

Characteristics of Penile Cancer at Tertiary Centre Hospital: A Nine Years Study from 2010-2019

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ABSTRACT

Background: Penile cancer is a rare and aggressive disease. The incidence in India, Africa, and South America ranges from 2.3 to 8.3 per 100,000. No data regarding incidence rates in Indonesia. The etiological factors include poor genital hygiene, phimosis, tobacco use, multiple sex partners, human papillomavirus (HPV) infection, and chronic inflammatory states. Squamous cell carcinoma (SCC) represents 95% of penile cancers. Progression and treatment of the disease cause devastating consequences and morbidity such as disfiguring penile amputation. This study aimed to assess the epidemiological characteristics of penile cancer in the city of Bandung, its associated risk factors, clinical manifestations, and compare the results with previous studies.

Methods: This was a descriptive study conducted at Hasan Sadikin Hospital Bandung from January 2010 to 2019. The study included all penile cancer patients that came to Urology Department. Variables such as age, history of circumcision, phimosis, HPV infection, marital status, smoking habit, educational level, age of onset, operation, histopathological results, history of multiple sex partners, location of the tumor, comorbidities, and staging are collected from the medical record and analyzed.

Results: A total of 13 penile cancer patients were involved with the age range from 28 to 67 years and 50.69 years on average. Most of them were smokers (69.2%) and uncircumcised (53.8%). All of the patients came at an advanced stage, and penectomy was done. Histopathologically, 84.6% were SCC. One of our patients was consulted by a haemato-oncologist for adjuvant chemotherapy (6 cycles of cisplatin and 5-fluorouracil).

Conclusions: Penile cancer is a rare neoplasm in Bandung, West Java. The characteristics of penile cancer patients found in our hospitals were on average 50.7 years old, and the most risk factors found were smoking and uncircumcised. Histopathologically, most of them were SCC. All patients came to seek medical treatment at an advanced stage and had undergone surgical penectomy.

INTRODUCTION

Penile cancer is a rare disease but remains to be a problem in developing countries. It is an aggressive disease with major psychological and social impacts, affecting self-esteem and body image [1–3]. The incidence in the United States is 1.5/100,000 annually, and 55% of the tumors are invasive while others are in situ [4]. The incidence is also modest in China and UK, where the rate is 0.6 per 100,000 men. In contrast, it is relatively common in India, Africa, and South America. The age-adjusted incidence in these countries ranges from 2.3 to 8.3 per 100,000 people [1]. In Indonesia, there is no data regarding incidence rates. Study in Bandung for 10 years (1976–1985) obtained penile malignancy constituted

6% of all malignancies in the Urology Division of Hasan Sadikin Hospital while Tranggono and Umbas at the Cipto Mangunkusumo and Dharmas Cancer Hospital Jakarta from 1994 to 2005 found 69 patients with penile malignancies [5,6]. The low incidence of this disease in developed countries in contrast to the high incidence in developing countries can indicate the association of the disease with socioeconomic status [2].

Penile cancer affects mainly men between 50 and 70 years of age although younger men under 35 years of age are common in Brazil [1]. SCC represents approximately 95% of penile cancers with progression and treatment of the disease that causes devastating consequences effects on patients' physical and mental health. It is a highly aggressive malignancy characterized

by early local regional penetration and lymphatic spread [3]. The remaining 5% of cases result from metastases from tumors in other organs or less frequent tumor types, such as sarcomas, melanomas, and lymphomas [2]. The etiology of penile cancer is multifactorial and has not been fully elucidated with the known etiological factors including poor genital hygiene, phimosis, tobacco use, multiple sex partners, human papillomavirus (HPV) infection, and chronic inflammatory states such as balanitis xerotic obliterans, and chronic lichen [2–4]. Therefore, religious, and cultural aspects related to circumcision in infancy have a fundamental role in the incidence of this tumor. Although circumcision is important in the prevention of penile cancer, populations with a better socioeconomic and cultural status where proper hygiene is performed also have low rates of this neoplasm [1,7].

The treatment methods most frequently used were local excision (36%), partial amputation (26%), laser therapy (16%), and total amputation (8%) [8]. Treatment varies depending on the pathology as well as the location of the lesion. Carcinoma In Situ (CIS) may be treated conservatively in reliable patients. Fluorouracil cream application or neodymium: yttrium aluminum garnet (YAG) laser treatment is also effective and preserves the penis.

Meanwhile, the goal of treatment in invasive penile carcinoma is complete excision with adequate margins. Patients who present with persistent enlarged inguinal nodes after undergoing treatment of the primary lesion followed by a 4- to 6-week course of oral broad-spectrum antibiotics treatment should be considered as metastatic disease, and sequential bilateral ilioinguinal node dissections should be performed. Patients who have an inoperable disease and bulky inguinal metastases are treated with chemotherapy (cisplatin and 5-fluorouracil) [9].

Progression and treatment of the disease cause devastating consequences and morbidity such as disfiguring penile amputation. This study aimed to assess the epidemiological characteristics of penile cancer in the city of Bandung.

METHODS

This is a descriptive study that was conducted at Hasan Sadikin Hospital Bandung based on the data collected from January 2010 to January 2019. Data was obtained from the Medical Records Office. All patients with penile cancer were eligible and included in the study. The demographics, presentation, treatment, and outcome of patients were reviewed and discussed.

Table 1. Patients’ characteristic according to demographic data

Characteristics	Cases (n=13)	Percentage (%)
Age		
<50	4	30.8
50–60	7	53.8
>60	2	15.4
Cigarette smoking		
Yes	9	69.2
No	4	30.8
Multiple sex partner		
Yes	4	30.8
No	9	69.2
Foreskin status (Circumcised)		
Yes	6	46.2
No	7	53.8
Location of tumor		
Glans	3	23
Body	5	38.5
Both	5	38.5
Comorbidity		
Hypertension	2	15.4
Diabetes Mellitus	2	15.4
COPD	1	7.7
HIV	1	7.7
Lung TB	1	7.7

HIV, Human Immunodeficiency Virus; COPD, Chronic Obstructive Pulmonary Disease; TB, Tuberculosis

Table 2. Staging, histology, and treatment of the patients

Characteristics	Cases (n=13)	Percentage (%)
Stage		
0	0	0
1	0	0
2	8	61.5
3	5	38.5
4	0	0
Histology		
Well-differentiated SCC	11	84.6
Epidermoid carcinoma penis	2	15.4
Treatment for primary tumor		
Total penectomy	5	38.5
Partial penectomy	8	61.5
Treatment for lymph nodes		
Superficial lymph node dissection	4	30.8
None	9	69.2
Urinary diversion		
Perineostomy	5	38.5
None	8	61.5
Adjuvant therapy		
Cisplatin, 5 FU	1	7.7

SCC, Squamous Cell Carcinoma; FU, Fluorouracil

RESULT

Demographic data of the patients are presented in **Table 1**. The study found a total of 13 patients with penile cancer from January 2010 until January 2019. The mean age was 50.69 years. Based on the lifestyle, most of the patients were cigarette smokers, and 4 patients had a history of multiple sexual partners. Based on the foreskin status, most of them were uncircumcised. Based on the location, tumors were in the penile shaft, in both glans and penile shaft. Diabetes mellitus and hypertension were found to be the most common comorbid in the patients.

Table 2 presents the staging, histopathological result, surgical procedure, and other treatments done in the patients. Most of the patients came at an advanced stage, stage 2, while the others came in stage 3. Histopathologically, the patients had squamous cell carcinoma. The surgical procedure in our center was penectomy that was done in all of the patients. Superficial lymph node dissection and perineostomy for urinary diversion fell in four patients respectively. One of the patients was referred to a haemato-oncologist for adjuvant chemotherapy. He had 6 cycles of cisplatin and 5-fluorouracil.

DISCUSSION

Penile cancer is a relatively rare neoplasm in the western world with an age-adjusted incidence rate of around 1 per 100,000 men [1]. One of the highest world incidences was found in India with the rate of 3.32/100,000 inhabitants [10]. The incidence of penile cancer varies significantly among different regions; by contrast, a decrease in incidence has been noted in the USA and Finland while an increase has been observed in the Netherlands and Denmark [8]. Our study shows that penile cancer was rare in Bandung as it is in most recent studies. The average age of cancer diagnosis in our study was 50.7 years, with the oldest of 67 years and the youngest of 28 years. This is consistent with the literature that penile cancer is typically a disease of middle-aged to older men, most commonly affecting those between 50 and 70 years of age, with a median age of 68 years. Younger individuals are also affected; approximately 22% of patients are less than 40 years and 7% are younger than 30 years. The disease has also been reported in children [11,12]. The study had the limitation that it only collected a small number of patients who were registered at the Hasan Sadikin Hospital, a national referral hospital in West Java province.

Socio-economic standing, smoking, phimosis, circumcision, and human papillomavirus are examples of factors known to influence the risk of penile cancer while neonatal circumcision is suggested to have a

protective effect [3,8]. An epidemiological study showed that tobacco smoking is a risk factor for the development of penile cancer. Another study also suggested a further risk factor is cigarette smoking, which is associated with a 4.5-fold increase in risk [10]. In our hospital, 9 patients (69.2%) were active smokers. We believe that cigarette smoking is an important risk factor for developing penile cancer. Our study, even though it did not offer a control group, demonstrates that more than one-third of the patients presenting with penile cancer were tobacco smokers

There is a worldwide geographic variation in the incidence that could be caused by differences in socioeconomic status, hygiene, religious, and cultural conditions. For example, the incidence of penile cancers ranges from 0.04 per 100,000 men in Jewish populations in Israel (high incidence of circumcision) in contrast to 3–4 per 100,000 men in countries such as Brazil, India, and Southern Africa. Although there is a lack of explanations regarding the pathogenesis, inflammation may represent a critical component in tumor development or progression as many penile cancers arise at sites of infection, chronic irritation, or injury [3]. Many proposed etiologies are underlying the development of penile cancer. One of them is a strong association between the presence of the prepuce and smegma which has been implicated in the carcinogenesis of penile cancer. The most important risk factors for the development of penile cancer are phimosis and genital hygiene. Studies showed in those that had never been circumcised, the risk was about 3 times higher than in those that were circumcised [10]. In this study, we found 7 (53.8%) of 13 patients were uncircumcised.

One of the most important risk factors for the development of penile cancer is the HPV infection, primarily HPV 16. There is an association between HPV infection and penile cancer in 30 to 50% of cases although the exact role of the infection in the genesis of this neoplasia has not yet been entirely clarified. HPV infections are, in turn, directly related to the number of lifetime sexual partners [10,12]. In our hospital, only 4 patients (44.4%) had a history of multiple sexual partners.

Penile cancer usually presents with a visible or palpable lesion on the penis, but it may be hidden under phimosis. It can also be associated with pain, discharge, bleeding, or foul odor. The location was most often distal (glans) according to what was described [12]. Our data showed the most common location of the tumor in 5 patients (38.5%) were in the penile glans. Likewise, tumors in both the glans and penile shaft were also found in 5 patients; only 3 patients (23.1%) had a tumor located in the penile shaft. Histopathologically, most of the tumors in our study were SCC. A total of 11 patients (84.6%) had SCC while the other 2 patients (15.4%) had epidermoid carcinoma

of the penis. This is consistent with previous studies that also show more than 95% of primary penile malignancies were SCC [2,11]. All other malignant lesions of the penis are much less common than penile SCC. The majority of the tumors were well and intermediate-graded (29 and 35%, respectively) [11,13].

The European Association of Urology (EAU) and the National Comprehensive Cancer Network have made a guideline for the treatment of penile cancer according to the T, N, and M staging categories. Treatment in this study refers to the guidelines of the EAU, which is to perform partial penectomy at T2 while in T3, total penectomy and perineostomy are performed [5,6]. The treatment of the primary tumor aims to complete tumor removal with as much organ preservation as possible without compromising oncological control. Local recurrence has little influence on long-term survival, so organ preservation strategies are justified. Penile preservation appears to be superior in functional and cosmetic outcomes to partial or total penectomy and is considered to be the primary treatment method for localized penile cancer [13,14]. However, Kieffer et al. [15] concluded penectomy and lymphadenectomy are associated with more problems with orgasm, body image, life interference, and urination.

Histological diagnosis with local staging must be obtained before using non-surgical treatments. With surgical treatment, negative surgical margins must be obtained. Local treatment modalities for small and localized penile cancer include excisional surgery, external beam radiotherapy (EBRT), brachytherapy, and laser ablation. Patients should be counseled about all relevant treatment options. The management of regional lymph nodes is decisive for patient survival. Cure can be achieved in limited lymph node disease confined to the regional lymph nodes. Radical lymphadenectomy is the treatment of choice. The multimodal treatment combining surgery and chemotherapy is often indicated [13,14]. Administration of topical chemotherapy as imiquimod or 5 Fluorouracil (5-FU) is given in carcinoma in situ. Meanwhile, in patients with pN2/pN3, adjuvant chemotherapy is recommended.

Prognosis is affected by tumor stage, grade, and, especially, the presence of lymph node involvement at diagnosis [11]. Factors associated with poor survival include lymphatic, blood, or perineural invasion, high histological grade, and locally evolved stage. Poor prognosis could be attributed to late diagnosis probably because patients are reluctant to consult although the tumor is rapidly symptomatic. Lymph-node metastasis at diagnosis involves about one-third of the patients and is responsible for significant immediate mortality. Evaluation of lymph node status is fundamental, but sentinel node technique or modified lymphadenectomy is recommended to investigate

intraclinical micrometastasis. Survival also decreases with age because of higher immediate mortality in the elderly and the less intensive treatment [16]. Our study underlines the fact that even within the context of a contemporary series of penile cancer patients, 100% of patients were diagnosed with advanced disease (Grade T2 or higher). This finding is of concern because it is evident that the advanced stage is strongly correlated with the degree of invasion and probability of regional and systemic metastases suggesting a worse prognosis for these patients. This finding is of concern because it is evident that the advanced stage is highly correlated with the rate of invasion and the likelihood of regional and systemic metastases suggesting a worse prognosis for these patients. These data suggest that patients delay seeking medical care because of either fear or ignorance. A national campaign is fundamental to alert the greater public about this present poorly known disease [10,17].

CONCLUSIONS

Penile cancer is a rare neoplasm in Hasan Sadikin Hospital, Bandung. The epidemiological profile study of these patients revealed that penile cancer is an aggressive disease that presents certain known and preventable risk factors identified in this report such as personal hygiene, smoking, uncircumcised, had a history of multiple sex partners, and being sixty years or older.

However, the low frequency of these cancers limits the possibilities for conducting clinical trials. More intensive research is strongly encouraged for the development of consensual recommendations.

DECLARATIONS

Ethics Approval and Consent to Participate

Ethical approval number LB.02.01/X.6.5/74/2021 and no consent needed.

Competing of Interest

The authors declare no competing interest in this study.

Acknowledgment

Not applicable.

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