

Metastatic Tumors of the Penis

A Report of 8 Cases and Review of the Literature

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Abstract: The purpose of this study was to report the clinical characteristics, treatments, and outcomes of secondary penile cancers and review the literature of this rare condition.

The records of 8 patients with metastatic penile cancer treated at our hospital from 2006 to 2013 were analyzed. A search of medical databases was conducted.

Patient symptoms included penile mass (n = 7, 5 had concomitant pain) and acute urine retention (n = 1). The primary cancers included bladder, lung, gastric, liver, and prostate malignancies and 1 case of pulmonary epithelioid hemangioendothelioma. The longest time from diagnosis of the primary cancer to metastatic penile cancer was 16 years and the shortest was 7 months. Six patients were treated with phallectomy, 1 with resection of the mass, and 1 with only a biopsy because of advanced metastatic disease. Five patients are deceased at the time of this report, and the longest and shortest survival times (from the diagnosis of primary cancer to the death) were 16 years and 9 months, respectively. The literature review identified 17 cases reported since 2011, bringing the total number of reported cases to 480. Genitourinary cancer, primarily bladder and prostate, account for approximately 70 of the primary cancer sites and gastrointestinal cancers account for approximately 21%. Approximately half of the patients had died of their disease within 1 year of the diagnosis of penile metastasis.

The prognosis of metastatic penile cancer is poor. Most primary cancers are in the urologic or gastrointestinal systems. Surgery and adjunctive therapy may improve symptoms, but fail to prolong survival.

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Abbreviations: CT = computed tomography, PET-CT = positron emission tomography-computed tomography, PSA = prostate specific antigen.

INTRODUCTION

Penile cancer is a rare malignancy, with a reported incidence ranging from 0.58 to 1.3 cases/100,000.^{1,2} The rate has been declining in recent decades,² however, the incidence is higher in many developing countries because of cultural and hygiene differences.^{3,4} Most cases of primary penile cancer are squamous cell carcinoma,⁵ and risk factors include exposure to the human papillomavirus, lack of neonatal circumcision, and exposure to tobacco.^{3,4,6,7}

Despite its abundant vascularization and extensive circulatory communication with neighboring organs, metastases from other cancers to the penis are rare and consequently lack an efficient treatment. These lesions are often associated with disseminated malignancy and have a poor prognosis.^{8–11} The survival time of patients with metastatic penile cancer is often no longer than 1 year.^{8–11} The first case of secondary penile malignancy was reported by Eberth in 1870.¹² In 1992, Perez et al¹⁰ provided a very complete review of 307 patients based on the primary cancer site. Since then, >100 cases have been reported and some literature reviews published.^{8,9,11} Most reviews, however, only summarize the origins of the cancer but not the survival or the treatment of patients.

From 2006 to 2013, 8 patients with metastatic penile cancer were treated at our hospital. The purpose of this study is to report our experience with treating these patients. In addition, we have performed a systematic review of the literature to provide a summary of metastatic penile cancer with respect to primary origins, clinical symptoms, treatments, and survival to provide more complete treatment choices and improve the prognosis of the disease.

CLINICAL STUDY

From 2006 to 2013, 8 patients with pathologically diagnosed metastatic penile cancer were treated and followed-up at our hospital. The median patient age was 66.4 years (range, 44–88 years). The symptoms of metastatic penile cancer included a penile mass (n = 7, 5 had concomitant pain) and acute urine retention (n = 1). One patient was admitted because of an abnormal persistent erection. The clinical characteristics of the 8 patients are summarized in Tables 1 and 2. This study was approved by the Institutional Review Board of Ninth People's Hospital, School of Medicine, Shanghai Jiao Tong University, and because of the retrospective nature of the study the requirement of written informed consent was waived.

TABLE 1. Clinical Characteristics of 8 Patients With Metastatic Penile Cancer

Patient	Age, y	Clinical Manifestations	Primary Cancer	Metastatic Site	Metastatic Lesion Size, cm	Metastasis to Other Sites	Time From Primary Lesion to Penile Cancer	Therapy of Primary Cancer
1	67	Penile mass, urine retention	Lung	Full length	6.5	No	3 y	Lobectomy + chemo/radiotherapy
2	62	Penile mass with pain	Lung	Root	4	No	7 mo	Chemotherapy
3	88	Penile mass	Bladder	Root	2	No	11 mo	Partial cystectomy
4	68	Penile mass with pain	Bladder	Middle	4	No	17 mo	Partial cystectomy
5	44	Abnormal erection	Liver	Full length	7	Lung, bone, retroperitoneum	16 y	Interventional chemotherapy
6	66	Penile mass with pain	Prostate	Full length	7	Liver, bone	Unknown	None
7	72	Penile mass with pain	Stomach	Root	3	No	30 mo	Radical resection of gastric cancer
8	64	Penile mass with pain	Bladder	Root	8	Right pelvic wall	17 mo	Total cystectomy

Among the 8 patients, the time from the diagnosis of the primary cancer to the presence of metastatic penile cancer varied significantly. The longest time (primary liver cancer) was 16 years and the shortest time was 7 months (primary lung cancer). Of the 8 patients, 5 are deceased at the time of this report and the longest and shortest survival times (from the diagnosis of primary cancer to the death) were 16 years and 9 months, respectively. The longest time from the diagnosis of penile cancer to death was 8 months.

Metastases were found in the root of the penis in 4 patients, in the middle of the penis in 1 patient, and involved the full length of the penis in 3 patients. In all cases, the tumor invaded the corpora cavernosum of the penis. Six patients were treated with phallectomy and 1 with resection of the mass and 1 with only a biopsy of the mass because of advanced metastatic disease. Seven of the patients received surgical intervention or radiotherapy/chemotherapy for the treatment of the primary cancer.

Histological examination showed advanced urothelial cancer in 2 patients, advanced papillary urothelial carcinoma (from bladder cancer) in 1, epithelioid hemangioendothelioma (from lung cancer) in 1, angiosarcoma (from liver cancer) in 1, metastatic poorly differentiated adenocarcinoma (from gastric cancer) in 1, adenocarcinoma

(prostate) in 1, and squamous cell carcinoma (from lung cancer) in 1. In addition, cancer thrombi were found in the penile vasculature of 5 patients. Summaries of the individual cases categorized by primary cancer site are presented below, and representative pathological images are shown in Figures 1 and 2.

Primary Lung Cancer

Two patients had penile metastasis from lung cancer. One patient received a lobectomy, and postoperative pathological examination showed squamous cell carcinoma. Postoperatively, the patient received chemotherapy with cisplatin and docetaxel and chest radiotherapy. Three years later, a solid nodule was noted at the junction of the penis and scrotum and gradually enlarged and extended to the penile body. The patient was admitted because of acute urine retention, and a corpora cavernosa biopsy showed infiltration of poorly differentiated cancer cells in the muscle and fibrous tissues, accompanied by necrosis and keratinization consistent with squamous cell carcinoma. Phallectomy and inguinal lymph node dissection was performed and 6 months later the patient died because of advanced lung cancer and respiratory failure. The other patient was diagnosed with pulmonary epithelioid hemangioendothelioma. At 7 months

TABLE 2. Treatment, Pathological Findings, and Follow-up of 8 Patients With Metastatic Penile Cancer

Patient	Surgery	Pathological Diagnosis	Postoperative Therapy	Survival Time
1	Phallectomy	Squamous cell carcinoma	Chemotherapy + radiotherapy	6 mo
2	Phallectomy	Epithelioid hemangioendothelioma	No	2 mo
3	Phallectomy	Advanced urothelial cancer	Bladder lavage	5 mo
4	Phallectomy	Advanced urothelial cancer	Bladder lavage	Alive (18 mo)
5	Phallectomy	Angiosarcoma	No	3 mo
6	Penis biopsy	Adenocarcinoma of the prostate	Endocrine therapy	8 mo
7	Resection of penile mass	Metastatic poorly differentiated adenocarcinoma	No	Alive (5 mo)
8	Phallectomy	Advanced invasive papillary urothelial carcinoma	No	Alive (1 mo)

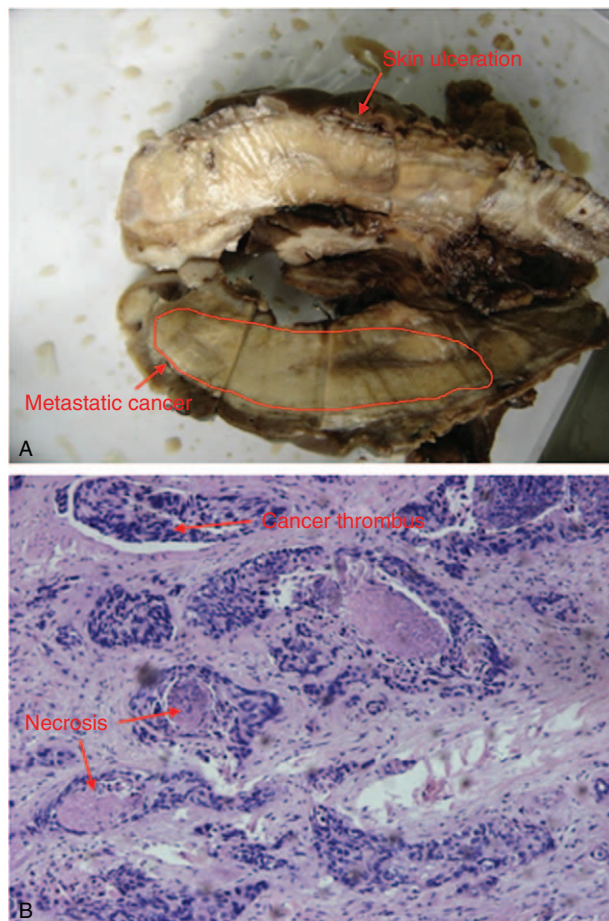


FIGURE 1. Penile metastasis from lung squamous cell carcinoma. (A) Longitudinal section of the corpora cavernosum of the penis after phallectomy. The cancer invaded the full-length penis (from balanus to root, red circle), and superficial skin ulceration was also observed. (B) Histological examination with hematoxylin and eosin stain (magnification $\times 200$) showed squamous cell carcinoma of the corpora cavernosum of the penis, moderately to poorly differentiated cells, with massive necrosis and cancer thrombus in the vasculature (red arrows).

after chemotherapy, a painful mass was found at the root of the penis. A biopsy of the mass was consistent with epithelioid hemangioendothelioma. A phallectomy was performed; however, 2 months later the patient died because of metastatic lung cancer and respiratory failure.

Primary Bladder Cancer

Three patients were diagnosed with penile metastasis from bladder cancer. All patients received partial or complete resection of the bladder prior to the diagnosis of penile metastasis. At 11 and 17 months after surgery, 2 patients developed a penile mass each and both received a phallectomy. Pathological examination in both cases revealed well-differentiated urothelial cancer. One patient died of dyscrasia because of advanced cancer 5 months later. The other patient was treated with chemotherapy by bladder lavage and is alive at 18 months after diagnosis without evidence of metastasis or recurrence of bladder cancer. The third patient received a total cystectomy for invasive urothelial carcinoma of the bladder and developed a

painful penile mass 17 months later. Phallectomy was performed and pathological examination was consistent with invasive papillary urothelial carcinoma. At 1 month postoperatively, the patient has developed emaciation, fatigue, poor appetite, and edema of both lower extremities.

Primary Gastric Cancer

Thirty months after radical resection of gastric adenocarcinoma the patient developed a painful penile mass. Biopsy showed metastatic poorly differentiated adenocarcinoma. Radiotherapy of the mass was ineffective and resection of the mass was performed. The patient refused postoperative radiotherapy and chemotherapy and is alive at 5 months after surgery with no evidence of metastasis by positron emission tomography-computed tomography (PET-CT).

Primary Liver Cancer

One patient was treated with interventional chemotherapy for hepatic angiosarcoma. Sixteen years later, he was seen with the complaint of an abnormal erection. The patient was treated with corpora cavernosum puncture and lavage; however, the symptoms recurred and a phallectomy was performed. The pathological diagnosis was metastatic angiosarcoma. Imaging studies showed metastasis to both lungs, right pubis, right ramus of the ischium, and retroperitoneum, and 3 months after surgery he died of dyscrasia because of advanced cancer.

Primary Prostate Cancer

One patient was seen with a complaint of a painful penile mass for 3 months. Biopsy of the mass revealed metastatic adenocarcinoma from the prostate. His blood prostate-specific antigen (PSA) level was 75 ng/mL. PET-CT showed metastasis to the liver and bone. Prostate biopsy showed prostate adenocarcinoma with a Gleason score of 5+4. He was treated with bilateral orchidectomy and oral casodex, and he died of liver failure 8 months later.

SYSTEMATIC LITERATURE REVIEW

Search Strategy and Study Selection

A search was conducted of MEDLINE, Cochrane, EMBASE, and Google Scholar on October 1, 2013 using combinations of the following search terms: penile cancer, malignant priapism, metastatic/metastasis, secondary. Inclusion criteria were malignant tumor metastatic to the penis and published after 2011 (inclusive). Non-English language publications were excluded. The search data from 2011 was selected because a prior comprehensive review was conducted by Zhu et al,¹¹ which included reports up to 2011.

Data Extraction

Studies were identified by the search strategy by 2 independent reviewers. Where there was uncertainty regarding eligibility, a third reviewer was consulted. The following information/data were extracted from studies that met the inclusion criteria: the name of the first author, year of publication, patient age, treatment, clinical course, and outcome.

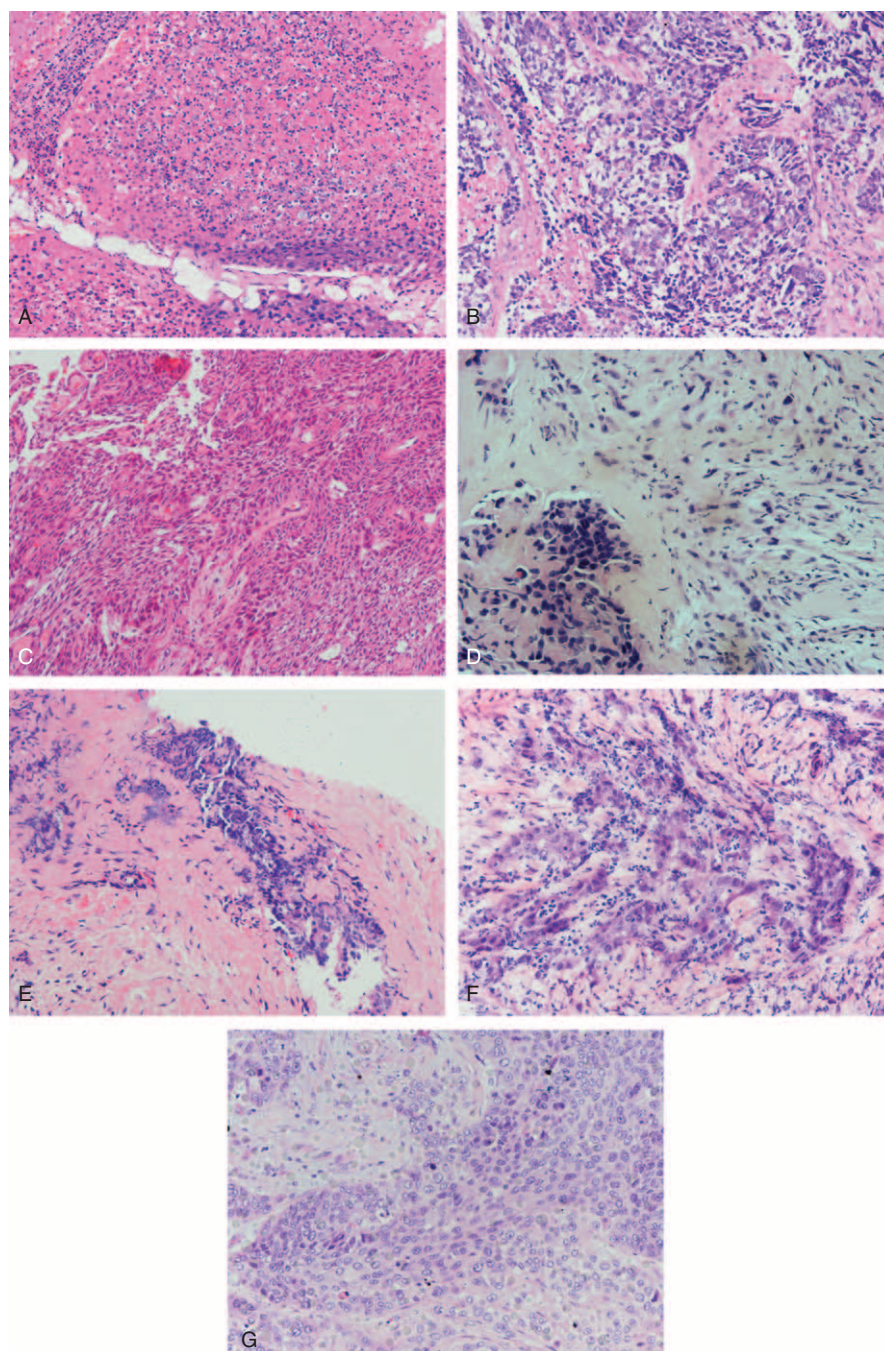


FIGURE 2. Representative histopathological images of penile metastases with different primary tumors. All images are hematoxylin and eosin stained, $\times 200$ magnification. (A) Epithelioid hemangioendothelioma, primary lung. (B) Advanced urothelial cancer, primary bladder. (C) Advanced urothelial cancer, primary bladder. (D) Angiosarcoma, primary liver. (E) Adenocarcinoma, primary prostate. (F) Poorly differentiated adenocarcinoma, primary stomach. (G) Invasive papillary urothelial carcinoma, primary bladder.

RESULTS

A flow diagram of the study selection is shown in Figure 3. A total of 239 potentially relevant studies were identified in the database search. After excluding nonrelevant studies and those not meeting the inclusion criteria, a total of 17 studies of metastatic penile cancer were included in the systematic review.^{13–29}

All included studies were new case reports since 2011 and published since the prior review of Zhu et al.¹¹ Of the 17 cases, 2 were from primary bladder cancer, 8 were from prostate cancer, 5 were from colon/rectal cancer, and 2 were from primary lung cancer. A summary of the 17 cases is presented in Table 3. A penile mass was the most common presenting symptom, and other symptoms included pain, priapism, urinary retention, and

TABLE 3. Clinical Characteristics of Patients With Metastatic Tumors to the Penis in the Reports Identified in the Systematic Review

Primary site	References	Age, y	Histological Type	Other Meta-static Sites	Location of Penis Meta-stasis	Clinical Presentation	Diagnosis Method	Treatment	Time From Primary Lesion to Penis Metastasis	Time From Penis Metastasis to Outcome	Outcome
Prostate	Messegueur et al ²⁵	57	Adenocarcinoma	Yes	G	Ulcerated mass	Biopsy	Palliative care	8 y	16 mo	AWD
	García et al ¹⁷	46	Adenocarcinoma	NA	S (CC)	No clinical symptoms	PET/CT, biopsy	Nonsurgical treatment	9 mo	NA	NA
	Nason et al ²⁶	92	Adenocarcinoma	No	G	Mass	Biopsy	Hormonal therapy	11 mo	3 mo	AWD
	Dijkstra et al ¹⁵	68	Adenocarcinoma	Yes	G	Induration, lower urinary tract symptoms	MRI, biopsy	Hormonal therapy	0*	NA	DOD, MM
	Pierro et al ²⁸	80	Adenocarcinoma	NA	S (CC)	Mass, induration, pain, dysuria	CT, MRI, ultrasoundography	Radiotherapy, chemotherapy, hormonal therapy	7 y	2 mo	DOD, MM
Bladder	Sánchez et al ²⁹	77	Adenocarcinoma	Yes	S (CC)	Induration, pain, hematuria, acute urinary retention	Ultrasoundography, biopsy	Radiotherapy, hormonal therapy	0*	4 mo	AWD
	Krpina et al ²²	64	Adenocarcinoma	Yes	G	Mass	CT, biopsy	Radiotherapy, chemotherapy	9 y	2 y	AWD, MM
	Lin et al ²³	84	Adenocarcinoma	NA	S (CC)	Priapism, pain	Ultrasoundography, MRI, biopsy	Surgical repair of priapism, palliative care	3 mo	NA	MM
	Ahmed et al ¹³	73	Urothelial carcinoma	Yes	S (CC)	Priapism, pain, penile edema	CT, MRI	Phallectomy	2 y	7 wk	DOD, MM
	Ajape and Bello ¹⁴	40	Bladder carcinoma	Yes	CC	Priapism, pain, penile gangrene	Corporeal aspiration cytology	Treatment declined	0*	NA	LFU
Rectum	Persec et al ²⁷	43	Adenocarcinoma	No	G	Ulcerated mass	CT, biopsy	Local excision	2 y	6 mo	DOD, MM
	Kimura et al ²¹	57	Adenocarcinoma	Yes	S (BF, CS)	Mass, bloody discharge	PET/CT, MRI, CECT	Phallectomy, chemotherapy	23 mo	>2 y	NED
	Dorsett et al ¹⁶	61	Adenocarcinoma	Yes	S, G	Mass	Biopsy	Phallectomy, radiotherapy	8 mo	4 mo	DOD
	Maestro et al ²⁴	70	Adenocarcinoma	Yes	G	Mass, induration	Biopsy	Chemotherapy	18 mo	1 y	DOD, MM
	Goris Gbenou et al ¹⁸	79	Adenocarcinoma	Yes	S	Mass, pain, urinary disorders	Biopsy	Circumcision, palliative care	3 y	6 mo	DOD
Lung	Karanikas et al ²⁰	59	Adenocarcinoma	Yes	S (BF, CS)	Mass	Ultrasoundography, MRI, biopsy	Radiotherapy, chemotherapy	1 mo	9 mo	AWD, bone marrow depression
	Haliloglu et al ⁹	57	Nonsmall cell carcinoma	Yes	S (CC)	Mass, priapism	Ultrasoundography, MRI, biopsy	Radiotherapy, pain management	0*	NA	AWD, MM

AWD = alive with disease, BF = Buck's fascia, CC = corpus cavernosum, CECT = contrast-enhanced computed tomography, CS = corpus spongiosum, CT = computed tomography, DOD = dead of disease, G = glans penis, LFU = lost to follow-up, MM = multiple metastases, MRI = magnetic resonance imaging, NA = not available, NED = no evidence of disease, PET = positron emission tomography, S = penile shaft.

*Synchronous diagnosis of primary lesion and penile metastasis.

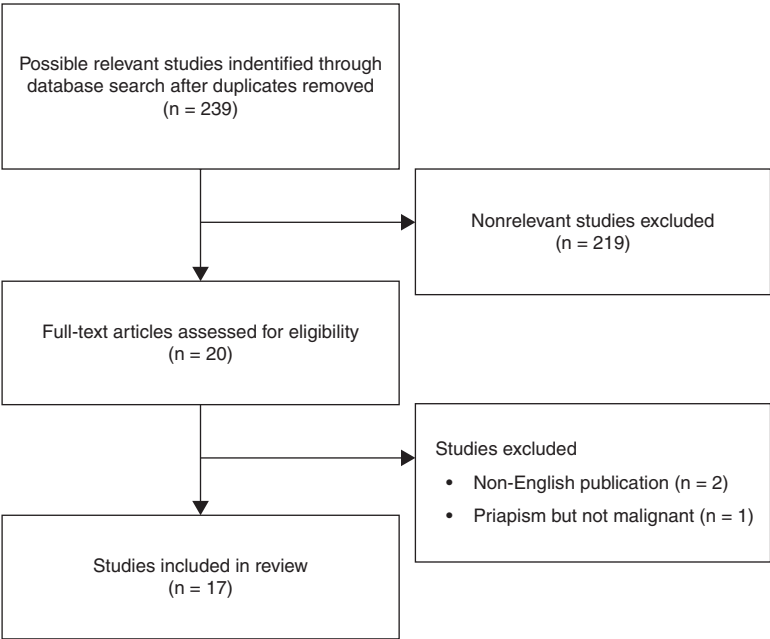


FIGURE 3. Flow diagram of study selection.

hematuria. In 1 case in which the primary site was prostate cancer, the patient had no symptoms associated with the penile metastasis. Various imaging studies were performed for diagnosis, but in the majority of cases a biopsy was performed. The time from diagnosis of the primary cancer to diagnosis of penile metastasis ranged from 3 months to 9 years, although in 3 cases diagnosis of penile metastasis was made at the same time as diagnosis of the primary cancer. Outcomes varied with the

primary cancer; however, approximately half of the patients had died of their disease <1 year of the diagnosis of penile metastasis. A summary of the primary cancer sites in cases of penile metastasis is shown in Table 4. The comprehensive review by Zhu et al¹¹ found a total of 455 reported cases of metastatic penile cancer. When the cases in the current report and the 17 found in the systematic review of the literature are added, there are a total of 480 reported cases of

TABLE 4. Summary of Primary Cancer Sites of Penile Metastases in Published Reports

Primary Cancer	Cases Reported by Zhu et al ¹¹	Cases in Present Report	New Cases Since 2011	Total Number of Cases (%)
Genitourinary	321	4	10	335 (69.8)
Bladder	138	3	2	143 (29.8)
Prostate	134	1	8	143 (29.8)
Kidney	31			31 (6.5)
Testis	12			12 (2.5)
Seminal vesicle	1			1 (0.2)
Ureter	2			2 (0.4)
Urethra	2			2 (0.4)
Renal pelvis	1			1 (0.2)
Gastrointestinal	94	2	5	101 (21.1)
Colon/rectum	78		5	83 (17.3)
Hepatobiliary + pancreas	7	1		8 (1.7)
Stomach	3			3 (0.6)
Esophagus	4	1		5 (1.0)
Anus	1			1 (0.2)
Tongue	1			1 (0.2)
Respiratory	22	2	2	26 (5.4)
Lung	18		2	20 (4.2)
Upper airway	4	2		6 (1.3)
Bone	3			3 (0.6)
Others	15			15 (3.1)
Total	455	8	17	480 (100.0)

metastatic penile cancer. Genitourinary cancer, primarily bladder and prostate, account for approximately 70% of the primary cancer sites in cases of metastatic penile cancer. Gastrointestinal cancers, primarily colon and rectal, account for approximately 21% of the primary sites, followed by respiratory (5%). Primary bone cancers and other malignancies account for only about 4% of the primary cancers.

DISCUSSION

The results of this report and literature review show that metastatic cancer to the penis is a rare disease with a poor prognosis. Most cases of metastatic penile cancer are from genitourinary malignancies, treatment is generally palliative, and approximately half of patients have died of their primary disease <1 year after the diagnosis of penile metastasis. Although the corpora cavernosum of the penis is rich in blood supply, metastatic penile cancer is not common. Since the first reported case of metastatic penile cancer in 1870,¹² 480 cases have been reported in English literature. The largest sample size of 17 cases was reported by Chaux et al.⁸

Metastatic penile cancer primarily is because of metastasis from malignancies of the urological system,^{8,30} which accounts for about 70% of primary cancers in patients with metastatic penile cancer (Table 4). Bladder cancer and prostate cancer account for 30% each followed by gastrointestinal cancers (21%) and lung cancer (4%).^{11,31} Primary bone cancer³² and malignant melanoma³³ have also been reported as the primary cancers in patients with metastatic penile cancer. In the present report, the urological cancers accounted for >50% of the primary lesions (3 from bladder cancer and 1 from prostate cancer).

The mechanism underlying the penile metastasis is still unclear.¹¹ Despite the rich blood supply to the penis, penile metastasis is rare. A number of mechanisms of metastasis have been suggested including direct tumor extension, retrograde venous spread, and arterial, lymphatic, or instrumental spread. Metastasis via blood circulation (especially the pelvic venous plexus and dorsal penile vein),³⁴ may explain the high proportion of primary cancers of genitourinary system and colon/rectum.³⁵ In the present report, cancer thrombi were noted in the vasculature in 5 cases, supporting this theory. On the basis of a direct or indirect connection of the penis with the bladder, prostate, and rectum via the iliac lymph nodes, some investigators propose that retrograde lymphatic metastasis is a cause of the penile metastasis,³⁶ which may explain why metastatic penile cancer often occurs in the skin, foreskin, and superficial fascia rich in lymph supply. In the present report, the 8 patients had no pelvic lymphadenectomy before or after treatment, and in those that survived for 18 months no lymphadenectomy was noted on computed tomography (CT). Our findings showed that metastasis primarily occurred in the corpora cavernosum of the penis shaft but not in the skin or foreskin. Previous reports have also shown that metastatic penile cancer is common in the shaft of the penis.^{8,11} These findings suggest that the possibility of lymph metastasis is lower than that of venous metastasis.

While direct invasion has been suggested because of the anatomic proximity of the prostate and bladder, the findings of Chaux et al⁸ do not support this as most metastases were found in the shaft of the penis, not the root. In our 8 patients, metastatic cancer was found at the root of the penis in 4 patients and invaded the full-length corpora cavernosum in 3 patients. Thus, the possibility of direct invasion of primary

cancer should be taken into account. In the 8 patients in this study, the penile metastatic cancer was very large at diagnosis, which is consistent with the view of Paquin et al³⁶ who proposed that the direct invasion should be taken into account when the metastatic penile cancer is large. Moreover, some investigators propose that the cancer cells might be seeded in the urethra during the transurethral resection of a prostate tumor (iatrogenic metastasis).⁸ While this is possible, in our report of 3 bladder cancer patients with metastatic penile cancer, only 1 received total cystectomy and urethral resection.

The most common clinical presentation of metastatic penile cancer is a penile mass (80%), and the mass is most frequently located in the shaft (71%) and less commonly in the head of the penis (24%) or foreskin (6%).^{8,10} Hematuria and pain are noted in some patients (7%).^{8,10} An abnormal erection is reported in 20% to 53% of patients with metastatic penile cancer.^{34,37,38} In these cases, histological examination shows metastatic cancer invading the vasculature, which explains the abnormal continuous erection and some investigators have called this condition "malignant abnormal erection."³⁹ In patients with a history of cancer, metastatic penile cancer should be included in the differential diagnosis of a continuous painful erection after excluding the consequence of drugs, trauma, and hematological diseases.

Few patients have metastatic penile cancer as the presentation of a primary malignancy.^{8,10,11} Of the 8 patients presented herein, only 1 patient with prostate cancer presented with metastatic penile cancer as the first symptom, and pathological examination showed the penile metastasis were from the prostate. The primary cancer and metastatic penile cancer are identified simultaneously in about 1/3 of patients, and metastatic penile cancer is diagnosed after the confirmation of the primary cancer (about 18 months after diagnosis of primary cancer) in about 2/3 of patients.^{8,10,11} The median time from the diagnosis of the primary cancer to the diagnosis of metastatic penile cancer in our patients (excluding the patient in whom penile cancer and prostate cancer were diagnosed simultaneously) was 44 months (range, 7–192 months), which was significantly longer than in previous reports. This might be attributed to our patients delaying seeing a physician after the onset of symptoms, which is suggested by the advanced disease in most patients. About 50% of patients have metastasis of the primary cancer to other organs at the time of diagnosis of metastatic penile cancer.^{8,10,11} In our report, 1/3 of patients had metastasis of the primary cancer to organs (lung, liver, and stomach).

Besides physical examination, Doppler ultrasonography is helpful for the early diagnosis of metastatic penile cancer. Ultrasonography can identify a mass in the corpora spongiosum penis and corpora cavernosum urethra. Ultrasonography has the advantages of being readily available, low cost, and has high patient acceptance. Magnetic resonance imaging (MRI) can determine the tumor size, depth, and site of cancer invasion and destruction of surrounding tissues.⁴⁰ CT is useful for determining the presence of retroperitoneal lymph node metastasis, but its accuracy is lower than that of lymphoscintigraphy.⁴¹ PET can be used to identify metastatic foci but is costly.⁴⁰ Penis cavernosography⁴² may also assist in the diagnosis of penile cancer but is gradually being replaced with noninvasive examinations.⁸ Currently, the diagnosis of metastatic penile cancer is dependent on pathological examination of a tissue specimen, and fine-needle aspiration cytology is frequently used. Comparison of the pathology of the primary cancer and metastatic penile

cancer is helpful for the diagnosis. In the present report, the pathology of the metastatic penile cancer was consistent with that of primary cancer in all cases.

Metastatic penile cancers are primarily squamous cell carcinoma and adenocarcinoma.^{20,43} Epithelioid hemangioendothelioma of the lung metastatic to the penis is very rare, and while epithelioid hemangioendothelioma of the lung is considered less malignant than other tumors, a study reported that a patient died at 11 months after the chest or abdominal wall metastasis.⁴⁴ Metastasis of a primary cancer to the penis usually indicates that the primary cancer is at an advanced stage and represents a poor prognosis. Treatment of metastatic penile cancer is usually palliative, and surgical intervention and urinary diversion are frequently performed.^{8,10,11} Although this therapy may not prolong survival time, it can relieve pain and improve the quality of life.^{8,11} Based on the histopathological diagnosis, chemotherapy, radiotherapy, and adjunctive endocrine therapy may be used after phallectomy. Unfortunately, these therapies fail to improve the prognosis, and there is no evidence demonstrating that one therapy is superior to another.^{8,9}

Previous reports have indicated that most patients died <6–12 months after the diagnosis of metastatic penile cancer, and few patients have been reported to survive for 2 years or more.⁸ Of the 8 patients in the current report, 3 were alive and 5 had died at a median of 4.8 months (range, 2–8 months) after the diagnosis of metastatic penile cancer. Of the 3 patients alive, 1 has survived for >18 months. In the report by Zhu et al,¹¹ 2 patients survived 22 months and 23 months, respectively. In their report of 17 patients, Chaux et al⁸ indicated that 1 patient with prostate cancer survived for 18 months. Whether penile metastasis from the urological system predicts a longer survival time is unclear.

There are some limitations of this report that should be considered. As case reports tend to be underreported, the actual incidence of metastatic penile cancer may be higher. The review was limited to English articles. There were 2 non-English studies that were identified and not included in the total number of reported cases of penile cancer. Both cases were in Japan and the primary tumors were in the esophagus⁴⁵ and kidney.⁴⁶

CONCLUSIONS

Metastatic penile cancer is a rare disease with approximately 480 reported cases. Metastasis to the penis typically indicates advanced stage disease and the prognosis is poor with half of patients dying <1 year of diagnosis. The most common primary tumor sites are the bladder, prostate, and colon/rectum. Treatment is palliative in most cases and achieved by phallectomy.

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