Metastasis in penile corpus cavernosum from esophageal squamous carcinoma after curative resection: a case report

Lingmin Song¹*, Yangmin Wang² and Guobin Weng¹

Abstract

Background: Metastasis in penile corpus cavernosum from esophageal squamous carcinoma is a rare but fatal disease, which was reported in cases without series studies.

Case presentation: An 84-year-old male smoker, who had a history of curative resection of esophageal squamous carcinoma 12 months before, presented with aggressive dysuria and penis pain for 1 month. Ultrasonic guided biopsy diagnosed metastatic squamous carcinoma from the primary in the esophagus. The accurately modulated conformal radiotherapy and non-steroidal antiinflammatory drugs achieved to alleviate the penis pain temporarily. But the disease progressed and disseminated in a short period. He died of multiple metastases and cancer cachexia in 4 months.

Conclusions: Primary esophageal cancer metastasis to penile corpus cavernosum refers to short onset time of metastasis, extensive dissemination, bad response to treatment and poor prognosis. Palliative therapy to patients with the disease could achieve temporary local symptom relief, but not prolong survival time. More research is necessary to understand the underlying mechanism of esophagheal metastasis.

Keywords: Penile metastasis, Esophageal carcinoma, Palliative therapy, Case report

Background

Esophageal cancer is one of the most deadly cancers worldwide, with extremely aggressive nature and 5-year survival of 15–25%, and the main metastatic organs are reported to be liver, lung, bone and brain [1]. Histologic types include squamous carcinoma, adenocarcinoma and undifferentiated carcinoma [2]. Despite the abundant blood supply, penile metastatic cancer, with a poor prognosis of 10-month median survival time, is uncommonly reported no more than 500 cases hitherto [3]. Among these cases, 69% of penile metastases were primarily from urogenital cancers and 19% from gastrointestinal cancer [4]. Since Gupta NM reported the first case of penile metastasis from esophageal cancer in 1989, only 9 cases were reported worldwide until now [5–13], which were all case reports without systematical study because of the rarity. The present study reports a new case about the clinical characteristic and management of penile metastases from esophageal cancer. Furthermore, we reviewed all the case reports to provide a summary of the clinical symptoms, treatments, survival and intended to speculate about the possible risk factors, research targets for this disease.

Case presentation

In September 2017, an 84-year-old male smoker, who had a history of curative resection of esophageal squamous carcinoma (pT3N0M0, phase IIA, moderately differentiated) 12 months before, presented with aggressive dysuria and penis pain for 1 month. He was in good performance status (ECOG = 1) with stage 2 hypertension for 30 years, which was under control by regular Nifedipine GITS. His physical examination revealed roughly normal appearance of the penis but several smooth, hard, fixed nodules (diameter from 0.5 cm to 2.5 cm) in the right penile corpus cavernosum, which compressed the penis urethra(Fig. 1a). MRI pelvis protocol scanning confirmed these masses, but did not detect any obvious metastasis in pelvic lymph nodes, bones or...
lumber, sacral vertebrae, (Fig. 1d). Gastroscopy with biopsy at the anastomosis detected no sign of local recurrence, and there was no radiographic evidence of pulmonary or mediastinal metastases by CT scan. After the failure of urethroscopy, retrograde urethrography showed a 2 cm-length urethrotomy about 5 cm proximal to external orifice (Fig. 1b), and he was catheterized (F12, Foley) in case of acute urinary retention. Ultrasonic guided biopsy from one of the nodules diagnosed metastatic squamous carcinoma from the primary in the esophagus (Fig. 1e). IHC revealed positive expression of CK8/18, CK5/6, P40, while negative expression of CK7, CK20. He refused positron emission tomography scan with CT, penectomy or chemotherapy. Then after paracentetic suprapubic cystostomy, we offered him accurately modulated conformal radiotherapy (total radiation absorbed dose: 6000 cGy/30 times) and non-steroidal antiinflammatory drugs (NSAIDs) to alleviate the penis pain. But 4 weeks later, the hard nodules in penile corpus cavernosum progressed; furthermore he developed severe back pain. MRI detected metastasis in the 4th and 5th lumber vertebrae. Since he still rejected further chemotherapy or radiotherapy, we treated him palliatively with paraspinal nerve block and three ladder analgesic programs of cancer to temporarily relieve the pain. After 10 weeks, he presented to us with cough, chest pain and recurrent dysphagia. CT scan revealed pulmonary infection, metastasis in both lungs and suspicious local recurrence in esophagus. He was discharged when pulmonary infection was cured, and the therapeutic regime turned to hospice care. In January 2018, he died of multiple metastases and cancer cachexia.

**Literature review**

We performed a search using PubMed and Chinese National Knowledge Infrastructure (CNKI), which offers medical literature research in China. As mentioned...
above, to the best of our knowledge only 9 cases of penile metastasis from esophageal cancer have been reported from 1989 to 2018. From these 10 cases, including the present and previous reports, we analyzed the clinical feature of the primary (Table 1) and the metastatic cancer (Table 2) in order to get some information for further study about this disease.

The average age was 58.1 ± 3.8 years, ranging from 40 to 84 years. Concerning the treatment to primary cancer, curative resection was conducted in 5 cases, partial esophagectomy in 2, chemotherapy and/or radiotherapy in 3. The pathological diagnoses of these primary cancers were exclusively squamous cell carcinoma, of which moderated differentiated account for 50% (5/10). The TNM stages of the primary cancer were pathological or clinical T3N0M0 to T4N1M1, which indicated the primary cancers were advanced, and metastatic when admitted in 4 cases. The time of penile metastasis since primary cancer diagnosed varied a lot, and the mean time was 9.3 ± 2.7 months, ranging from concurrent to more than 24 months. The clinical manifestation included painless (4/10) or painful mass (3/10), necrosis in glans with pain (2/10), dysuria (4/10), and priapism (2/10). The metastatic site could locate in any portion or the full length of penile corpus cavernosum, but none reported in cavernous spongiosum, skin or foreskin. Furthermore, metastases in other organ or lymph node were reported simultaneously in 6 cases. The present case reported the penile metastasis ad the first site and successively metastasis to other organs in 3 months The prognosis was dismal regardless of the methods of treatment to metastases, since the survival time was 5.4 ± 1.4 months (ranging from 1 month to 12 months).

Discussion and conclusions
The present report and analysis of literature review reveal that metastasis in penile corpus cavernosum from esophageal squamous carcinoma is a rare disease with a survival time of less than 12 months after diagnosed and poor treatment response. Since this disease is only reported in case reports, there might rarely be reliable evidence from lager data of prospective or retrospective series studied. However, a little more information can be gathered from these cases available. Thereupon, we get conscious of some characteristics of this disease: the primary cancers were exclusively squamous cell carcinoma and local advanced, even metastatic when admitted in a few cases; the metastatic site exclusively located in penile corpus cavernosum, but not in cavernous spongiosum, skin or foreskin; metastasis to other sites simultaneously were detected in most cases, and progressed rapidly with a poor prognosis.

It is widely accepted that the possible mechanisms of metastasis include direct invasion, hematogenous or lymphatic dissemination, iatrogenic spread [3]. Obviously, anatomic proximity is necessary for direct invasion, such as large metastatic mass in the root of penis from the prostate and bladder [14] Penile metastasis from genitourinary system and colon/rectum via pelvic venous plexus and dorsal penile vein was presumed by Abeshouse and Kumer with the evidence of presentation of cancer thrombi in vasculature [15, 16]. While Paquin proposed

| Author          | Age (year) | Primary treatment          | Pathology                               | Stage             | Postoperative Therapy            |
|-----------------|------------|----------------------------|-----------------------------------------|-------------------|----------------------------------|
| Gupta N M       | 40         | Radiotherapy               | Poorly differentiated squamous cell carcinoma | Can’t evaluate    | –                                |
| Pai A           | 51         | Curative resection         | Moderately differentiated squamous cell carcinoma | pT3N1M0           | Adjuvant radiotherapy            |
| Zou C           | 61         | Curative resection         | Moderately differentiated squamous cell carcinoma | pT3N1M0           | Radiotherapy plus chemotherapy    |
| Numakura K      | 68         | Curative resection         | Poorly differentiated squamous cell carcinoma | pT3N0M0           | –                                |
| Kobayashi Y     | 61         | Curative resection         | Well differentiated squamous cell carcinoma | pT3N0M0           | Adjuvant chemotherapy            |
| López-Aramburu MA | 57       | Chemotherapy               | Squamous cell carcinoma                 | ct3N1M1           | –                                |
| Morán PE        | 53         | Chemotherapy plus Radiotherapy | Moderately differentiated squamous cell carcinoma | ct4N1M1           | –                                |
| Li XM           | 57         | Lower esophagectomy       | Squamous cell carcinoma                 | Can’t evaluate    | –                                |
| Tang ZJ         | 49         | Middle esophagectomy      | Moderately differentiated squamous cell carcinoma | Can’t evaluate    | –                                |
| Song LM         | 84         | Curative resection         | Moderately differentiated squamous cell carcinoma | pT3N0M0           | –                                |
retrograde lymphatic metastasis to penis might basically locate in the skin, foreskin, because of the abundant lymph supply and widely connection of the penis with pelvic organs via the iliac lymph nodes [14]. Urethra or cavernous spongiosum might be involved by transurethral resection of the prostate or bladder cancer via iatrogenic spread [17]. Because of the anatomical distance, it seems obvious that esophageal cancer does not metastasis via direct invasion, venous or lymphatic dissemination, and iatrogenic spread to the penis. Therefore, we speculate arterial dissemination be the metastatic pathway, which simultaneously indicates the progression and widespread dissemination of the primary cancer.

The treatment, including surgical excision, urinary diversion, radiotherapy, chemotherapy and the combination of these, is usually palliative and relieve local symptom temporarily, but may not delay the progression or prolong survival time. The poor response to treatment lead to the dismal prognosis no more than 6-month's median survival time not only in penile metastasis from esophageal cancer but also from other primary cancers [3, 9]. However, little is known about the exact mechanism or molecular biology feature of penile metastasis especially from esophageal cancer, which needs to be verified by further research.

Primary esophageal cancer metastasis to penile corpus cavernosum is a rare but fatal condition, which refers to short onset time of metastasis, extensive dissemination, bad response to treatment and poor prognosis. Palliative therapy to patients with the disease could achieve temporary local symptom relief, but not prolong survival time. The rarity of the disease limits clinical study and biochemistry research on it, as well as our understanding of the underlying mechanisms of metastasis for effective treatment and better prognosis.

Table 2 Treatment, pathological findings, and follow-up of 9 patients with metastatic penile cancer

| Author         | Time of penile metastasis | Clinical manifestation                  | Metastatic site           | Other metastasis simultaneously | Diagnosis method | Pathology                           | Treatment of metastasis                          | Survival time |
|----------------|---------------------------|----------------------------------------|---------------------------|----------------------------------|------------------|-------------------------------------|-----------------------------------------------|---------------|
| Gupta NM       | 1 week                    | Painful nodules                        | Dorsal shaft              | Not mentioned                    | Open biopsy      | Squamous cell carcinoma            | Polydrug chemotherapy                           | 6 weeks       |
| Pai A          | 9 months                  | Painful nodules                        | Full length               | Lymph node in left hilir, subcarinal and left supraclavicular | Fine needle aspiration | Squamous cell carcinoma            | Palliative chemotherapy                           | alive in 6 months |
| Zou C          | 6 months                  | Painless mass                          | Shaft                     | Right thigh; lymph nodes in left neck | Excisional biopsy | Moderated differentiated squamous cell carcinoma | Resection of penile mass; Palliative external beam radiation | 5 months       |
| Numakura K     | 24+ months                | Dysuria, Penile pain Necrosis in glans | Full length               | Brain, liver and eyes            | Excisional biopsy | Squamous cell carcinoma            | Total penectomy, chemotherapy                    | 3 months       |
| Kobayashi Y    | 2 months                  | Painless mass                          | Glans and shaft           | Abdominal lymph nodes and spleen | Open biopsy      | Squamous cell carcinoma            | Chemotherapy                                         | 5 months       |
| López-Aramburu MA | Simultaneously penile metastasis was the first symptom | Pain, Necrosis in glans | Glans and distal shaft       | Right humerus                    | Excisional biopsy | Squamous cell carcinoma            | Partial penectomy                                  | 1 month        |
| Morán PE       | 24+ months                | Painless mass, Dysuria                 | Glans and shaft           | Pelvic lymph node                | Open biopsy      | Squamous cell carcinoma            | Chemotherapy plus radiotherapy                    | Withdrawing, loss to follow up |               |
| Li XM          | 9 months                  | Priapism, Painless nodule, Dysuria     | Shaft                     | Not mentioned                    | Excisional biopsy | Squamous cell carcinoma            | Total penectomy                                  | 10 months      |
| Tang ZJ        | 4 months                  | Priapism                               | Shaft                     | Not mentioned                    | Excisional biopsy | Moderately differentiated squamous cell carcinoma | Total penectomy                                  | Not mentioned  |
| Song LM        | 12 months                 | Dysuria, Painful nodules               | Right shaft               | Not detected                     | Ultrasound guided biopsy | Moderately differentiated squamous cell carcinoma | Radiotherapy                                  | 4 months       |

Table 2: Treatment, pathological findings, and follow-up of 9 patients with metastatic penile cancer.
Abbreviations
cGy: Centigray; CK: Cytokeratin; CNKI: Chinese National Knowledge Infrastructure; CT: Computed Tomography; ECOG: Eastern Cooperative Oncology Group; IHC: Immunohistochemistry; MRI: Magnetic Resonance Imaging; NSAIDs: Non-steroidal antiinflammatory drugs

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Authors’ contributions
LS and YW cared for the patient. LS and GW wrote this manuscript. We were all responsible for writing and editing the manuscript. All authors have read and approved the final manuscript.

Ethics approval and consent to participate
This report was approved by Ethnic Committee of Lanzhou General Hospital, PLA, China. The patient’s legal representative (his daughter) provided written informed consent.

Consent for publication
Written consent from the patient’s legal representative (his daughter) for publication was obtained.

Competing interests
The authors declare that they have no competing interests.

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Author details
1. Department of Urology, Ningbo Urology & Nephrology Hospital, Ningbo 315192, Zhejiang, China. 2. Department of Urology, Lanzhou General Hospital, PLA, Lanzhou, Gansu, China.

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References
1. Johnson MD, Huang W, Jr WW. Esophageal cancer: risk factors, screening and endoscopic treatment in Western and eastern countries[J]. World J Gastroenterol. 2015;21(26):7933.
2. Allen DC. Oesophageal carcinoma[J]. Lancet. 2013;381(9846):400–12.
3. Zhang K, Da J, Yao HJ, et al. Metastatic tumors of the penis: a report of 8 cases and review of the literature.[J]. Medicine. 2015;94(1):e132.
4. Cocci A, Hakenberg OW, Cai T, et al. Prognosis of men with penile metastasis and malignant priapism: a systematic review[J]. Oncotarget. 2018;9(2):2923–30.
5. Gupta NM. Penile metastases from esophageal carcinoma[J]. Am J Gastroenterol. 1989;84(3):339–40.
6. Pai A, Sonawane S, Purandare NC, et al. Penile metastasis from esophageal squamous carcinoma after curative resection.[J]. Ann Thorac Cardiovasc Surg. 2008;14(4):38–41.
7. Zou C, Yu D, Qi W, et al. Penile and intramuscular metastases from esophageal squamous cell carcinoma: a rare case report and review of the literature[J]. Can Urol Assoc J. 2014;8(11–12):E875.
8. Numakura K, Tadachi K, Shimoda J. A case of metastatic tumor of penis from esophageal carcinoma.[J]. Hinyokika Kyokai Journal of Japanese Urological Association. 2008;54(12):795–7.
9. Kobayashi Y, Nozawa M, Kikuchi T, et al. Penile metastasis from esophageal cancer: a case report.[J]. Hinyokika Kyokai Journal of Japanese Urological Association. 2013;59(5):315–8.
10. López-Aramburu MA, Viguri DA, Rosa AJ, et al. Penile metastasis like first sign of esophagus carcinoma.[J]. Actas Urologicas Españolas. 2009;33(3):318–20.
11. Morán PE, Di CSC, Soto Poveda AM, et al. Penile metastasis of esophageal squamous cell carcinoma.[J]. Actas Urológicas Españolas. 2010;34(3):297–9.