

## The Clinical Features of Penile Cancer Patients at Sanglah General Hospital Bali-Indonesia

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**Objectives:** To explore clinical characteristics, treatment modalities and outcomes after the follow-up of penile cancer patients.

**Method:** We reviewed penile cancer patients during 8 years, started from April 1993 to March 2001. The data collected through medical record consisted of patient identities, history takings, physical and pathological findings, treatment modalities and their follow-up after 3±4 years

**Results:** During eight years of study there were 46 patients aged 58±3 years. Out of 46 patients, 33 patients (72%) have history of urogenital infection and 40 patients (87%) with phymosis. With regard to physical examination, 24 patients (52%) presented as stage III (Jackson classification). Pathological findings showed that 100% patients were keratinizing squamous cell carcinoma. Partial penectomy alone was carried out in 21 patients (46%), total penectomy alone was done in 17 patients (37%), and total penectomy with lymph node dissection was done in 8 patients (17%). During the follow-up, majority of the patients (42) showed no complications or recurrence, only 2 patients showed recurrent tumor and the rest 2 were lost to follow-up.

**Conclusions:** During eight years at Sanglah General Hospital there were 46 penile cancer patients, mean of age was 58±3 years. Predispositioning factors were urogenital infection and phymosis. All of them were keratinizing squamous cell carcinoma. Total or partial penectomy with or without lymph node dissection was carried out with good results.

**Keywords:** penile, cancer, urogenital, squamous, carcinoma.

### INTRODUCTION

Penile cancer is a rare malignant disease. In USA, this malignancy was reported only in 1: 100,000 of male population or less than 1% of cancer cases on men. In other parts of the world such as Africa, South America and Asia cases of penile cancer reach 10 – 20% of cancer that affects men. The peak incidence age is 60 years.<sup>1-4</sup> Some studies revealed a varying incidence, for example at the National Taiwan University Hospital there were 71 cases within 20 years, at Maria Skodowska-Curie Cancer Center Warsaw - Poland there were 64 cases within 9 years and at the Hospital Universitario San Carlos-Madrid there were 13 cases within 22 years.<sup>2,5,6</sup>

Until recently, the etiology of penile cancer is unclear. It is still believed that the risk factors are pnyosis, chronic inflammation, and the papilloma virus (HPV). Many researchs shows a strong relationship between these three factors and penile cancer.<sup>7-9</sup> Some other researches also proved that smoking habits, trauma, and plural change of sexual partners to also be risk factors.

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The latest discovery stated a meaningful correlation between lichen cherosis and the occurrence of penile cancer.<sup>10</sup> It was also found that there was a triple decrease in the risk of penile cancer on men who underwent circumcision as babies. Out of 1,193 penile cancer patients in India, only 0.02% was Moslems much less compared to the Hindus, in which circumcision is not compulsory for males.<sup>4</sup> One research found that the penile cancer incidence increased in men who have a history of change in sexual partners of more than 30 times.<sup>4</sup> HPV infection in penile cancer patients invasively reaches 70-100%, mostly of the type 16 HPV.<sup>7,10</sup> Treatment of penile cancer is based on the staging. Conservative treatment for in situ penile cancer is still accepted. Surgery is the primary treatment on most penile cancers. The prime procedure of surgery on invasive cancer is a complete excision within adequate margin. This surgical procedure may include circumcision, partial penectomy or even total penectomy. Many literatures reveal the 'wait and watch' policy in the treatment of the lymphadenectomy by applying antibiotics for 4 - 6 weeks. If there is no response with antibiotics then it is suggested to conduct ilioinginal lymph node dissection uni or bilaterally, using the Cabanas technique or the modified technique introduced by Catalona.<sup>1,6,11,12</sup> In

other reports, there was an increase in the survival rate for high-risk patients by applying surgery that is more aggressive. Lymph adenectomy prophylaxis should be considered to decrease morbidity and mortality rates.<sup>13,14</sup> Adjuvant therapy which coincides with surgery is implemented to increase the overall survival rate. It is applied in the form of chemotherapy, radiotherapy, or a chemo radiotherapy combination. Four anti-cancer agents often used as chemotherapy are bleomycin, methotrexate, cisplatin and 5-fluorouracil. For palliative objectives, radiotherapy and chemotherapy are usually applied.<sup>(15,16,17)</sup> Chances of survival for the penile cancer patients depend on whether there is metastasis to the surrounding lymph nodes. The 5 years survival rate in a negative node reaches 65 – 90%, an inguinal positive node reaches 30 – 50% whereas a patient with a positive node up to the iliac glands decrease down to below 20% in chances of survival.<sup>14</sup>

## METHODS

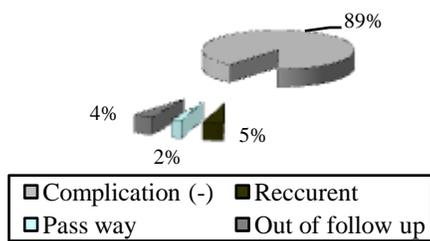
A descriptive study was conducted at the Sanglah General Hospital Denpasar. This study was carried out by an evaluation of demographic data, disease history, clinical findings, treatment modalities and patients hospitalized development after therapy. Penile cancer patients from April 1993 to March 2001 at Sanglah General Hospital Bali-Indonesia were included in this study. The inclusion criteria were those who diagnosed as penile cancer based on histopathologic examination. Patients who did not agree to follow the treatment procedures were excluded from the study. During the study, 46 patients were included. After the treatment was completed, the patient were regularly checked through polyclinic visits every week in the first month, every month in the 5 following months, and every 3 months in a year and every 6 months in the following year. Medical examination including patient's complained physical examination and some supporting examination if necessary. The follow up was conducted for 96 months from April 1993 to March 2001 or an average of 52.8 months for each patient.

## RESULTS

There were 46 penile cancer cases during the study with the average ages of  $58.4 \pm SD 3.2$  years. The youngest patient was 47 year and oldest 72 year. Their educational backgrounds are 27 (58.7%) from elementary schools, 10 (21.7%) junior high and 9 (19.6%) who have not graduated from elementary or no educational background at all. Their occupational backgrounds were mostly farmer 22 (47.8%), trader 7 (15.2%), driver 12 (26.1%) and others 5 (10.9%). Twenty (43.5%) cases were husbands with one wife,

18 (39.1%) had 2 wives and 5 (10.9%) had more than 2 wives, whereas there were 3 (6.5%) patients unmarried. All (100%) patients were Hindus. Forty cases had a history of phymosis, whereas the history of urinary tract infection was found in 33 (72%) cases. None (0%) of the patients had circumcision. Eight patients had phymosis but had no urinary tract infection. Urinary tract infection was diagnosed if the patient sought medication for their complain of dysuria. Three (6.5%) patients had penile cancer with stage I, 18 (8.28%) were in the stage II, 24 (52.2%) of the stage III and the remaining 1 patient was known to be in stage IV. The results of histopathologic examination showed that all of these penile cancer cases are of the squamous cell carcinoma (Table 1).

The treatment modality of penile cancer at Sanglah General Hospital is slightly different with those written in references. The difference is that inguinal lymph node biopsy was conducted in all penectomy patients, both partially and totally. The biopsy is executed either on palpable or non-palpable lymph nodes. From the 46 cases only 21 (45.7%) partial penectomy were done. Meanwhile total penectomy without the inguinal lymph node dissection were done in 17 (36.9%) patients and total penectomy with lymph node dissection were done in 8 (17.4%) patients. All patients who underwent lymph node dissection were given adjuvant bleomycin chemotherapy. Radiotherapy, which accompanied total penectomy and lymph node dissection, was done in 2 patients. During the follow up, it was found that outpatient clinic up to March 2001 regularly visited. It was shown that 41 (89.1%) patients still in good condition, 2 (4.3%) had relapse in of which patients were in the grade III. Those patients had penectomy, lymph node dissection and given bleomycin. One patient with stadium IV died 4 months after operation and 2 patients were loss to follow up (Figure 1).



**Figure 1 Treatment Outcome of Penile Cancer**

## DISCUSSION

The mean age of the penile cancer in our series was 58.4 years. The patients come from the low

social economic background, which is reflected, by their educational levels and occupational backgrounds. Therefore, sexual activity cannot be accurately obtained in our study, since it may grossly reflected only by the number of wives.

**Table 1. Baseline characteristics of the penile cancer patients**

Characteristics	Number	Percentage (%)
Total	46	100.0
Age	58.4±SD3.2	
Education		
Elementary school	27	58.7
Junior high	10	21.7
No graduate/illiteracy	9	19.6
Occupation		
Farmer	22	47.8
Trader	7	15.2
Driver	12	26.1
Others	5	10.9
Marital status		
-Married		
1 wife	20	43.5
2 wives	18	39.1
More than 2 wives	5	10.9
-Unmarried	3	6.5
Religion		
Hindu	46	100.0
Underlying disease		
Phimosis	40	87.0
Urinary tract infection	33	72.0
Circumcision	0	0
Stage		
Stage I	3	6.5
Stage II	18	39.1
Stage III	24	52.2
Stage IV	1	2.2
Lymph node biopsy		
Palpable	8	17.4
Non palpable	38	82.6
Biopsy:		
node (+)	13	28.3
Palpable	6	75.0
Non palpable	7	18.4
Histopathologic		
Squamous cell carcinoma	46	100
Lymph node metastases		
Stage I	0	0
Stage II	2	11.1
Stage III	10	41.7
Stage IV	1	100
Surgery treatment		
Partial penectomy	21	45.7
Total penectomy	17	36.9
Total penectomy + dissection	8	17.4

All of patients had no history of circumcision. The circumcision is not commonly carried out among the Balinese, because the majority of Balinese population is Hindus. Some studies showed that circumcision produced a triple decrease of penile cancer risk and the incidence reach only 0.02%.<sup>4</sup> One theory

postulates that smegma accumulation under the phimotic foreskin results in chronic inflammation leading to carcinoma.<sup>1,4</sup> This fact indicates a strong correlation between the practice of circumcision and low penile cancer incidence. That should be taken into consideration is the presence of the human papilloma virus (HPV) infection that is not specifically observed in this study.

In our study, most (52,2%) penile cancers were in stadium III. It may be caused by a delay in case finding and diagnosis. This situation may relate to lack of awareness among the patients to seek medical help in early stage of their illness. This data is different from what was found in developed countries, where most of penile cancer was found in stadium I. In some reports, squamous cell carcinoma is the most frequent histopathologic finding, that is more than 85%.<sup>1,3,4,9,12</sup> Meanwhile our data showed that all (100%) penile cancers were as squamous cell carcinoma.

The treatment of penile cancer at Sanglah General Hospital does not follow the 'wait and watch' policy to define whether or not the palpable lymph node needs dissection. Moreover, all patients who have undergone penectomy are applied lymph adenectomy for biopsy on both palpable and non-palpable lymph nodes. Surprisingly, this procedure gives an 11.1% positive node on stadium II penile cancer and 41.7% positive nodes on stadium III. Besides that, simultaneous biopsy and the main surgery can help a prompt decision for further surgery is necessary. It may provide advantages in the prevention of cancer spread and can reduce mortality rate. Late lymphadenectomy can decrease the survival rate by 50%. This measurement supported by Ravi et al who stated that it is necessary to consider prophylaxis lymphadenectomy in order to decrease the morbidity rate on the 'wait and watch' policy.<sup>12,14</sup> This authors found that there were 9.6% positive nodes from 52 patients who were undergoing biopsy of inguinal lymph node (inguinal pick). The sensitivity of this procedure was 72%.<sup>14</sup> However, negative result of this procedure does not rule out the spread of the vicious regional cells to the surrounding lymph nodes.

This study is an historical cohort that re-evaluated medical records during the past 8 years, from 1993 through 2001. The mean follow up of our patients was 52,8 months, therefore we can not determine the 5 year survival rate. In the regard with treatment outcomes, our study found that only 2 patients (4.3%) were recurrent and all were from the stadium III. One report showed that the recurrent rate was 11%.<sup>6</sup> Other studies also showed the survival rate simultaneously increases with the decrease of the stadium, where the 5 year survival

rate on stadium III is 66.7% while stadium I reach 100%. In total, the 5 year survival rate on penis squamous cell carcinoma is 78%.<sup>1,8,9,12</sup>

## CONCLUSION

During 8 years of retrospective study, there are 46 penile cancer cases. Most of them come from the lower social economic background and the dominant associated factors of penile cancer are psmosis and lower urinary tract infection. All cases are squamous cell carcinoma, which are mostly in the stadium II. Lymph node biopsy is a regular procedure in addition to main surgical treatment. There is a low recurrent rate after an average 52.8 months of follow up.

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