of metastasis from the colon and rectum, lungs and breast are reported [4–6]; however, urethral metastasis secondary to esophageal cancer has not previously been reported.

Urethral metastasis was diagnosed by histopathological analysis of the sample obtained via transurethral biopsy. Cystoscopy revealed a smooth nodular mass that did not extend to the surrounding urothelium. Primary urethral tumors commonly extend beyond or above the surface. Moreover, they exhibit a cobble appearance with a papillary surface [2]. In our case, the tumor's characteristics differed from the typical primary urethral carcinoma. Microscopically, it was diagnosed as a squamous cell carcinoma. The carcinomatous component was negative for GATA-3 and uroplakin II on immunohistochemical analysis. However, these markers were positive on the surface of the normal urothelium surrounding the tumor. GATA-3 and uroplakin II are novel markers for primary urethral carcinoma and are positive in 99 and 80% of malignant urothelial tumors, respectively [7]. The immunohistochemical findings, in this case, indicated metastasis of esophageal cancer to the urethra, and the tumor might have arisen from the stroma, which is beneath the urothelium.

The proposed hypotheses for urethral metastasis include the lymphatic, arterial or venal routes or direct invasion, although direct invasion is anatomically impossible. Kaushal *et al.* [8] reported a case of inguinal lymph node metastasis from a gastroesophageal junction carcinoma. The patient had bilateral inguinal lymph node swelling with multiple enlarged paraaortic, iliac and pelvic lymph nodes. The authors hypothesized that metastasis was due to the retrograde flow through paraaortic nodes to the pelvic and inguinal nodes. While our patient had right inguinal node swelling, he did not have pelvic lymph node metastasis; therefore, it is likely that the underlying mechanisms differ. In a study describing unexpected sites of metastases secondary to esophageal cancer, distal isolated metastases via the lymphatic route were scarcely explained. The authors postulated that tumor embolisms pass through the main artery to the distal isolated organs [9]. We propose that distal urethral tumors flow into the right inguinal lymph node via the hematologic route. Although inguinal lymph node metastasis secondary to esophageal cancer is rare, we should consider the possibility of a urethral tumor in patients presenting with inguinal lymph node swelling.

Herein, we report a case of urethral metastasis secondary to esophageal squamous cell carcinoma. Despite its rarity, medical oncologists should consider this diagnosis in cancer patients presenting with dysuria.

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CONFLICT OF INTEREST STATEMENT

No conflicts of interest.

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ETHICAL APPROVAL

This case report was approved by the institute's Institutional Review Board.

CONSENT

Written consent was obtained from the patient for this publication.

GUARANTOR

Ikumi Kuno is the guarantor of this article.

REFERENCES

1. Zhang Y. Epidemiology of esophageal cancer. *World J Gastroenterol* 2013;**19**:5598–606. <https://doi.org/10.3748/wjg.v19.i34.5598>.
2. Zhang M, Adeniran AJ, Vikram R, Tamboli P, Pettaway C, Bondaruk J, et al. Carcinoma of the urethra. *Hum Pathol* 2018;**72**:35–44. <https://doi.org/10.1016/j.humpath.2017.08.006>.
3. Karaosmanoglu AD, Onur MR, Karcaaltincaba M, Akata D, Ozmen MN. Secondary tumors of the urinary system: an imaging conundrum. *Korean J Radiol* 2018;**19**:742–51. <https://doi.org/10.3348/kjr.2018.19.4.742>.
4. Tefilli MV, Stefani SD, Mariano MB. Urethral metastasis of lung carcinoma with germinative cell features. *Int Braz J Urol* 2003;**29**:431–3. <https://doi.org/10.1590/s1677-55382003000500008>.
5. Karakose A, Aydogdu O, Atesci YZ. Unusual urethral metastasis from colon carcinoma presenting with difficult urination and hematuria. *Curr Urol* 2013;**7**:152–4. <https://doi.org/10.1159/000356269>.
6. Tanaka Y, Okabe T, Okada K, Kiriya T, Yoshida O. Metastatic urethral tumor from carcinoma of the breast: a case report. *Acta Urol Jap* 1981;**11**:1393–7. <https://doi.org/http://hdl.handle.net/2433/123236>.
7. Leivo MZ, Elson PJ, Tacha DE, Delahunt B, Hansel DE. A combination of p40, GATA-3 and uroplakin II shows utility in the diagnosis and prognosis of muscle-invasive urothelial carcinoma. *Pathology* 2016;**48**:543–9. <https://doi.org/10.1016/j.pathol.2016.05.008>.
8. Kaushal G, Anand S, Raja K, Chandrasekar S, Pottakkat B, Gnanasekaran S. Inguinal mass: an unusual presentation of gastroesophageal junction adenocarcinoma. *Int J Adv Med Health Res* 2017;**4**:85–7. https://doi.org/10.4103/IJAMR.IJAMR_54_17.
9. Shaheen O, Ghibour A, Alsaid B. Esophageal cancer metastases to unexpected sites: a systematic review. *Gastroenterol Res Pract* 2017;**2017**:1657310. <https://doi.org/10.1155/2017/1657310>.