The Prevalence of Penile Cancer in Patients With Adult Acquired Buried Penis

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OBJECTIVE	To determine the prevalence of penile cancer in patients with adult acquired buried penis (AABP). Penile cancer is a rare but aggressive cancer. Several case reports have recently been published that indicate that AABP may increase the risk of penile cancer.
MATERIALS AND METHODS	A retrospective review was conducted of adults diagnosed with AABP and penile cancer between January, 2008 and December, 2018 seen at a tertiary referral center. Demographics including age, BMI, comorbidities, etiology of AABP, smoking history, circumcision status, and premalignant lesions (condyloma, lichen sclerosus [LS] carcinoma in situ [CIS]) were recorded. For patients with penile cancer, AJCC staging, grade, TNM staging and treatments were recorded. Basic descriptive statistics were performed for the overall cohort. We used Chi-square tests and Fisher exact tests to compare differences between patients with benign pathology and patients with malignant or pre-malignant pathology.
RESULTS	We identified 150 patients with the diagnosis of AABP. The prevalence of penile squamous cell carcinoma was 7%. There was a 35% rate of premalignant lesions. This study is limited by its retrospective and single-institution nature.
CONCLUSION	AABP is a condition that incorporates multiple risk factors for penile cancer. The prevalence of penile cancer appears to be higher in patients with AABP; however, more data are needed to confirm these initial findings. Patients with AABP should be counseled on these risks and should be considered for buried penis repair if a physical examination cannot be performed. UROLOGY 133: 229−233, 2019. © 2019 Elsevier Inc.

Adult acquired buried penis (AABP) is increasing in incidence due to the obesity epidemic. This condition has been defined as "a condition in which the penile shaft is invisible below the surface of the prepubic skin and/or scrotum.[1]" Because the penile shaft is hidden under overhanging adipose tissue, it oftentimes cannot be exhumed for urination or hygiene. Patients with AABP have urinary dribbling and pooling within the adipose layers that bury the glans leading to an environment of chronic inflammation, recurrent infections, and ultimately poor quality of life. Fortunately, surgical intervention has resulted in substantial improvements in quality of life.[2]

There is rising concern, however, that quality of life may not be the only indication for surgical intervention. Several case reports have been published suggesting that buried penis may increase the risk of penile cancer.[1,3]

Penile cancer is a rare malignancy with an incidence of 0.81 per 100,000 persons in the US and Europe.[4,5] Penile cancer has a 5-year survival rate of 50% (between 11% and 85% depending on stage) and its treatment is highly morbid.[6,7] Well-known risk factors for penile cancer include uncircumcised status, phimosis, poor genital hygiene, human papillomavirus (HPV) types 16 and 18, immune compromise, UVA phototherapy, lichen sclerosis, and tobacco use.[5] Obesity has also been associated with an increased risk of penile cancer and more advanced disease at presentation.[8,9]

While a direct causal link between AABP and penile cancer has not been established, patients with AABP may inherently possess multiple risk factors for penile cancer including functional phimosis, poor genital hygiene, morbid obesity and chronic inflammation of the penile skin and glans. Patients with AABP are challenging to examine due to obesity and a penis that is often difficult to exhume, which could result in delayed diagnosis of penile lesions. More studies are needed to better define the relationship between AABP and penile cancer so urologists can counsel, monitor, and treat patients appropriately.

We hypothesize that the prevalence of penile cancer in patients with AABP is higher than the general population, and in this study we seek to define the prevalence of penile cancer in our population of patients with AABP.

MATERIALS AND METHODS

Study Population

We performed a retrospective chart review to identify patients who carried the diagnosis code of AABP (ICD-9 code 607.89 and ICD-10 code 752.65) or those who underwent operative repair of buried penis between January, 2008 and December, 2018. We performed an additional search to identify patients who carried the diagnosis code of penile cancer (ICD 9 code 9.187.1-9 and ICD-10 code C60.9 and D09.9) to ensure no cases were missed. Demographic information collected included age, BMI, medical comorbidities, etiology of AABP (lymphedema, cicatrix, or obesity), smoking history, circumcision status and timing of circumcision, HPV and HIV status, and the presence of premalignant lesions (condyloma, lichen sclerosus, CIS). If patients underwent a surgical procedure for their AABP, American Society of Anesthesiologists (ASA) physical classification and final surgical pathology were recorded.

Study Aims

The primary study aim was to record the concurrent diagnosis of penile cancer and AABP. The various benign pathologies on escutcheonectomy specimen were recorded and included: chronic inflammation, hyperkeratosis, balanitis, and squamous hyperplasia. Premalignant lesions from escutcheonectomy were recorded and included condyloma, CIS, or lichen sclerosis. For patients with penile cancer, oncologic data and staging using the TNM Staging 8th edition (2017) was recorded. Treatments types—topical therapy, local excision, partial penectomy, total penectomy, inguinal lymph node dissection, chemotherapy, and radiation were recorded.

Statistical Analysis

Basic demographic and clinical characteristics of the overall cohort were summarized. We used Chi-square tests and Fisher exact tests to compare differences between patients with benign surgical pathology and patients with pre-malignant or malignant surgical pathology. We performed all data management and analyses in STATA and R v13.2 (R Foundation for Statistical Computing, Vienna, Austria), using the ggplot2 for graphics. All tests were 2-sided, and the probability of a type I error was set at .05. The institutional review board approved the study.

RESULTS

Two hundred and seventy-two patients were identified with the diagnosis code of buried penis from an institutional search and from operative reports. Seventy-one patients were excluded after chart review revealed they did not carry the diagnosis and 53 duplicates were removed. Twenty-one patients were identified with the diagnosis of penile cancer. Four patients were removed as they did not carry the diagnosis of penile cancer. An additional 8 patients were removed as they did not also have the diagnosis of buried penis and finally duplicates (also in the AABP cohort) were removed. Ultimately, the final cohort was 150 patients with AABP (Fig. 1).

The median age of the AABP cohort was 54 years and the median BMI was 42.9 kg/m^2. For the majority of patients (95%), obesity was the etiology of their buried penis (Table 1). There were 11 patients (7%) in our cohort who had a diagnosis of penile cancer. Of the 150 patients in our cohort, 51 (35%) had at least one premalignant lesion on physical examination. Forty-four patients (30%) had lichen sclerosus, 10 patients (7%) had condyloma, and 2 patients (1%) had CIS. Pathology results were available for 73 patients (Tables 2 and 3). Of the patients with benign pathology, 61% had evidence of chronic inflammation (N = 39), 25% (N = 16) had hyperkeratosis, 9.4% had lichen sclerosus (N = 6), and 3.1% (N = 2) had balanitis.
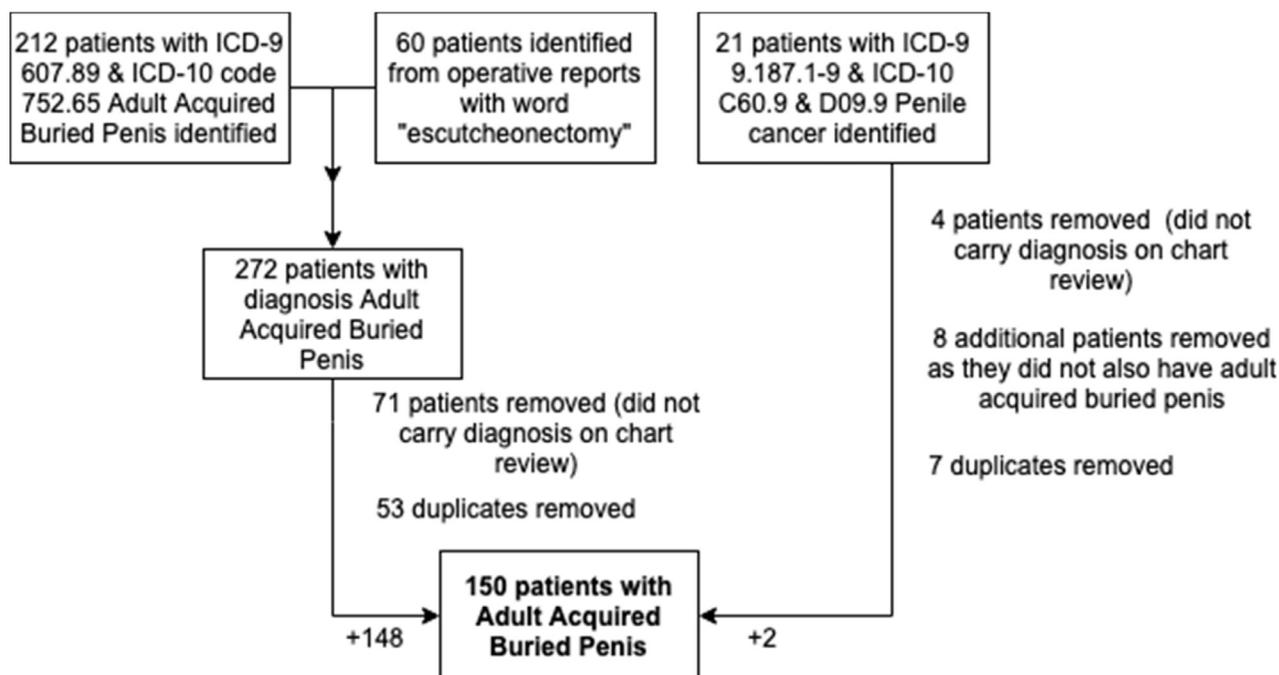

Figure 1. Search strategy and developing cohort of patients with adult acquired buried penis.

Table 1. Demographic characteristics of entire cohort (n = 150).

Characteristics	AABP (N = 150)
Median age (IQR)	55 (42-67)
Median BMI (IQR)	43 (36-49)
Median ASA classification (IQR)	3 (2-3)
Comorbidities (%)	Percent of cohort (N)
Respiratory (OSA, COPD, asthma)	57 (38%)
Diabetes	77 (51%)
Hypertension	98 (65%)
Fournier's gangrene	9 (6%)
Etiology of AABP (%)	
Lymphedema	20 (13%)
Cicatrix	48 (32%)
Obesity	143 (95%)
Risk factors (%)	
History of tobacco use	79 (53%)
Circumcision status	
Circumcised	62 (41%)
Uncircumcised	8 (5%)
Unknown	80 (53%)
Age at circumcision (%)	
Neonate	21 (34%)
Child	20 (32%)
Adult	12 (19%)
Unknown	9 (15%)
HPV status (%)	
Positive	5 (3%)
Negative	2 (1%)
Unknown	150 (95%)

Note: Some patients had more than one circumcision procedure. Circumcision was defined as removal of preputial skin and initial age was recorded.
Obstructive sleep apnea (OSA), chronic obstructive pulmonary disease (COPD).

When evaluating risk factors for penile cancer, 79 patients (53%) reported a smoking history. Circumcision status was known in 70 patients; of these, 62 (89%) of patients reported circumcision, 8 patients (11%) reported no circumcision, and the other 80 patients had a circumcision status that was not documented. Among the 62 patients with recorded circumcision, 21 (34%) had neonatal circumcision, 20 (32%) had circumcision as a child, 12 (19%) had adult circumcision and in 9 patients (15%) the timing of circumcision is unknown. Only a very small number of the overall cohort had HPV or HIV statuses recorded.

Patients with penile cancer were slightly older with a median age of 58 years. There were more patients with a smoking history (73%) within this cohort. When a comparison of demographic characteristics between patients with benign pathology and patients with malignant or premalignant pathology was performed using Chi squared tests and Fishers exact test, patients with premalignant or malignant lesions surprisingly were more likely to have a lower BMI and were more likely to have lymphedema listed as the etiology of AABP (Table 2).

The circumcision status of patients who developed penile cancer was unknown for 6 patients (55%) while 1 patient (9%) had never been circumcised and 4 (36%) underwent neonatal or child circumcision. Pathology data were available for 8 of the patients with penile cancer. Four patients had AJCC stage 1 penile cancer and 3 patients had AJCC stage 2 penile cancer and 1 patient had AJCC stage 4 penile cancer. Patients underwent a variety of treatments in a stepwise fashion for their penile cancer—7 (64%) underwent local excision, 4 (36%) underwent partial penectomy, 3 (27%) underwent total penectomy, and 5 (45%) underwent inguinal lymph node dissection as part of their treatment (Supplementary Table 1).

DISCUSSION

Penile cancer is extremely rare and is estimated to account for less than 1% of malignancies in the US and Western Europe.[5] We report a penile cancer prevalence of 7% in a population of patients with AABP. Further, we report a rate of premalignant lesions including condyloma, carcinoma in situ, and lichen sclerosus of 35%. We included lichen sclerosus as a premalignant lesion given evidence that it is frequently found in specimens of invasive penile cancer at rates of approximately 33% and there is a strong association with non-HPV related penile carcinomas.[10] We reported these lesions based on clinical examination

Table 2. Comparison of demographic characteristics between patients with benign pathology and patients with malignant or pre-malignant pathology.

Characteristics	Benign N = 57	Malignant or Premalignant N= 15	P Value
Median age (IQR)	64 (54-69)	51 (40-66)	.13
Median BMI (IQR)	44 (38-48)	35 (31-43)	.01
Median ASA classification	3	3	.15
Comorbidities (%)			
Respiratory (OSA, COPD, Asthma)	21 (37)	7 (47)	.42
Diabetes	27 (47)	4 (27)	.24*
Hypertension	34 (42)	9 (60)	.88
Etiology of AABP (%)			
Lymphedema	0 (0)	9 (60)	
Cicatrix	23 (40)	5 (33)	.62
Obesity	54 (95)	14 (93)	1*
History of tobacco use	23 (40)	13 (86)	.002*

The sample for this table only includes patients who underwent surgery, and therefore have pathologic data available. Malignant and/or premalignant lesions were compared to benign lesions. Benign lesions included chronic inflammation, hyperkeratosis, balanitis, or squamous hyperplasia. Premalignant lesions include condyloma, CIS, or lichen sclerosus. Differences between groups were compared using chi-squared test.
Obstructive sleep apnea (OSA), chronic obstructive pulmonary disease (COPD).
* Fisher-Exact test was used to compare differences between groups when cell sizes were <5.

Table 3. Premalignant lesions and benign pathology within AABP population.

Premalignant lesions based on physical examination	Percent of cohort (N = 142)
Presence of premalignant lesion (any type)	35% (N = 51)
Condyloma	7% (N = 10)
CIS	1.4% (N = 2)
Lichen sclerosus	31% (N = 44)
Benign pathology report findings	Percent of Cohort (N = 64)
Chronic inflammation	61% (N = 39)
Hyperkeratosis	25% (N = 16)
Lichen sclerosus	9.4% (N = 6)
Condyloma	1.5% (N = 1)
Balanitis	3.1% (N = 2)
No pathologic findings	19% (N = 12)
Squamous hyperplasia	3.1% (N = 2)

Note: Some patients had more than one premalignant lesion so numbers will not add up to the cohort total. Presence of premalignant lesions was based on physical examination and in 8 patients, the phallus was unable to be exhumed for examination. Some patients had more than one benign pathology on their final pathology. Percentages will not add up to 100.

findings as the pathologic changes are subtle and often not included on pathology reports for AABP specimens which is likely because of the large (ie. 30-50 lb) specimens provided at the time of buried penis surgery.[10] At least 36% of our AABP patients with penile cancer (N = 4) were previously circumcised and 41% of our overall AABP cohort. Within our cohort of patient with AABP, although circumcision status is only known in 45% (N = 70), we believe that the majority of our cohort is likely circumcised as 90% of patients in our cohort with a documented circumcision status are circumcised. Although our cohort is not a random population sample, data from CDC estimate that up to 80% of males in our region undergo neonatal circumcision[11,12]. Prior circumcision may not be an absolute protective factor against penile cancer in patients who eventually develop AABP.[13]

AABP is a condition that combines multiple risk factors for penile cancer including functionally uncircumcised status, functional phimosis due to cicatrix formation, and poor hygiene. Penile burying creates a moist environment with chronic inflammation and this was seen pathologically in the majority of our patients' surgical specimens (Table 2). While 2 patients with penile cancer had Human Papilloma Virus, the most likely pathway to carcinogenesis in this population is chronic inflammation.[14]

Patients with AABP are often referred to a specialist at a tertiary referral center to discuss potential surgical options intended to improve their quality of life. However, based on our findings, patients should perhaps also be counseled on the potential increased risk of penile cancer and premalignant lesions. Patients with AABP are often instructed to lose weight or referred for gastric bypass procedures prior to urologic referral or prior to being offered surgical correction by an urologist. However, this condition rarely corrects with weight loss alone as weight loss often spares the suprapubic fat pad and skin laxity with massive weight loss often just exacerbates penile burying.[15] Thus, many of these patients require surgical treatment even after weight loss and these delays could result in progression of any malignant or premalignant lesions.

Examination of the buried penis is difficult and sometimes impossible in the setting of a tight cicatrix. This makes early detection and prompt treatment of penile cancer in these patients challenging especially since many of these patients report not visualizing their phallus for years. Multiple studies in patients with penile cancer have shown that physical examination is the most reliable tool to estimate tumor size and invasion into the corpus cavernosum when compared to MRI and ultrasound.[16,17] However, in the AABP population, performing a comprehensive physical examination can be difficult or impossible due to inability to exhume the penis, like the 8 patients in our cohort.

Our study finding of 7% prevalence of penile cancer in patients with a diagnosis of AABP is eye-opening. Identification and treatment of this condition is relatively new and the number of patients with this condition is on the rise. More reports are needed from other institutions to describe the true prevalence of penile cancer in this cohort of patients. Limitations include the retrospective nature and possible limited generalizability of our findings from a single institution and a major tertiary referral center. Given the retrospective nature of the study based on electronic medical records, several important data points including several risk factors for penile cancer—sexual practices, hygiene practices, immunosuppression status, socioeconomic status, UVA exposure, circumcision status and details including timing of circumcision, circumcision revisions are missing for a large portion of our cohort. Unfortunately, we cannot delineate the timing from development of penile burying and length of time required to develop premalignant lesions or penile cancer.

CONCLUSION

Penile cancer is an aggressive and rare disease. The prevalence of penile cancer appears to be higher in patients with AABP, however more data are needed to confirm these initial findings. In addition, premalignant lesions including carcinoma in situ, condyloma, and lichen sclerosus are common in this population. Patients with buried penis should be counseled on these risks and should be considered for surgical treatment particularly when patients cannot undergo an adequate physical examination.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.urology.2019.07.019.

References

1. Abdulla A, Daya D, Pinthus J, Davies T. Buried penis: an unrecognized risk factor in the development of invasive penile cancer. *Can Urol Assoc J*. 2012;6:E199–E202. https://doi.org/10.5489/cuaj.11226.

2. Theisen KM, Fuller TW, Rusilko P. Surgical management of adult-acquired buried penis: impact on urinary and sexual quality of life outcomes. *Urology*. 2018;116:180–184. https://doi.org/10.1016/j.urology.2018.03.031.

3. Manwaring J, Vourganti S, Nikolavsky D, Valente AL, Byler T. Pannus is the new prepuce? Penile cancer in a buried phallus. *Case Rep Urol*. 2015;2015: 403545. https://doi.org/10.1155/2015/403545.

4. Hernandez BY, Barnholtz-Sloan J, German RR, et al. Burden of invasive squamous cell carcinoma of the penis in the United States, 1998-2003. *Cancer*. 2008;113(10 Suppl):2883–2891. https://doi.org/10.1002/cncr.23743.

5. Douglawi A, Masterson TA. Updates on the epidemiology and risk factors for penile cancer. *Transl Androl Urol*. 2017;6:785–790. https://doi.org/10.21037/tau.2017.05.19.

6. Hakenberg OW, Compérat EM, Minhas S, Necchi A, Protzel C, Watkin N. EAU guidelines on penile cancer: 2014 update. *Eur Urol*. 2015;67:142–150. https://doi.org/10.1016/j.eururo.2014.10.017.

7. Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2017. *CA Cancer J Clin*. 2017;67:7–30. https://doi.org/10.3322/caac.21387.

8. Barnes KT, Smith BJ, Lynch CF, Gupta A. Obesity and invasive penile cancer. *Eur Urol*. 2013;63:588–589. https://doi.org/10.1016/j.eururo.2012.11.046.

9. Barnes KT, McDowell BD, Button A, Smith BJ, Lynch CF, Gupta A. Obesity is associated with increased risk of invasive penile cancer. *BMC Urol*. 2016;16:42. https://doi.org/10.1186/s12894-016-0161-7.

10. Velazquez EF, Cubilla AL. Lichen sclerosus in 68 patients with squamous cell carcinoma of the penis: frequent atypias and correlation with special carcinoma variants suggests a precancerous role. *Am J Surg Pathol*. 2003;27:1448–1453.

11. Morris BJ, Bailis SA, Wiswell TE. Circumcision rates in the United States: rising or falling? What effect might the new affirmative pediatric policy statement have? *Mayo Clin Proc*. 2014;89:677–686. https://doi.org/10.1016/j.mayocp.2014.01.001.

12. Owings, M, Uddin S, Williams S. Trends in Circumcision for Male Newborns in U.S. Hospitals: 1979−2010.

13. Alzubaidi AN, Hahn AE, Gelhaus PT, et al. Circumcision, buried penis, and obesity in a contemporary cohort of patients with penile cancer. *Urol Practice*. 2019;6:243–248.

14. Stratton KL, Culkin DJ. A contemporary review of HPV and penile cancer. *Oncology (Williston Park, NY)*. 2016;30:245–249.

15. Fuller TW, Theisen KM, Shah A, Rusilko PJ. Surgical management of adult acquired buried penis. *Curr Urol Rep*. 2018;19:22. https://doi.org/10.1007/s11934-018-0768-1.

16. Lont AP, Besnard APE, Gallee MPW, van Tinteren H, Horenblas S. A comparison of physical examination and imaging in determining the extent of primary penile carcinoma. *BJU Int*. 2003; 91:493–495.

17. Kayes O, Minhas S, Allen C, Hare C, Freeman A, Ralph D. The role of magnetic resonance imaging in the local staging of penile cancer. *Eur Urol*. 2007;51:1313–1318. https://doi.org/10.1016/j.eururo.2006.11.014. discussion 1318-1319.