Penile Intraepithelial Neoplasia (PeIN) in a young man with the clinical appearance of Buschke Lowenstein Tumor

Fiona Wongkar1*, Ni Nyoman Ayu Sutrini2

ABSTRACT

Background: The incidence of penile cancer in the general population is rare. Epidemiologically, penile cancer occurs less than 1% compared to other types of cancer. Penile Intraepithelial Neoplasia (PeIN) is a precancerous lesion of invasive squamous cell carcinoma characterized by dysplastic changes of squamous epithelium with the intact basement membrane. This case report aims to increase understanding of Penile Intraepithelial Neoplasia (PeIN), especially with the clinical appearance of the Buschke Lowenstein Tumor, diagnosis, examination, and appropriate management.

Case Presentation: A 21-year-old Balinese man presented with a lump on his genitalia without itching, pain, and a lesion that bleeds easily, which has appeared since January 2022. The patient denied complaints of the genitals. Venerological status was within normal limits. Fourteen days after surgery, multiple lumps appeared, recurred, and increased in number and size. On 1-month observation after the second surgery, the patient denied complaints of the genitals. Venerological status was within normal limits.

Conclusion: HPV-related Penile Intraepithelial Neoplasia (Warty subtype) with the clinical appearance of Buschke Lowenstein Tumor was reported in a 21-year-old Balinese man treated with Glans Resurfacing surgical excision with satisfactory results characterized by no functional abnormalities both during urination or erection.

Keywords: Buschke Lowenstein Tumor, penile cancer, Penile Intraepithelial Neoplasia.

INTRODUCTION

The incidence of penile cancer in the general population is rare. Epidemiologically, penile cancer occurs less than 1% compared to other types of cancer. Penile cancer generally occurs in the sixth decade, and the incidence increases with age. The incidence of penile cancer is lower in Asian males than in Hispanics. Risk factors associated with squamous cell carcinoma of the penis are a history of uncircumcision, genital warts, urinary tract infection, urethral strictures, smoking, and phimosis.

Penile Intraepithelial Neoplasia (PeIN) is a precancerous lesion of invasive squamous cell carcinoma characterized by dysplastic changes of squamous epithelium with the intact basement membrane. According to WHO in 2016, Penile Intraepithelial Neoplasia (PeIN) is classified based on the incidence of HPV as HPV-related and non-HPV-related. PeIN is mostly located on the glans penis, mucous membranes, or prepuce. The clinical appearance of PeIN is reddish or ulcerated plaques and can occur along with secondary infections. Infectious conditions such as genital herpes and condyloma acuminata that co-occur are a challenge to diagnose PeIN.

Buschke Lowenstein Tumor is a clinical form of condyloma acuminata. It is a sexually transmitted infection with a clinical appearance of an exophytic tumor that bleeds easily, which has appeared since January 2022. He complained that the lump was getting bigger and bigger. Physical examination showed multiple hyperpigmented papules and plaques with well-defined oval and corn shapes that vary in size with a dense consistency and a verrucous surface. Laboratory tests showed negative on Hep-B and HIV tests. The patient also had a biopsy of the lump where the results showed Penile Intraepithelial Neoplasia. The patient was treated with 6 cycles of TCA 80% once a week, but it did not improve, so circumcision and surgical excision were carried out on June 2022. Fourteen days after surgery, multiple lumps appeared, recurred, and increased in number and size. On 1-month observation after the second surgery, the patient denied complaints of the genitals. Venerological status was within normal limits.

Conclusion: HPV-related Penile Intraepithelial Neoplasia (Warty subtype) with the clinical appearance of Buschke Lowenstein Tumor was reported in a 21-year-old Balinese man treated with Glans Resurfacing surgical excision with satisfactory results characterized by no functional abnormalities both during urination or erection.

Keywords: Penile Intraepithelial Neoplasia (PeIN), Buschke Lowenstein Tumor, penile cancer, Penile Intraepithelial Neoplasia.
CASE REPORT

A 21-year-old Balinese man came to the Dermatology and Venereology Polyclinic Bali Mandara General Hospital complaining of a lump on his genitals. The lump appeared in January 2022. The patient complained that the lump was getting bigger and bigger. The patient did not complain of itching, pain, or lesions that bleed easily. The patient never had a similar complaint before.

In February 2022, the patient was treated with 6 cycles of TCA 80% once a week, but it did not improve. In June 2022, circumcision and surgical excision were carried out. Fourteen days after surgery, a new lesion began to appear in the form of multiple recurring lumps without pain and itching. Twenty days after surgery, the lesion increased in number and size. In October 2022, a biopsy and second surgical excision were carried out.

The patient denied a history of using drugs or applying traditional oils. The patient also denied a history of co-morbidities. There was no family history of malignancy. Based on social history, the patient was a student, smoking 3 cigarettes per day, and did not consume alcohol, narcotics, and illegal drugs. The patient had been sexually active since 19, had intercourse with three partners, and did not use condoms. History of intercourse with the same sex was denied. The patient claimed to have been in contact with a partner who previously had complaints of genital warts. History of HPV vaccination showed the first dose was given in September 2022 using Gardasil.

Physical examination showed that the patient was in good general condition with composit mentis awareness. The visual analog scale (VAS) was 0, the patient's weight was 57 kg, and the height was 173 cm with a Body Mass Index of 19 kg/m², which was in the normal category. Generalist status was within normal limits. Lymph node enlargement was not found. On venereological status in the glans region of the penis, multiple hyperpigmented papules and plaques were found with well-defined oval and corn shapes that vary in size with a dense consistency and a verrucous surface.

Laboratory tests were complete blood count, Hepatitis B, HIV, and tissue biopsy. The results showed normal complete blood test results, negative Hep B, and negative HIV. Venereal Disease Research Laboratory (VDRL) and Treponema Pallidum Haemagglutination Assay (TPHA) examinations have never been carried out. Biopsy examination showed histomorphology in accordance with the description of Penile Intraepithelial Neoplasia.

The working diagnosis of this case was Buschke Lowenstein Tumor and HPV-related Penile Intraepithelial Neoplasia (Warty subtype). The management given to the patient was surgical excision surgery and periodic observation. In 1-month observation after the second surgery, the patient denied complaints of the genitals. Venereal Status was within normal limits.

DISCUSSION

Penile Intraepithelial Neoplasia (PeIN) is a precancerous lesion of invasive carcinoma. According to National Cancer Institute Surveillance Epidemiology in the United States, 37% of penile cancer cases are PeIN. Intraepithelial neoplasia is more common in the head, neck, hands, back, oral cavity, and nails. The incidence of the penis is rare. PeIN can occur in the area of
Complaints of itching and easy bleeding or redness with well-defined borders. SOLITARY OR MULTIPLE PLAQUES OF SKIN COLOR, REDNESS WITH WELL-DEFINED BORDERS. FIGURE 5. PROMINENT KOilocytosis.

Penile Intraepithelial Neoplasia is included in the precancerous lesions of Squamous Cell Carcinoma in Situ (SCCIS). SCCIS that can occur in the genital area is Bowen disease, Bowenoid Papulosis, and Erythroplasia of Queyrat. According to the 8th edition of the American Joint Committee on Cancer (AJCC), PeIN is classified as Tis where T represents Tumor and Is means In Situ.

According to WHO 2016, Penile Intraepithelial Neoplasia (PeIN) is classified based on the incidence of HPV as HP-related PeIN and non-HPV-related PeIN. HPV-related PeIN is more often found in young men. Based on the histopathological results, PeIN can be classified into four subtypes: differentiated, basaloid, warty, and basaloid-warty. Based on the histomorphology in the differentiated type, atypical epithelial cells are prominent in the lower layers with squamous maturation and eosinophilic cytoplasm. In the basaloid subtype, monotonous basophilic cells are found with high apoptotic and mitotic. Koilocytosis, parakeratosis, and acanthosis cells are found in the warty subtype. Koilocytosis is more prominent in the upper one-third and can be found in the parakeratotic layer and occasionally in fibrovascular. Koilocytosis is a vacuolated cell with clear cytoplasm with a “halo” around that occurs as a result of HPV infection. Preventive measures against HPV infection can be in the form of vaccination. The vaccine is indicated in Indonesia is a bivalent vaccine that protects against HPV 16 and 18 and a quadrivalent vaccine, which protects against HPV 16, 6, 11, and 18. The vaccine is indicated in men aged 9 to 26 to prevent external genital lesions such as condyloma acuminata, Anal Intraepithelial Neoplasia, and PeIN. Based on WHO recommendations and the American College of Obstetrics and Gynecologists (ACOG), HPV vaccination is the primary prevention of HPV-related diseases. Vaccination is also recommended for HPV DNA-positive patients. There is no data on the efficacy of HPV vaccination against PeIN due to its low incidence.

In this case report, the patient was a male, aged 21 years, who complained of multiple hyperpigmented papules and plaques with well-defined horns above them, varying in size of more than 3 cm with a dense consistency and a verrucous surface. The patient admitted a history of active sexual intercourse since 19 and did not use condoms with more than 1 partner. The patient had sexual intercourse with a partner who complained of similar lumps on her genitals. The patient had not received the HPV vaccine before. The patient has no history of circumcision. Based on the history taking and physical examination, the initial diagnosis was Buschke Lowenstein Tumor.

The patient was treated with 6 cycles of TCA 80% once a week, but it did not improve, so surgical excision and circumcision procedures were carried out. This is in accordance with the previous clinical practice guidelines that if one method does not show improvement as much as 6 times, it can be replaced with another. Twenty days after the first surgery, the patient had a recurrence, and similar complaints arose as previously experienced. The patient then underwent second surgical excision, and a biopsy was performed. The biopsy results showed that the histomorphology was appropriate for Penile Intraepithelial Neoplasia (PeIN) with microscopic features of acanthosis, parakeratosis, squamous maturation of the epithelium with the upper third of the surface epithelial layer showing koilocytosis accompanied by dilution of blood vessels. The final diagnosis was HPV-related Penile Intraepithelial Neoplasia (Warty subtype).

Various therapeutic modalities can be used for Penile Intraepithelial Neoplasia, such as topical agents (5-Fluorouracil, Imiquimod 5%), local destructive agents such as photodynamic therapy, laser therapy, namely ablative carbon dioxide (CO2) or neodymium: yttrium-aluminum-garnet (Nd: YAG), cryotherapy, curettage, and electrocautery. However, surgical excision is the main choice as it has the highest efficacy rate and lowest recurrence compared to other therapies. Surgical excision includes Mohs, Glans.
resurfacing, and Glanectomy. The patient underwent Glans Resurfacing on Condyloma Acuminata and PeIN lesions. In addition, the patient also received education regarding the prevention of sexually transmitted infections, methods of transmission, and education on maintaining genital hygiene.\textsuperscript{3,4,7,18}

The transformation from PeIN to invasive carcinoma is 10 – 30%. The prognosis is that 74% of recurrences occur within the first two years, and 66% occur locally. After the first five years, recurrence is up to 92%. Therefore, the European and National Swedish guidelines recommend the follow-up of cases for the first five years. As much as 48% of cases recur after excision and progress to 2% invasive carcinoma. Thus, follow-up after surgical excision is needed to see if there is a recurrence of PeIN.\textsuperscript{3,4,7} In this case report, the additional laboratory diagnosis is not comprehensive, which causes the final diagnosis cannot to be decided for such a long time. Suggestions for future study, an additional laboratory can be added to the report will be comprehensive. Also, additional research for this disease is still needed due to the lack of study that has been conducted in the hope of confirming the diagnosis and treatment.

CONCLUSION

HPV-related Penile Intraepithelial Neoplasia (Warty subtype) with the clinical appearance of Buschke Lowenstein Tumor was reported in a 21-year-old Balinese man who was treated with Glans Resurfacing excision surgery with satisfactory results characterized by no functional abnormalities both during urination and erection.

CONFLICT OF INTEREST

The author reports no conflicts of interest in this work.

ETHICAL CONSIDERATIONS

The Bali Mandara General Hospital ethics committee approved this study. Informed consent has been provided prior to the case study being conducted.

FUNDING

None.

AUTHOR CONTRIBUTION

All authors contributed to the study through the conceptual framework, data gathering, and case report writing.

REFERENCES