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THE RARE CASE OF NON-METASTATIC PENILE CANCER IN UROLOGY SERVICE OF ALIABAD TEACHING HOSPITAL

Penile cancer is a very rare cancer of urogenital system of males which occurs in one in every 100000 individuals annually. Senescence, poor personal hygiene, and existence of prepuce are the contributing risk factors. About 95% of the cases are of squamous cell carcinoma type. Metastasis to the nearby lymph nodes indicates poor prognosis. Hence, physical examination, especially palpation of the inguinal region is vital to diagnose the disease and predict the prognosis. The best treatment choice is surgery, and, in case of lymphatic metastasis to the inguinal region, dissection of the lymph nodes.

An 80-year-old man, complaining about a painless ulcer in his penis, was hospitalized on July 14, 2019 in the urology service of Aliabad Teaching Hospital. The patient had been suffering from the ulcer for three years. The ulcer had been small in size for the first two years. It, then, had enlarged and caused urinary retention for one year. Thus, cystostomy had been performed. The ulcer was inspected red which was occupying the distal half of the penis. Moreover, the glans was completely destroyed. However, the inguinal lymph nodes were found normal in size in palpation. Biopsy indicated a squamous cell carcinoma. A partial penectomy was consequently carried out.

This particular case implies that penile ulcers especially in the glans could be the primary sign of a penile cancer. Therefore, the patient had better be consulted regarding biopsy, pathological examinations and early diagnosis and treatment.

Key words: Penile cancer, squamous cell cancer, penectomy.

Introduction

Penile cancer is the most rare tumor of male genitourinary system, the annual occurrence of which is 1/100000 individuals in the world. It occurs a lot less frequently in the Jewish and Islamic societies due to early customary circumcision, suggesting that circumcision decreases the likelihood of a penile cancer to a great extent.

Common risk factors of the disease include chronic inflammatory diseases such as phimosis, balanoposthitis, balanitis xerotica obliterans, phototherapy with ultraviolet radiation, multiple sexual partners, and history of condyloma, cigarette smoking, and Human Papilloma Virus types 6, 11, 16 and 18 which can be transmitted from the infected partner during sexual intercourse. Smegma is thought to be carcinogenic, so circumcision decreases chances of developing the disease.

In terms of microscopic classification, more than 95% of the cases are squamous cell carcinoma. It is believed that SCC originates from penile intraepithelial neoplasia, or *in situ*.

Pathogenesis of the disease includes transcription of viral oncogenes E6 and E7 by cells which are

infected with Human Papilloma Virus types 16 and 18. The E6 oncogene targets P53 gene, but the E7 oncogene targets RB1 gene. P53 and RB1 are tumor suppressor genes, which prevent overgrowth of body cells. Transformation of these genes by E6 and E7 results in uncontrollable growth of cells and formation of cancers, as a result, Glans penis is involved in around 48% of the cases [1-6].

Clinical manifestations of the disease varies a lot, the beginning sign of which could range from a small area of erythema and skin induration to a deep ulcer or lesion. As the disease develops, pain, prickling, secretions, bleeding, and mephitis would likely appear. Clinical symptoms might be delayed due to psychological factors and the patient would not want to see a doctor in the early stages of the disease.

Size, location, and other characteristics of the lesion and the meatus should thoroughly be assessed in physical examination of the patient. Furthermore, palpation of the inguinal lymph nodes is vitally important because the tumor's initial lymphatic metastasis targets the superficial and deep inguinal lymph nodes and then the pelvic and periaortic lymph nodes. Metastasis to distant organs, which is seen only in the late stages of the disease, is not usual and occurs in only 1-10 percent of the cases.

Surgical intervention approach is chosen according to the location and size of the lesion, and patient's demand in order not to remove the penis so as to have sexual intercourse. Treatment of Penile Intraepithelial Neoplasia (PIN) includes topical.

Imiquimod or 5-Fluorouracil, circumcision, local excision, and laser ablation therapy. If the tumor is well-differentiated, a penile sparing surgery, which includes removing of the lesion and maintaining the penis, is carried out. In case the inguinal lymph nodes are involved, dissection and removal of the lymph nodes is recommended.

It is considered one of the rarest cases of male genitourinary system, especially in societies where boys are circumcised. In Afghanistan, where majority of male population are circumcised, it is very rare. Nonetheless, the pathology can occur. As a result, all penile lesions should be assessed thoroughly in terms of being malignant and treated accordingly. On the other hand, penile cancers usually suggest penile amputation, which is unacceptable to the patient. For instance, in the case being presented, the patient, in spite of being very elderly, had not agreed with penile amputation for three years. Amputation of penis could cause psychological problems in the patient, so the treatment of the condition is also somewhat challenging.

Material. Case Report

On August 14, 2019, an 83-year-old man was referred to and hospitalized in Aliabad Teaching Hospital, Urology Service. His chief complaints included an ulcer with prickling and mild pain in the distal end of his penis. According to his explanation, the problem had begun as erythema and induration in the glans three years ago. The erythema and induration had then increased and enlarged gradually

over time and had ultimately developed to an ulcer. The ulcer had, subsequently, increased in size, and besides destroying the glans, it had developed toward the shaft of the penis. As the ulcer had been enlarging, mild pain, prickling, secretions, and nasty smell had appeared. Consequently, since one year before his referral to hospital, he had been suffering from dysuria and then urinary retention. The patient was first taken to a primary clinic, where he was fitted with a suprapubic catheter. As the patient explained, he had first used topical over-the-counter medicine. Then, he had just agreed with dressing of the wound. The doctors he had referred to had recommended biopsy and amputation of the penis, which he had rejected.

The patient was not complaining about any sexually transmitted diseases. Similarly, he was not a smoker and had only one sexual partner. Nobody else in his family had had the same problem and all his other organs and systems had normal function.

In physical examination of the external genitourinary organs, a big ulcer was inspected. The ulcer had completely occupied glans penis and shaft up to the base of the penis. Moreover, the ulcer was red in color with some white spots of fibrin on it. Some black and necrotic ulcers were visible on the edges of the lesion. In addition, necrotic points were noticed in the tip of penis, whereas meatus was not visible (figure 1). Scrotum was normal in inspection, while the suprapubic catheter was visible in the suprapubic region. Inguinal region was symmetrical and no prominence was found in the area. The patient was slim and cachexic. Palpation of the inguinal region revealed no abnormality and no sign of enlargement of the lymph nodes was found.



Figure 1: showing large penile lesion involving glans and penile shaft Laboratory examination of urine read as below:

Glucose nil
 pH... 6
 Albumin... (+)
 RBC... 0-1
 WBC 30-32
 Epithelial cells... 2-3
 Laboratory examination of blood was reported as following... Monocytes... 2%
 Eosinophils... 2%
 Lymphocytes... 35%
 Neutrophils... 61%
 WBC 6000
 Hb... 12.6
 Urea 37mg/dl
 Creatinine 0.97mg/dl
 Glycaemia... 126mg/dl
 HBS Negative
 HCV Negative
 HIV Negative

In addition to the mentioned laboratory examinations, a chest x-ray was carried out, in which the lungs looked normal and no sign of metastasis was seen.

A biopsy of the ulceration was performed which indicated squamous cell carcinoma with moderate differentiation. Before the surgical operation was carried out, abdominopelvic and inguinal ultrasonography had been ordered to assess lymph nodes which was reported as normal.

The patient, with the diagnosis of moderately differentiated squamous cell carcinoma, was prepared for a partial penectomy. After using spinal anesthetics in supine position and draping, a circular incision was made 1cm proximal to the tumor. All superficial vessels identified and ligated. The corpus spongiosum was dissected and separated from corpora cavernosa. The corpora cavernosa were transected and the corpus spongiosum was transected then, all bleeding points controlled. The urethra was then spotted and brought out on the ventral surface of penile stump. Corpora cavernosa were repaired in tow layers. The meatus was inverted and implanted into the skin of the base of the penis afterwards. A Foley catheter was inserted and the patient, whose vital signs were normal, was transferred to recovery room (figure 2).

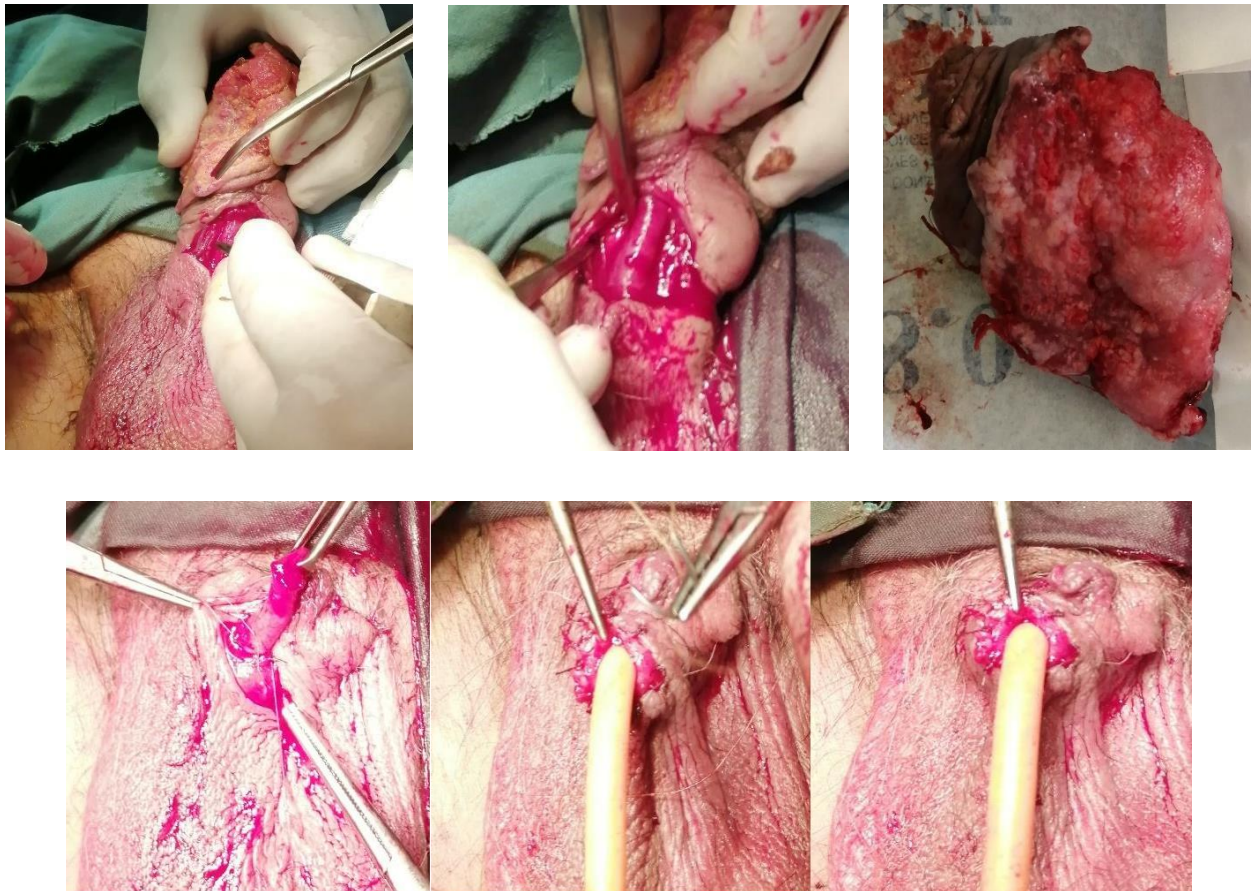


Figure2: showing steps of operation with excised tumor and final appearance of urethral opening with foley catheter applied to it.

Discussion

Penile cancer is the most uncommon malignant tumor of male genitourinary system, which is reported in 1/100000 people every year. Similarly, this was the first penile cancer case ever recorded in urology service of Aliabad Teaching Hospital.

The most common type of primary penile cancer is squamous cell carcinoma which constitutes more than 95% of the cases [7, 8, 9], as was the reported case.

The risk factors which are thought to contribute to the occurrence of the condition include old age, chronic inflammatory diseases of glans and prepuce such as phimosis, smoking, multiple sexual partners, Human Papilloma Virus, which is transmitted from the infected individuals, poor hygiene of genital organs, positive history of condyloma, and radiotherapy with ultraviolet radiation [2, 9, 4, 5, 6]. The patient discussed in this case was elderly, 80 years old. However, he didn't complain about any chronic inflammatory disease of glans and prepuce, was not a smoker, had only one sexual partner, and didn't explain positive history of condyloma. The patient had not carried out any laboratory exams to detect HPV, which might have contributed to the disease, besides old age.

Circumcision, which is a cultural and religious matter in Jewish and Muslim societies, is considered to decrease the likelihood of the disease to as many as 5 times because smegma, which located underneath the prepuce, is carcinogenic. The mentioned patient had been circumcised in his childhood.

Primary penile cancers metastasize via lymphatic vessels to superficial and deep inguinal, and pelvic lymph nodes [10, 11]. Moreover, they can metastasize via veins to the liver, the lungs, bones, the brain, the heart, the skin, and even to the breasts [8, 10,]. Lymphatic metastasis of the cancer implies poor prognosis. Therefore, palpation of the inguinal lymph nodes in physical examination of the patients is deadly essential [6]. Nonetheless, in spite of normal lymph nodes, there is a possibility of 20% micro metastasis [2]. CT-Scan, MRI, and PET could be used in order to better detect lymphadenopathy in the inguinal and pelvic regions

[10,4]. The inguinal lymph nodes were palpated normal in physical examination. Furthermore, pelvic, inguinal and abdominal ultrasonography were found normal. The chest x-ray, ordered to find out metastasis to the lungs, were normal. On the other hand, CT-Scan, MRI, and PET, to further investigate inguinal lymph nodes, and bone scanning, to assess metastasis to the bones, were not carried out.

Treatment of penile cancers include partial or total penectomy. However, total penectomy is not very common contemporarily. Partial penectomy is carried out with or without inguinal lymph nodes dissection [11, 4]. In addition, a 2cm margin is used in partial penectomy [8], but studies have shown that dissecting a few millimeters of margin is safe in terms of malignant cells [18]. In this case, partial penectomy was carried out without intervention to the inguinal lymph nodes and 1cm of margin was dissected. The marginal cells were reported normal according to pathology.

Conclusion

Primary or secondary penile cancer, which appears as erythema, induration and ulcer in penis, is a rare pathology of the male genitourinary system. Due to its uncommonness, it could be treated as a benign or precancerous lesion. Thus, it requires more attention and precision to differentiate it from benign ulcers [14].

The patients may not represent any of the risk factors and only complain about penile ulcer. Nevertheless, physicians should not neglect the likelihood of a penile cancer, which can a potential threat to the patients' lives. Thus, they had better accomplish thorough examination and investigations to find out whether the patients or their partners are infected with HPV or not.

Early diagnosis and treatment are vitally necessary for the patients because the problem can be eliminated by merely a penile sparing surgery, in which the patient's sexual productivity is preserved. In case the patient refers to the doctor very late, it is better to carry out CT-Scan of the pelvis, abdomen and even the thorax, bone scan and

Fine Needle Aspiration Biopsy of the inguinal lymph nodes, and merely ultrasonography and a simple chest x-ray are not sufficient [15].

References

1. Antwerpen I, Gstrein L, Moskovszky L, et al. Primary urethral squamous cell carcinoma: a unique manifestation of a penile tumor. *J Int Med Res.* 2019;47(2):999-1004. doi:10.1177/0300060518813506
2. Astigueta, Juan Carlos. (October 05,2015) Endoscopic Inguinal lymphadenectomy in Penile Cancer: Case Report and literature Review. *Ecancermedicalscience.* VL - 9doi: 10.3332/ecancer.2015.57
3. Lau WD, Ong CH, Lim TP, Teo C. Penile cancer: a local case series and literature review. *Singapore Med J.* 2015;56(11):637-640. doi:10.11622/smedj.2015174
4. Marchionne E, Perez C, Hui A, Khachemoune A. Penile squamous cell carcinoma: a review of the literature and case report treated with Mohs micrographic surgery. *An Bras Dermatol.* 2017;92(1):95-99. doi:10.1590/abd1806-4841.20175009
5. Öztürk Hakan. Penile mucinous carcinoma: A case report. *Oncology letters.* Mar 01.2015; 9: 1293-1296. Doi:10.3892/ol.2014.2839
6. Solakhan M, Bulut E (2018) Penile Cancer: Case Report. *Int Arch Urol Complic* 4:045. doi.org/10.23937/2469-5742/1510045
7. Ahmad S W, Daze R P, Arvaneh S, et al. (July 08, 2019) Painful Penile Plaques: A Rare Case Report of Rectal Adenocarcinoma with Cutaneous Metastasis to the Penis. *Cureus* 11(7): e5095. doi:10.7759/cureus.5095
8. Franceschini, G., Sanchez, A.M., Di Leone, A. et al. Penile cancer metastasizing to the breast: a case report. *J Med Case Reports* 10, 53 (2016). <https://doi.org/10.1186/s13256-016-0829-3>
9. Ikpi Edet, Konneh Solomane, Yunusa Bashir, Camara Ansumana, Clark Alberta, Subah Sean, Alele David, Sroden Monica. (January 01,2018) Penile Cancer in Liberia: A Case Report and Review of the Literature. *J Health.* Jan 01,2018; 10: 1132-1139. Doi: 10.4236/health.2018.108086
10. Campi R, Sessa F, Cocci A, Sforza S, Greco I, Cito G, Vanacore D, Raspollini MR, Serni S, Lapini A, Carini M, Minervini A. Surgical management of a rare case of giant penile cancer. *Minerva Urol Nefrol.* 2019 Aug;71(4):421-425. doi: 10.23736/S0393-2249.18.03238-1. Epub 2018 Nov 7. PMID: 30421592.
11. Chen CF, Tang TY, Chen M, Chen LC. Penile metastasis from recurrent sarcoma in a teenager: a case report. *BMC Urol.* 2019;19(1):81. Published 2019 Sep 2. doi:10.1186/s12894-019-0511-3
12. Guo LC, Li G, Wang XM, Zhang M, Huang JA, Chen YB. Penile metastases from primary lung cancer: Case report and literature review. *Medicine (Baltimore).* 2017 Jun;96(26): e7307. doi: 10.1097/MD.0000000000007307. PMID: 28658136; PMCID: PMC5500058.
13. Kim Brian, Garcia Francisco, Touma Naji, Moussa Madeleine, Izawa Jonathan. A rare case of penile cancer in situ metastasizing to lymph nodes. *Canadian Urological Association journal = Journal de l'Association des urologues du Canada.* Dec 01,2007; 01: 404-407. Doi: 10.5489/cuaj.458
14. Kiptoon DK, Ngugi PM, Rana FS. Cancer of the penis: case report. *East Afr Med J.* 2009;86(4):196-200. doi:10.4314/eamj.v86i4.46952
15. Vanthoor J, Thomas A, Tsaor I, Albersen M; and in collaboration with the European Reference Network for rare urogenital diseases and complex conditions (eUROGEN). Making surgery safer by centralization of care: impact of case load in penile cancer. *World J Urol.* 2020 Jun;38(6):1385-1390. doi: 10.1007/s00345-019-02866-9. Epub 2019 Jul 10. PMID: 31292733.