



Penile Metastases: A Report of 2 Cases and Literature Review

Salim Said Al Busaidy^{1*}, Said Abdallah Al-Mamari¹, Qais Mohamed Al Hooti¹, Atheel Ahmad Kamona² and Murtadha Taqi Al Qubtan³

¹Department of Urology, Royal Hospital, Oman

²Department of Radiology, Royal Hospital, Oman

³Department of Colorectal Surgery, Royal Hospital, Oman

Abstract

Penile metastases represent a rare clinico-pathological entity which carries an extremely grim prognosis regardless of the primary tumor site. Their origins are most frequently from the urogenital organs and rectum and they are particularly aggressive with a rapid progression to death. Due to the scarcity of the reported cases, there are no international guidelines or consensus on management.

We present 2 cases of penile metastases arising from rectal and bladder carcinomas and review the literature. The patients presented with rectal bleeding and hematuria respectively. The first case had a stage T4 N1 rectal tumor which was initially managed with neoadjuvant chemo-radiotherapy followed by laparoscopic low resection of the rectal tumor, colorectal anastomosis and defunctioning ileostomy. Penile metastases occurred within 3 months and the patient was further treated with external beam radiation therapy. The second patient presented with a stage T3b N1 bladder tumor and had poor general health. Penile metastases were also noted synchronously at the time of presentation and chemotherapy was advised, however he did not consent to the treatment.

Keywords: Penile metastasis; Malignant priapism; Bladder cancer; Penile tumor; Rectal cancer

Introduction

Despite harboring an abundant vascularization with extensive communication to the neighboring pelvic organs, the penis is a very rare site for metastatic disease and this paradox remains unexplained.

The majority of reported cases of penile metastases arise from the genitourinary tract, especially the bladder and the prostate. The other common sites are the rectum and sigmoid colon however less frequent, distant sites have also been described [1-3].

Total penectomy has been advocated by some authors for isolated penile secondary lesions or as an alternative to palliative radiotherapy in the presence of severe symptoms. Radiotherapy and chemotherapy have also been suggested for locally advanced malignancies while chemotherapy alone is reserved for disseminated diseases [2-4]. The prognosis is very poor and approximately half of the patients are reported to die within one year of the diagnosis [2-4]. Furthermore, there is no consensus on the management of the disease.

Case Presentation 1

A 54-year-old man with a history of hypertension, diabetes mellitus and coronary artery bypass presented with rectal bleeding, anemia and weight lost. The carcinoembryonic antigen (CEA) was 26 ng/ml at presentation. A colonoscopy revealed a circumferential lower rectal tumor which was histopathologically reported as a moderately differentiated papillary adenocarcinoma. An abdominal computed-tomography (CT) scan revealed enlarged para-aortic lymph nodes and a magnetic resonance imaging (MRI) study of the pelvis showed a 10cm tumor infiltrating the anorectal junction with suspicion of invasion of the prostate. The patient had neoadjuvant chemo-radiotherapy to the pelvis with 3D Conformal Radiation Therapy (3DCRT), mixed photons to a dose of 50.4 Gy/28. This produced significant disease regression as evidenced by a repeat MRI and subsequently he underwent a low laparoscopic resection of the rectal tumor and colorectal anastomosis with defunctioning ileostomy. The final histopathology revealed a papillary adenocarcinoma and reactive hyperplasia in small adjacent lymph nodes. Four months post-operatively the CEA level was elevated

OPEN ACCESS

*Correspondence:

Salim Said Seif Al Busaidy, Department of Urology, Royal Hospital, PO Box 1201, Postal Code 111, Muscat, Oman, Tel: (+968) 99326041; (+968) 24541337;

E-mail: salimalbusaidy@hotmail.com

Received Date: 08 Aug 2016

Accepted Date: 24 Sep 2016

Published Date: 28 Oct 2016

Citation:

Al Busaidy SS, Al-Mamari SA, Al Hooti QM, Kamona AA, Al Qubtan MT. Penile Metastases: A Report of 2 Cases and Literature Review. *Clin Surg*. 2016; 1: 1167.

Copyright © 2016 Al Busaidy SS. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

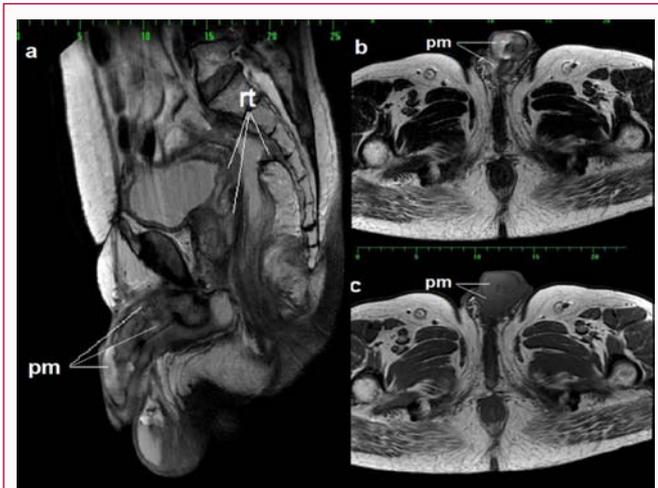


Figure 1a-b: Sagittal and axial T2-weighted images showing multiple penile metastases (pm) which are hyperintense in signal intensity, along with evidence of rectal tumour (rt) recurrence directly invading the prostate, the seminal vesicles and the presacral fascia as seen on the sagittal sequence. c. T1-weighted axial image showing a penile mass which is iso-/hyperintense.

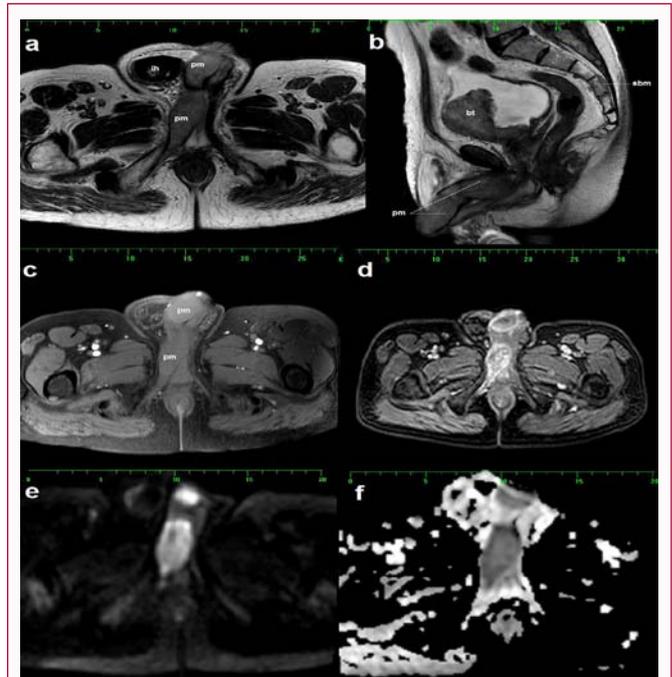


Figure 3a-b: Axial and sagittal T2-weighted images showing multiple penile metastases (pm) which are of intermediate signal intensity, along with the large urinary bladder tumor (bt) and sacral bones metastasis (sbm), beside a right inguinal hernia (ih). c-d. T1-weighted axial fat suppression with and without intravenous Gadolinium, showing multiple penile masses which are iso-/hyperintense on the non-contrast T1-weighted image, and intensely and heterogeneously enhancing on the post-contrast study. e-f. Diffusion-weighted images (b-factor 600 sec/mm) and ADC map sequences showing features of diffusion restriction.

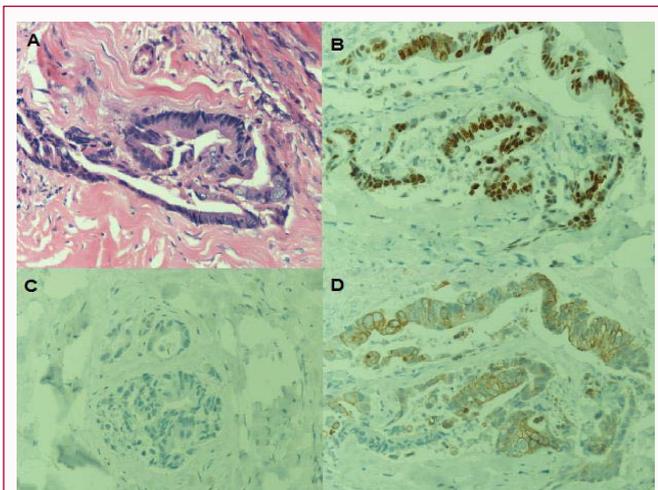


Figure 2: Histopathology of the penile lesion showing features of metastatic cancer from rectal adenocarcinoma. A. H&E at 20x. B. CDX2 positive at 20x. C. CK7 negative at 20x. D. CK20 positive at 20x.

at 122 ng/ml and a pelvic MRI revealed a recurrent 1.7 x 1.2 cm ill-defined mass at the anorectal junction, a 4 cm presacral mass and newly developed multiple necrotic penile masses (largest 3.5 x 2.7 cm) consistent with metastases (Figure 1). An incisional biopsy of one of the penile nodules confirmed metastatic rectal adenocarcinoma, positive for CK20 and CDX2 but negative for CK7 and PSA (Figure 2). The patient was prescribed a combination of Capecitabine and Bevacizumab as palliative chemotherapy. A repeat pelvic MRI at 6 months showed increase in size of the penile masses as well as significant progression of the rectal tumor with direct invasion of the ureters, seminal vesicles, prostate and urinary bladder. The patient's general condition rapidly deteriorated and he died 11 months after the initial presentation.

Case Presentation 2

A 70 year old male presented with a 5 month history of painless hematuria. He was a chronic smoker with other comorbidities. A suprapubic mass was clinically palpable and another firm painless

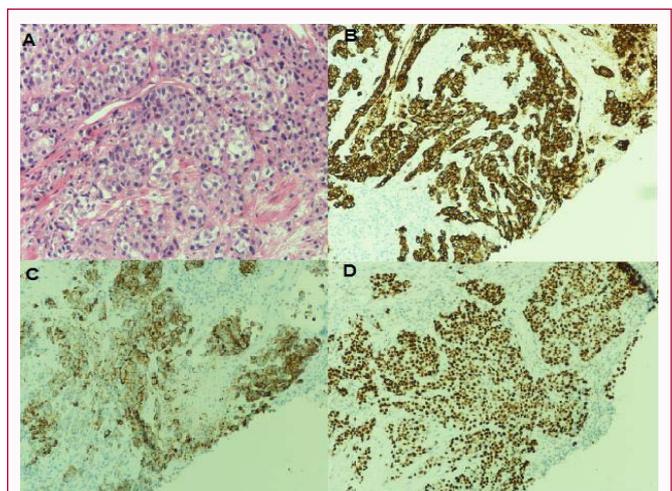
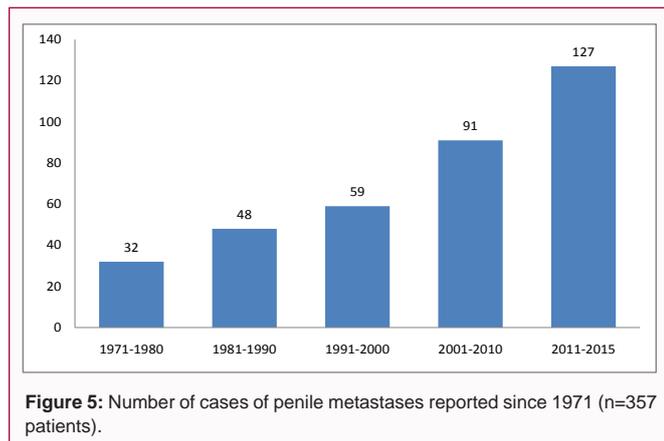


Figure 4: Histopathology of the penile lesion showing features of metastatic urothelial cancer. A: H&E at 3 x 20 x. B. CK7 positive at 10 x. C. CK20 positive at 10 x. D. p63 positive at 10 x.

mass, 5 x 4 cm was palpable at the root of the penis. An abdominal CT scan was performed which demonstrated a 7.2 x 5.7 x 8 cm bladder tumor with normal upper urinary tracts. Routine laboratory investigations were normal and a transurethral resection of the tumor was performed which histopathologically revealed a high grade pT2 urothelial carcinoma. Chest, abdomen and pelvic contrast enhanced CT scan revealed stage IIIB N1 disease and a pelvic MRI demonstrated an infiltrating bladder tumor with enlarged lymph nodes, a metastatic



lesion of the sacral bone and multiple penile metastases (Figure 3). The penile masses were seen at the right corpus cavernosum, the largest being 4 x 2.2 cms.

An incisional biopsy of a penile lesion confirmed the presence of a metastasis, consistent with urothelial cancer and the cells were positive for CK7, CK20, P⁶³ and negative for PSA (Figure 4). Chemotherapy was offered although the patient did not consent for the treatment.

Discussion

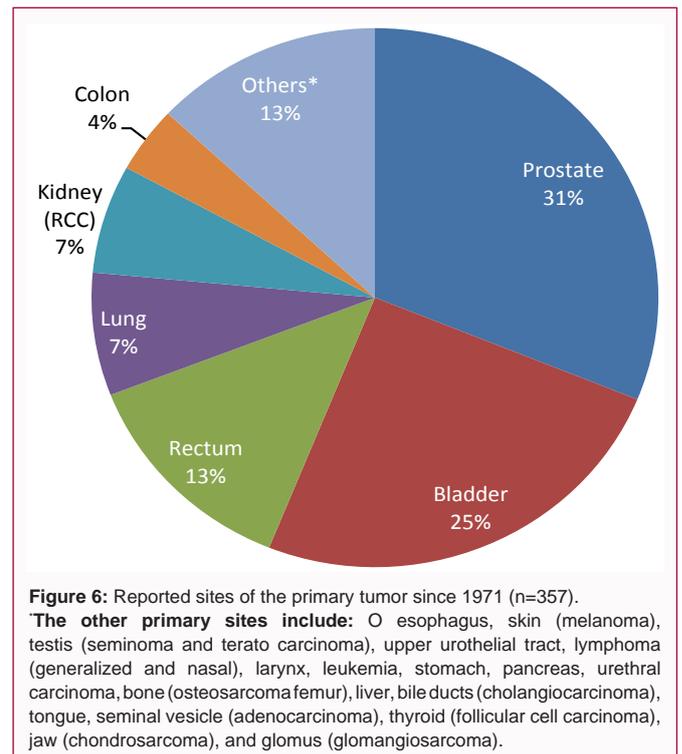
A literature review was conducted however in view of the difficulty in retrieving information before 1970, data were obtained from References [1,5,6]. The data from 1971 to the present day were collected by a review of PubMed/Medline database using keywords “penile metastasis” and “malignant priapism”.

The number of patients reported until 1970 was 165 whereas 357 cases have been documented from 1971 to date excluding the present study (Figure 5). An overall total of 522 patients have been reported in the literature. Figure 5 shows a steady increase in the number of reported cases over the decades since 1971. There is no evidence to explain this increase but it may be attributable to the easier reporting opportunities and the widespread availability of the internet rather than a genuine change in the disease pattern.

Eberth [7] reported the first case of penile metastasis in the literature in 1870 from a rectal carcinoma and since then there have been few isolated cases and only a handful of small series dealing with this subject. Ellis and Epstein [8] presented the largest series to date comprising of 29 cases of penile metastases from prostatic adenocarcinoma.

The distribution of the primary tumor sites since 1971 has been reviewed in this study (Figure 6) which compares with that of Cherian et al. [9], who documented 360 cases [9].

The average age at presentation depends on the primary disease, which is 60-70 years for cancers of the pelvic organs, kidney and lung, however the age is much younger for cancers of the skin and nasopharynx [1,3]. Clinical manifestations of penile metastases vary widely and usually include penile nodules, penile pain, malignant priapism and skin lesion which must be differentiated from pre-malignant and malignant lesions, such as Bowen’s disease, erythroplasia of Queyrat and squamous cell carcinoma [10]. Some investigators have suggested that malignant priapism is the most commonly encountered sign in penile metastasis and it is commonly suspected in any patient with malignant disease who develops



priapism [1,11-13]. However other series have documented penile nodule as the most frequent sign (60%), followed by malignant priapism (20-53%) [3,10,14]. Other less common presentations include obstructive voiding symptoms and hematuria.

The interval between diagnosis of the primary tumor and the penile metastasis varies widely, ranging from a synchronous presentation to 16 years from the initial treatment, especially for relatively slow growing malignancies such as prostate adenocarcinomas [3,15,16]. Tu SM et al. [17], found a mean interval of 50 months among 12 patients with primary prostate carcinomas [17], while Zhu et al. [4], reported a mean interval of 26.4 months in 8 patients with primary bladder cancers [4]. In exceptional cases, penile metastases have been found before the diagnosis of the primary which was only reached after further investigations were initiated by the result of the penile biopsy [10].

Prostatic cancers with a propensity to develop penile metastases display considerably more ductal features histopathologically than the general group [8]. This has been documented earlier by Tu SM et al. [17], who also observed the likelihood of these tumors spreading to viscera rather than to bones [17]. Furthermore, they noted the tendency to develop persistent or recurrent urinary symptoms despite androgen-suppression therapy [17].

In 1956, Paquin and Roland [1] proposed several mechanisms to explain the spread of malignant cells to the penis which are still in favor today. These mechanisms include retrograde venous spread which is considered as the commonest [9], retrograde lymphatic spread, arterial spread, direct extension and secondary embolization [10,18]. Iatrogenic tumor spread by instrumentation is controversial since isolated corpus spongiosum involvement is an extremely rare event [10]. The corpus cavernosum remains the commonest site of penile metastases, but other anatomical structures can also be involved such as the penile skin, the corpus spongiosum and the glans [10,11].

Table 1: Recent studies of penile metastases from urothelial bladder carcinoma.

Study	Number of cases	Treatment of the penile lesion	Patients progress at the time of publication
Zhang K et al. [3]	3	Penectomy	- 1 patient died within 5 months - 1 patient was in poor condition at one month - 1 patient was alive at 18 months
Kumar N et al. [23]	2	EBRT	- 1 patient had a partial response and improvement of quality of life - 1 patient died at 2 months
Zhu YP et al. [4]	8	- 4 patients treated with penectomy + chemotherapy - 1 patient treated with EBRT only - 3 patients treated with chemotherapy only	Mean survival: 11.4 months (range: 4- 23)
Chaux A et al. [10]	6	Not available	Mean survival: 6 months (range 0.25-18)
Berkmen et al. [2]	7	- all patients treated with total penectomy - 1 patient had adjuvant chemotherapy	Mean survival: 12.5 months (range 6-21)

The accuracy of MRI imaging has been well documented especially when the lesions are right in the middle of the corpora cavernosa or spongiosa, a feature which differentiates them from primary lesions. These lesions may appear in T2 iso-/hyper intense as in our cases, or hypointense and showing non-specific enhancement after Gadolinium injection [19,20]. The patient's clinical history and the multiplicity of the lesions are valuable clues in reaching the diagnosis of penile metastasis. The role of (18F-) fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (¹⁸F-FDG PET/CT) has also been documented especially for urothelial tumors [21,22].

The diagnosis is usually confirmed by an incisional biopsy of the nodule as was performed in our patients however fine needle aspiration cytology is adequate [3,23]. Penile metastases from prostatic adenocarcinoma are associated with high Gleason's score (≥ 8) [17] which may not always produce high serum PSA levels [24]. High serum CEA can also be found surprisingly under these clinical circumstances [17].

Secondary penile lesions generally appear in the setting of multiple metastases, whatever the primary sites [17]. Few isolated penile metastases have also been reported [2,25-28]. Total phallectomy should only be advocated for isolated penile metastasis provided the primary tumor has been totally excised and shows no recurrence. The procedure is also justified for palliation when the patient presents with malignant priapism or ulcer with intractable pain. Other possible management options, namely radiotherapy and chemotherapy are reserved for unresectable primary lesions.

In a review by Paquin and Roland [1] in which 21 patients with penile metastases from bladder primaries were treated by penectomy or radiotherapy, there was rapid progression to death with a mean interval of 3.95 months (range 1-17) regardless of the treatment rendered. More recent publications have shown only a modest improvement of a few months in the mean overall survival and the prognosis remains very poor with approximately half of the patients succumbing to the disease within one year of the diagnosis (Table 1). Demonstrates the treatment options and prognoses of recent studies of urothelial bladder cancers with penile metastases.

Conclusion

Penile metastases from pelvic or distant organs area rare clinico-pathological entity and there are no guidelines nor consensus regarding the optimal management of this disease. The prognosis is very poor regardless of the primary site or the treatment offered. Further studies and research may shed more light and information on the more efficacious treatment options.

References

1. Paquin AJ Jr, Roland SI. Secondary carcinoma of the penis. A review of the

literature and a report of nine new cases. *Cancer*. 1956; 9: 626.

- Berkmen F, Ayyildiz A. Metastatic penile carcinoma: a study of nine cases and review of the literature. *Afric J Urol*. 2005; 11: 22-26.
- Zhang K, Da J, Yao HJ, Zheng DC, Cai ZK, Jiang YQ, et al. Metastatic tumors of the penis: a report of 8 cases and review of the literature. *Medicine (Baltimore)*. 2015; 94: e132.
- Zhu YP, Yao XD, Zhang HL, Shen YJ, Huang D, Ye DW. Penile metastasis from primary bladder cancer: a study of 8 cases and review of the literature. *Onkologie*. 2012; 35: 196-199.
- Abeshouse BS, Abeshouse GA. Metastatic tumors of the penis: a review of the literature and a report of two cases. *J Urol*. 1961; 86: 99-112.
- Weitzner S. Secondary carcinoma in the penis. Report of three cases and literature review. *Am Surg*. 1971; 37: 563-567.
- Eberth CJ. Krebmetastasen des corpus cavernosum penis. *Virch Arch*. 1870; 51: 145-145.
- Ellis CL, Epstein JI. Metastatic prostate adenocarcinoma to the penis: a series of 29 cases with predilection for ductal adenocarcinoma. *Am J SurgPathol*. 2015; 39: 67-74.
- Cherian J, Rajan S, Thwaini A, Elmasry Y, Shah T, Puri R. Secondary penile tumours revisited. *Int Semin Surg Oncol*. 2006; 3: 33.
- Mearini L, Colella R, Zucchi A, Nunzi E, Porrozzio C, Porena M. A review of penile metastasis. *Oncol Rev*. 2012; 6: e10.
- Moricchetti D, Mazzucchelli R, Lopez-Beltran A, Cheng L, Scarpelli M, Kirkali Z, et al. Secondary neoplasms of the urinary system and male genital organs. *BJU Int*. 2009; 104: 770-776.
- Hizli F, Berkmen F. Penile metastasis from other malignancies. *Urol Int*. 2006; 76: 118-121.
- Otta R, Gordillo C, and Olivier C. Early penile metastasis as the first sign of urothelial carcinoma spread. *Int J Urol*. 2013; 20: 740.
- Chaux A, Amin M, Cubilla AL, Young RH. Metastatic tumors to the penis: a report of 17 cases and review of the literature. *Int J Surg Pathol*. 2011; 19: 597-606.
- Pomara G, Pastina I, Simone M, Casale P, Marchetti G, Francesca F. Penile metastasis from primary transitional cell carcinoma of the renal pelvis: first manifestation of systemic spread. *BMC Cancer*. 2004; 4: 90.
- Krpina K, Markić D, Spanjol J, Valencić M, Fuckar Z. Penile metastases of prostate cancer. *Acta Clin Croat*. 2011; 50: 431-433.
- Tu SM, Reyes A, Maa A, Bhowmick D, Pisters LL, Pettaway CA, et al. Prostate carcinoma with testicular or penile metastases. Clinical, pathologic, and immunohistochemical features. *Cancer*. 2002; 94: 2610-2617.
- Murhekar KM, Majhi U, Mahajan V, Satheesan B. Penile metastasis from rectal carcinoma. *Indian J Cancer*. 2007; 44: 155-156.
- Rocher L, Glas L, Cluzel G, Ifergan J, Bellin MF. Imaging tumours of the penis. *Diagn Interv Imaging*. 2012; 93: 319-28.

20. Lau TN, Wakeley CJ, Goddard P. Magnetic resonance imaging of penile metastases: a report on five cases. *Australas Radiol.* 1999; 43: 378-81.
21. Rouanne M, Alhammadi A, Vilain D, Radulescu C, Leuret T. Value of positron emission tomography in diagnosing synchronous penile metastasis from urothelial bladder cancer. *World J Surg Oncol.* 2015; 13: 276.
22. Wang YL, Fang N, Zeng L, Wu ZJ, Cui XJ. 18F-FDG PET/CT Findings of Metastasis to Spongy Body of Penis From Urothelial Carcinoma of Bladder. *Clin Nucl Med.* 2016; 41: e251-252.
23. Kumar N, Bhattacharyya T, Mandal AK, Gupta N, Rajwanshi A, Kumar R. Penile metastasis secondary to bladder cancer: a report of two cases. *Indian J Palliat Care.* 2014; 20: 57-60.
24. Pierro A, Cilla S, Digesù C, Morganti AG. Penile metastases of recurrent prostatic adenocarcinoma without PSA level increase: A case report. *J Clin Imaging Sci.* 2012; 2: 44.
25. Demuren OA, Koriech O. Isolated penile metastasis from bladder carcinoma. *Eur Radiol.* 1999; 9: 1596-8.
26. Thyavihally YB, Tongaonkar HB, Gupta S, Gujral S. Primary seminal vesicle adenocarcinoma presenting as isolated metastasis to penis responding to chemotherapy and hormonal therapy. *Urology* 2007; 69: 778.e1-3.
27. Sofikerim M, Gülmez I, Tokat F, Er O, Gülmez I. Epidermoid carcinoma of the lung with isolated penile metastasis. *Can J Urol.* 2007; 14: 3643-3645.
28. Liu S, Zeng F, Qi L, Jiang S, Tan P, Zu X. Malignant priapism secondary to isolated penile metastasis from a renal pelvic carcinoma. *Can Urol Assoc J.* 2014; 8: E558-560.