

Penile metastases from primary lung cancer

Case report and literature review

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Abstract

Background: Metastasis to the penis from primary lung cancer is quite rare. To improve the understanding, we present a case diagnosed as penile metastasis from primary lung cancer and review the literature.

Methods: One case report and retrospectively analysis penile cancer patient secondary from primary lung cancer.

Results: The patient complained of perineal pain and burning on urination for about 2 months. On physical examination, painful nodular masses at the base of left side of the corpora cavernosa were found. 18F-fluorodeoxyglucose positron emission tomography/CT (PET/CT) scan showed that maximum standardized uptake value (SUV_{max}) in left side corpora cavernosa and right hilar increased to 12.0 and 13.5 respectively. On flexible bronchoscopy checking, stenosis of the opening of apical segmental and posterior segmental bronchi of right upper lobe was found. The lateral segmental bronchi of left lower lobe was obstructed by a neoplasm. The pathological result was primary pulmonary adenosquamous carcinoma (ASC). Two months later, total penectomy was performed. The pathological result was penile ASC derived from pulmonary. On reviewing the literature, there are 39 cases reported. The patient we present is the 40th one. The average age at diagnosis was (60.5 ± 10.7) years old. The most common symptom was mass, followed by priapism, pain. The overall survival time was (4.5 ± 3.9) months.

Conclusions: The penis may be a site of metastasis from lung cancer, especially for old patient. Metastasis to the penis usually indicates that the primary lung cancer is at an advanced stage and the prognosis is very poor.

Abbreviations: ASC = adenosquamous carcinoma, CEA = carcinoembryonic antigen, MRI = magnetic resonance imaging, PET/CT = 18F-fluorodeoxyglucose positron emission tomography CT, SUV_{max} = maximum standardized uptake value.

Keywords: case report, lung cancer, metastasis, penile cancer, perineal pain

1. Introduction

Penile cancer is an uncommon malignancy with an incidence of < 1 per 100,000 men in the United States.^[1] The penis has a rich and complex vascular and lymphatic supply, but it is surprising that metastasis to the penis is such a rare clinical entity. Since the first reported case of metastatic penile cancer in 1870, there are total 504 reported cases to date.^[2] Most metastatic lesions originate from the neighboring genitourinary and pelvic organs, mainly bladder, prostate, and rectosigmoid colon, which account for nearly 75%. And penile metastasis from extrapelvic primaries

constitutes 25%.^[3] Metastatic penile cancer from primary lung cancer accounts for 4% to 6.2%.^[4,5] Herein, we report a case who presents penile metastasis as the first sign of primary lung cancer. The study is approved by the Ethics Committee of the First Affiliated Hospital of Soochow University. And the patient's son provided written informed consent for the information and images to be included in this article for publication. Also, we review the literature on penile metastases from primary lung cancer, and discuss its clinical features, diagnosis, therapy, and prognosis.

2. Case report

A 64-year-old male patient was admitted to our hospital with perineal pain and burning on urination for about 2 months. He denied fever, blood-stained sputum, malaise and emaciation. He was a heavy smoker with 30 pack-year smoking history. He had a history of chronic prostatitis for 10 years. On physical examination, the patient appeared well. He had no barrel chest and no clubbing fingers. Palpable painful nodular masses at the base of left side of the corpora cavernosa were found, the biggest one as broad bean in size. The glans was normal, without redundant prepuce. Testis and epididymides were normal too. The inguinal lymph nodes didn't show hints of enlargement. Magnetic resonance imaging (MRI) scan was performed. Abnormal signal in left side corpora cavernosa was found, 5.2 cm × 2.4 cm in size. The lesion was characterized by isointense on T1WI (Fig. 1A), slightly high signal intensity on T2WI and hyperintense on diffusion weighted imaging (Fig. 1B and C).

Editor: Levent Dalar.

LG and GL contributed equally to this work as co-first authors.

The authors have no funding and conflicts of interest to disclose.

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Medicine (2017) 96:26(e7307)

Received: 20 December 2016 / Received in final form: 23 May 2017 / Accepted: 26 May 2017

http://dx.doi.org/10.1097/MD.0000000000007307

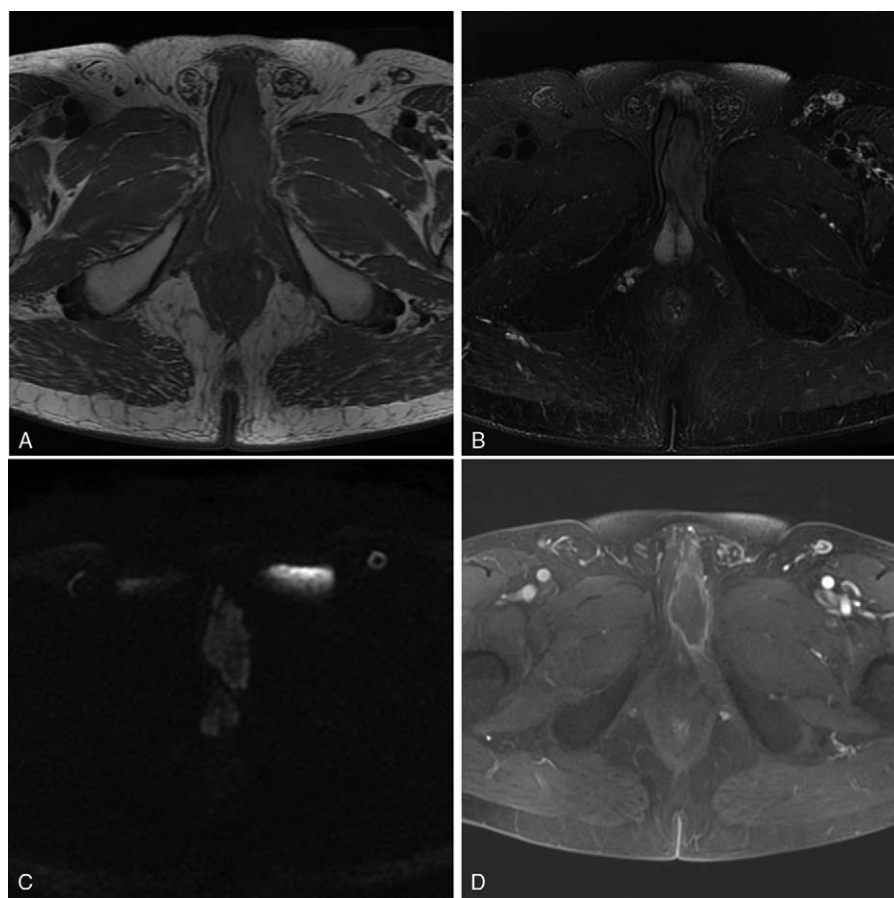


Figure 1. MRI of the pelvis: (A) T1-weighted image shows an isointense tissue mass located at the base of the left corpora cavernosa with irregular margins. (B) T2-weighted image shows slightly hyperintense lesion (about 5.2 cm × 2.4 cm) on the base of the left corpora cavernosa. (C) On DWI, the lesion is demonstrated hyperintense. (D) T1-weighted MR image with fat signal suppression, after Gadolinium injection, shows prominent ring enhancement in the lesion. DWI = diffusion weighted imaging, MRI = Magnetic resonance imaging.

After Gadolinium administration it showed prominent ring enhancement (Fig. 1D). Pelvic MRI was negative. Then, PET/CT scan was performed. The uptake in the enlarged base of left side corpora cavernosa was very intense ($SUV_{max} = 12.0$) (Fig. 2A). A mass measured in 3 cm × 2 cm with $SUV_{max} = 13.5$ was found in right hilar, and the posterior segmental bronchi of right upper lobe was obstructive (Fig. 2B). Enlargement of the mediastinal and hilar lymph nodes were also detected. Laboratory findings showed elevated serum levels of carcinoembryonic antigen (CEA, 21.17 ng/mL, normal for smoker 0–10.0 ng/mL), CA199 (192.97 U/mL, normal 0.00–37.00 U/mL), CA125 (40.5 U/mL, normal 0.00–30.20 U/mL), and CYFRA211 (6.49 ng/mL, normal 0.00–3.30 ng/mL). The patient denied biopsy of penis. The flexible bronchoscopy was arranged for him. Stenosis of the opening of apical segmental and posterior segmental bronchi of right upper lobe was found (Fig. 2C). The lateral segmental bronchi of left lower lobe was obstructed by a neoplasm (Fig. 2D). Samples were taken from both sides, and the pathological results were ASC (Fig. 3A–F). The patient denied local therapy on penis, such as penectomy and local radiotherapy, and he did not have operation opportunity for lung cancer either, so he received 2 cycles of chemotherapy consisting of carboplatin (400 mg/m², AUC = 5) and docetaxel (75 mg/m²). But his condition did not improved and penis pain became deteriorated. Serum tumor markers all increased than before,

which listed as CEA 25.21 ng/mL, CA199 219.81 U/mL, CA125 79.5 U/mL, and CYFRA211 6.81 ng/mL. Two months after his first visit to doctor, total penectomy was performed finally. During the operation, we found that the multiple infiltrative nodules in left side corpora cavernosa fused together, rigid, without distinct margins, adhered to right corpora cavernosa and corpus spongiosum. The pathological result was penile ASC derived from pulmonary (Fig. 3G–L). After operation, he did not receive chemotherapy anymore, his perineal pain relieved significantly, but he died of disease progression 11 months after penectomy (Fig. 4).

We searched literature from <http://www.ncbi.nlm.nih.gov/pubmed> and <http://med.wanfangdata.com.cn>. There are 21 papers published in English and 5 papers in Chinese, which included 39 patients of penis metastases from primary lung cancer in all; our present patient was the 40th one (Table 1).^[6–10]

3. Discussion

The common sites of metastasis of primary lung cancer are regional lymph nodes, brain, bone, adrenal gland, and lung. 15% of primary lung cancer patients have extrapulmonary symptoms as the first sign to the diagnosis.^[11] Metastasis to the penis from primary lung cancer is quite rare and is usually considered to be end-stage with short survival. The fact that the penis is not

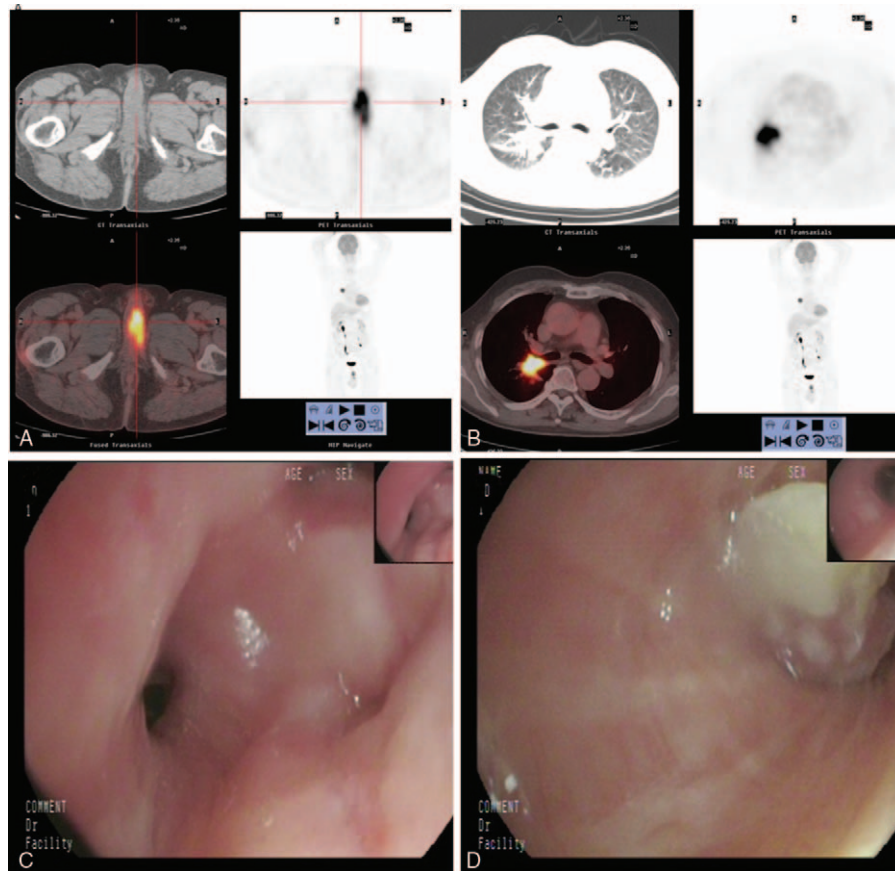


Figure 2. (A) Axial CT, PET-CT fusion, and PET images of pelvis demonstrate focus high uptake of 18F-fluorodeoxyglucose (FDG) in the base of left side corpora cavernosa; SUV_{max} of lesion is 12.0. (B) Axial CT, PET-CT fusion, and PET images of chest show a mass measured 3 cm \times 2 cm with uptake intense in the right hilar; SUV_{max} of lesion is 13.5. The posterior segmental bronchi of right upper lobe is obstructive. (C) Flexible bronchoscopy image shows stenosis of the opening of apical and posterior segmental bronchi of right upper lobe. (D) Flexible bronchoscopy image shows the lateral segmental bronchi of the left lower lobe obstructed by a neoplasm. CT=computed tomography, PET/CT= 18F-fluorodeoxyglucose positron emission tomography CT, FDG= 18F-fluorodeoxyglucose.

examined routinely may lead to the low incidence of the disease to some extent.^[12]

The median age of diagnosis is (60.5 ± 10.7) years old, although the incidence of primary lung cancer increases among older subgroups and there is also an increasing tendency in young adults.^[13] We can easily find from Table 1 that all histological types of primary lung cancer could transfer to penis. Squamous cell carcinoma is the most common one, which accounts for nearly to 60%. The location of primary lung cancer does not have relationship to the secondary penile cancer. Among the 22 patients with exactly location recorded, left side accounts for 10 cases, right side 11 cases, and 1 case we provided affects both sides of lung field simultaneously. No difference of distribution in lung lobe is found in the 40 cases.

Clinical manifestations of penile metastases vary widely. Penile mass is the most common symptom (45%), which measured (3.5 ± 2.4) cm in size, and followed by priapism (the so-called malignant priapism), penile or perineal pain, problems in voiding. There is an interesting case which presents as erectile dysfunction with the mechanism to be elucidated.^[14] The mass is most frequently located in the shaft and less commonly in the head of the penis or foreskin. One case located in foreskin (2.5%), 4 cases (10%) in glans penis, 34 cases (85%) in the shaft. Bilateral involvement of corpora cavernosa is seen in most of cases. The fact that the corpora

cavernosa communicate freely through an incomplete midline septum may be the underlying reason.

The rarity of metastatic involvement of the penis has been a clinical enigma because of its rich blood supply and being an end organ with respect to arterial, venous and lymphatic systems. It is generally accepted that lung cancer spreads to penis through the arterial route.^[2]

Almost one-third of all penile metastases are generally detected at the same time as primary tumor, whereas the remaining two-thirds are detected several months later than the discovery of primary tumor.^[15] In our review, nearly half of the patients (45%) are diagnosed at the same time, while 22.5% patients were detected (12 ± 11) months after the diagnosis of primary lung cancer. There are nearly one-third patients (27.5%) whose penis is the sole metastasis location apart from the primary lung cancer.

Besides physical examination, several diagnostic modalities can be used to confirm the clinician suspicion. Non-invasive modalities, such as ultrasound scan, color doppler ultrasonography, CT, and MRI are being increasingly used to diagnose and stage the disease. MRI can determine the tumor size, depth, and site of cancer invasion and destruction of surrounding tissues. On T1-weighted images, these lesions usually have low signal intensity, similar to the surrounding corpora cavernosa. On T2-weighted imaging, they appear non-homogenous with low to intermediate signal intensity seen clearly against the high

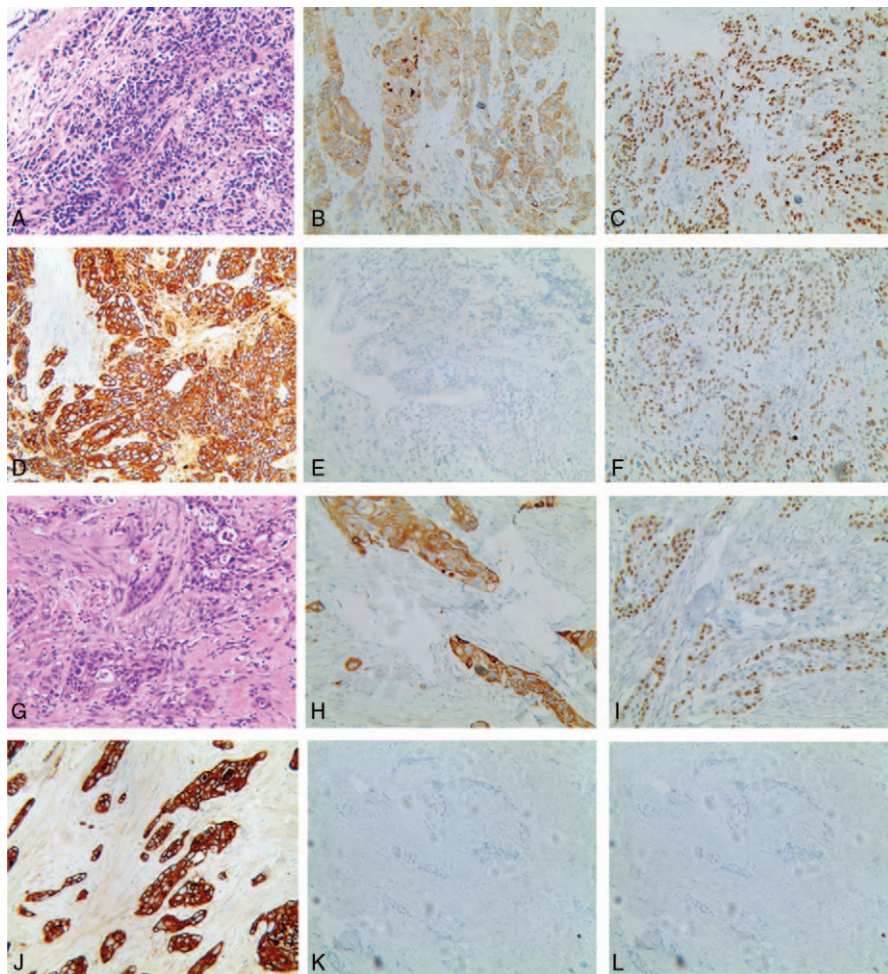


Figure 3. (A–F) Histopathological findings show adenosquamous carcinoma changing for samples from the right upper lobe of the lung. (A) HE × 200, (B) CK5,6 × 200, (C) P40 × 200, (D) CK7 × 200, (E) NapsinA × 200, (F) TTF-1 × 200. (G–L) Histopathological findings show adenosquamous carcinoma changing for samples from penis. (G) HE × 200, (H) CK5,6 × 200, (I) P40 × 200, (J) CK7 × 200, (K) NapsinA × 100, (L) TTF-1 × 200. CK5/6, P40 are markers for squamous carcinoma; CK7, NapsinA, TTF-1 are markers for adenocarcinoma. H&E=hematoxylin and eosin.

background intensity of the corpora cavernosa.^[16] PET/CT can be used to identify metastatic foci although it is so expensive. Biopsy or fine-needle aspiration helps to differentiate between metastasis and primary tumors.

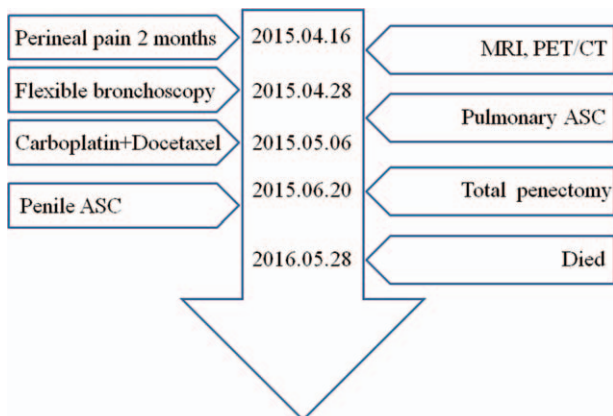


Figure 4. The timeline of interventions and outcomes for the case.

The choice of treatment for penile metastatic cancer generally depends on the histological type of the primary lung cancer, the size, location, and number of metastatic tumors, patient age, and general health status. Unfortunately, systemic therapy and local therapy (surgery, radiation therapy), or a combination of these treatments, hardly improve the prognosis. Palliative local resection or radiation treatment can relieve pain and improve the quality of life.^[17–19] In our review, 40% patients denied any therapy, 32.5% received chemotherapy, and 15% received local radiotherapy. More than two-thirds of the patients were dead at 6 months after diagnosis of the penile metastasis, less than one-fifth were alive at 12 months.^[20,21] The overall survival time is (4.5 ± 3.9) months.

In conclusion, the penis may be a site of metastasis from primary lung cancer. Since primary lung cancer remains the leading cause of cancer-related deaths worldwide and since the prolongation of survival in lung cancer patients, more cases of penile metastasis might be detected in the future. Metastasis to the penis usually indicates that the primary lung cancer is at an advanced stage and the prognosis is very poor. Early detection, then appropriate management of penile metastasis will be more important.^[22]

Table 1
Summary of penile metastasis from primary lung cancer.

No.	Age, years	Histology type	Location of lung cancer	Diagnosis means of penis metastasis	Metastatic site	Penile lesion size, cm	Clinical manifestations	Metastasis to other sites	Time metastasis to penile, M	Penis therapy	OS, M	References
1	62	AC	RS	Amputation	CC,GP	2.4	Pain	YES	ST	CTH	7	[2]
2	57	SCC	NR	Phallectomy	CC	NR	Mass	NO	ST	CTH	4	[3]
3	62	EHE	NR	Phallectomy	CC,CS	4	Mass, pain	NO	7	CTH	2	[5]
4	67	SCC	NR	Phallectomy	CC,CS,GP	6.5	Mass, UR	NO	36	CTH+RTH	6	[5]
5	33	EC	NR	NR	CC,CS	NR	UR, priapism	YES	NR	NR	<1	[6]
6	43	SCC	NR	Amputation	CC	NR	Mass, priapism	YES	NR	NO	3	[6]
7	45	SCC	NR	NR	CC,CS,GP	NR	UR	YES	NR	NO	NR	[6]
8	49	SCC	RMB	FNA	CC,CS	5	Mass	YES	6	TTH	>15	[6]
9	50	SCC	NR	NR	CC	NR	Priapism	NR	NR	NO	NR	[6]
10	50	EPC	LS	FNA	CC,CS	3	Dysuria, pain	NO	NR	CTH+RTH	4	[6]
11	51	SCC	NR	NR	CC	NR	Mass, priapism	NO	NR	CTH	NR	[6]
12	51	AC	LLL	FNA	CC,CS,GP	2	Dysuria, SP, ulceration	YES	ST	CTH	<2	[6]
13	52	SCC	LMB	FNA+ autopsy	CC,CS	10	Pollakisuria, BU	YES	ST	NO	1	[6]
14	54	LCC	NR	NR	CC	NR	Mass	YES	NR	RTH	7	[6]
15	55	EPC	RML	FNA	GP	2.5	Ulceration	NO	ST	NO	6	[6]
16	55	AC	LUL	FNA	CC,CS,GP	1	SP, pain	YES	ST	RTH	2	[6]
17	57	NSCLC	LMB	Amputation	CC	2	ED, mass	YES	ST	RTH	NR	[6]
18	59	AC	RLL	FNA	CC	1.8	Mass	YES	1	CTH+RTH	>5	[6]
19	64	SCLC	NR	Amputation	GP	NR	Mass	NR	NR	NO	>12	[6]
20	65	SCC	NR	NR	NR	NR	Mass	YES	NR	CTH	3	[6]
21	65	SCC	NR	FNA+ autopsy	CC,GP	NR	Priapism	YES	ST	RTH	3	[6]
22	67	SCC	NR	NR	CC	NR	SP	YES	NR	NO	<1	[6]
23	67	SCC	RLL	FNA+ autopsy	CC,CS,GP	NR	UR, priapism	YES	17	NO	<1	[6]
24	67	SCC	RLL	FNA	CC	3	Mass	YES	24	NO	<1	[6]
25	67	SCC	NR	FNA	CC,CS	NR	Dysuria	YES	6	No	2	[6]
26	67	SCC	LUL	FNA	Foreskin	0.6	Mass	NO	ST	CTH	6	[6]
27	69	SCC	NR	Amputation	CC	NR	Pain, priapism	NR	NR	NO	3	[6]
28	70	SCC	NR	NR	CC,CS	NR	Pain, priapism	YES	NR	NO	2	[6]
29	72	AC	NR	NR	CC	NR	UR, priapism	NR	NR	NO	1	[6]
30	75	SCC	RH	FNA	CC	6	Mass	YES	6	RTH	3	[6]
31	75	SCC	RUL	FNA	CC	1	Mass	NO	ST	CTH	NR	[6]
32	77	SCLC	NR	FNA	GP	1	Mass	YES	6	CTH	3	[6]
33	78	SCC	RLL	Autopsy	CC	4	Mass	YES	ST	NO	<1	[6]
34	60	AC	LUL	FNA	CC,CS,GP	NR	Priapism	YES	ST	CTH	3	[7]
35	81	SCC	RUL	FNA	CC,CS	3.9	Priapism, pain	YES	ST	RTH	3	[8]
36	55	SCC	LH	FNA	CC,CS	2	Mass	NO	ST	CTH	6	[9]
37	46	SC	RUL	FNA	CC	NR	Priapism, pain	NO	ST	NO	12	[10]
38	51	AC	LLL	Phallectomy	GP	NR	Pain, ulceration	YES	ST	CTH	3	[10]
39	68	SCC	LH	FNA	CC,CS	NR	Priapism	NO	ST	NO	12	[10]
40	64	ASC	RS+LS	Phallectomy	CC	0.5	Pain	YES	ST	CTH	>14	Present case

AC=adenocarcinoma, ASC=adenosquamous carcinoma, BU=burning on urination, CC=corpora cavernosa, CS=corpus spongiosum, CTH=chemotherapy, EC=epithelial carcinoma, ED=erectile dysfunction, EHE=epithelioid hemangioendothelioma, EPC=epidermoid carcinoma, FNA=fine needle aspiration, GP=glans penis, LCC=large cell carcinoma, LH=left hilar, LLL=left lower lobe, LMB=left main bronchus, LS=left side, LUL=left upper lobe, NR=not recorded, NSCLC=non-small cell lung cancer, OS=over survival time after penile metastasis, RH=right hilar, RLL=right lower lobe, RMB=right main bronchus, RML=right middle lobe, RS=right side, RTH=radiotherapy, RUL=right upper lobe, SC=sarcomatoid carcinoma, SCC=squamous cell carcinoma, SCLC=small cell lung cancer, SP=swelling of penis, ST=same time, TTH=target therapy, UR=urinary retention.
 No. 40th is the patient we present, No. 1–39 from the literature.

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