Penile cancer: an analysis of socioeconomic factors at a southeastern tertiary referral center

Matthew McIntyre, MD,[1] Avi Weiss, MD,[2] Amy Wahlquist, MS,[1]
Thomas Keane, MD,[1] Harry Clarke, MD,[1] Stephen Savage, MD[1]

[1]Medical University of South Carolina, Charleston, South Carolina, USA
[2]Urology Specialist of Nevada, Las Vegas, Nevada, USA

MCINTYRE M, WEISS A, WAHLQUIST A, KEANE T, CLARKE H, SAVAGE S. Penile cancer: an analysis of socioeconomic factors at a southeastern tertiary referral center. The Canadian Journal of Urology. 2011;18(1):5524-5528.

Introduction: *Penile cancer is rare, often presenting in later stages. We sought to determine if factors potentially related to access to care were associated with worse outcomes.*

Methods: *We performed a retrospective review of all patients with the diagnosis of penile cancer over a 14 year period at the only tertiary referral center in the state. We collected data on multiple factors potentially associated with access to care.*

Results: *Fifty-five patients with penile cancer were identified. The average age was 57 years. Of the 55 patients, 23 patients (42%) had private insurance carriers, 16 (29%) had Medicare/Medicaid, 13 (24%) had no insurance, one had VA benefits, and no data was available on two patients. Typically, 4% of patients seen at our institution are uninsured. Pathologic tumor stage distribution was Tis (n = 9), Ta (1), T1 (15), T2 (16), and T3 (4). Nodal disease was present in 11, four of whom (38%) were uninsured, and metastatic disease was present in three. Of the 55 patients, eight admitted to greater than two alcoholic drinks per day three, of whom 38% presented with advanced disease. School district graduation rate was also calculated and similar among all groups. Univariate and multivariate modeling revealed no factors associated with delay to care.*

Conclusions: *Patients presenting to a referral center in the southeastern United States with penile cancer more commonly lack health insurance. Additionally, patients who are heavy alcohol users or are uninsured present with advanced disease. These factors contribute to poorer prognosis in these patients.*

Key Words: penile cancer, socioeconomic, alcohol, delay to care

Introduction

Penile cancer is a relatively rare cancer in the United States. It accounts for 0.4% to 0.6% of malignant cancers among men in the United States and Europe.[1] Previous studies have shown that greater than 50% of patients will present with symptom duration of greater than 6 months prior to presentation.[2] This is especially important since penile cancer has dramatically higher cure rates for local disease versus disease that has progressed to regional or metastatic spread. Many theories have been put forward to explain the potential delay to presentation.[3] These factors include reluctance to address medical problems, concern about potentially disfiguring surgery, as well as potential barriers to access to care. Penile cancer has also been shown to be related to poor hygienic practices as well as potentially related to sexually transmitted diseases.[4] Various public programs have sought to help reduce the risks of similar diseases through education.[5]

Due to the many potential variables associated with the development, presentation and treatment of penile cancer, there is potential for a disproportionately large socioeconomic effect when compared to other

Accepted for publication November 2010

Address correspondence to Dr. Matthew McIntyre, 96 Jonathan Lucas Street, CSB 644, PO Box 250620, Charleston, SC 29425 USA

malignancies. If this could be identified, more effective prevention strategies could be implemented, particularly in a malignancy with clear targets for prevention. As a regional tertiary referral center that includes significant rural areas, we sought to determine if we could identify putative socioeconomic factors that portended poorer outcomes in our patient population.

Methods

After obtaining Internal Review Board approval, we retrospectively reviewed our database of patients diagnosed with penile cancer between 1994 to 2008. We collected preoperative data on baseline patient demographics, length of symptoms (less than 6 months or longer than 6 months), tumor stage, presence or absence of nodal disease, tumor metastasis, treatment choice, recurrence, death due to disease, and loss to follow up. We specifically sought to identify factors potentially related to access to care including insurance provider, distance to referral center, alcohol use, and smoking history. We used univariate and multivariate logistic regression models to try and identify any variable that was related to delay to care. Chi-square tests were also used to compare categorical factors across groups for variables that might limit access to care. All statistical calculations were performed using SPSS 16.

Results

We identified 55 patients with the diagnosis of penile cancer during the study dates. Baseline parameters are included in Table 1. Seven patients (13%) had documented previous circumcisions. The average age at presentation was 57 years old. Nineteen patients (35%) had symptoms greater than 6 months duration, 11 (20%) patients had symptoms for less than 6 months, and no data was available for 25 (45%). Of those with symptoms for greater than 6 months in duration, only four (21%) did not have any insurance.

Tumor stage of patients at presentation was T1 (27%), T2 (29%), T3 (7%), Tis (16%), while data was unavailable for 10 (18%). Table 2. Eleven patients presented with nodal disease while three patients had distant metastatic spread. Nodal status was defined by clinical and pathologic criteria. In some cases with grossly metastatic nodes, surgical pathology was not obtained. Forty-four (80%) patients underwent standard surgical excision, seven (13%) patients underwent Mohs micrographic surgery, and no data was found on four (7%). Four (7%) patients had recurrent disease. Five (9%) of the study patients were known to have died of the disease. Twenty-five patients (45%) were lost to follow up. Seventy-six percent of patients lost to follow up had some type of insurance.

In our patient population the average distance to the medical center from patient reported zip code was 82 miles. The average high school graduation rate in our study was 79%, while the state average is 75%. Twenty-three patients (42%) had private insurance carriers, 16 (29%) had Medicare/Medicaid, 13 (24%) had no insurance, one (2%) had VA benefits, and no data was available on two (4%). Current statistics show that 16.1% of state residents do not have insurance.[6] Eight patients (15%) admitted to greater than two alcoholic drinks per day.

TABLE 1. **Basic characteristics grouped by length of symptoms**

	Total n = 55 (%)	**> 6 months duration n = 19**	**< 6 months duration n = 11**
Age	57.2	54	57.8
Distance in miles	82.1	59.5	87.6
> 2 alcoholic drinks per day	8 (14.5)	2 (10.5)	2 (18)
Current or former smoker	20 (36)	10 (52)	8 (72)
Have an insurance provider	40 (72)	15 (78)	7 (63)
Were referred from outside institutions	42 (76)	17 (89)	7 (63)
Marital married	26 (47)	12 (63)	5 (45)
Surgical intervention			
Standard surgical approach	44 (80)	17 (89)	10 (90)
Mohs	7 (13)	2 (11)	

Length of symptom data was unavailable for 25 patients

TABLE 2. **Tumor stage, grade, nodal metastasis, distant metastasis**

Stage	n = 55 (%)
Tis	9 (16.4)
Ta	1 (1.8)
T1	15 (27.3)
T2	16 (29)
T3	4 (7.3)
T4	0
No data	10 (18.2)
Grade	
Well differentiated	20 (36.4)
Moderately differentiated	10 (18.2)
Poorly differentiated	11 (20)
No data	14 (25.4)
Nodal metastatic disease	11 (20)
Distant metastatic disease	3 (5.4)

When we examined the factors that may have limited access to care we found that distance from referral center was similar among all groups. Of the 11 patients with nodal disease, four (36%) did not have any form of insurance, compared to 21% of the patients without nodal disease (p = 0.285). Three of the eight (38%) patients who admitted to greater than two alcohol drinks per day presented with advanced disease compared to 17% of those without advanced disease (p = 0.181).

Thirty patients had data on length of symptoms prior to presentation. Univariate logistic regression modeling was performed using these patients examining age, graduation rate, distance from referral center, greater than two alcoholic drinks per day, tobacco use, insurance, nodal metastasis, delay to treatment after diagnosis, and standard surgical intervention versus Mohs to see if any of these had a significant relationship with length of symptoms greater than 6 months. No patients had distant metastatic disease in this group. In the univariate models, no statistically significant variables were identified. A multivariate regression model excluding the variables that could not be solved (due to small sample sizes) in univariate modeling as well as delay to surgical treatment and recurrences did not reveal significant relationships with length of symptoms when adjusting for other variables.

Discussion

Penile cancer is a rare disease in the United States which makes studying it somewhat difficult. Previous studies by Goodman et al[7] using the SEER database have shown the highest rates to occur among Hispanic and African-American males and in the southeastern United States. This fact makes our institutional experience somewhat unique given its geographic location and demographic makeup of the local and surrounding population.

As previously stated, most patients with penile cancer will have an extended duration of symptoms prior to presentation.[2] In the present study at least 20% presented with symptoms for greater than 6 months duration. From our data, this delay in presentation does not seem to be due to a lack of access to care or a lack of medical insurance provider as a majority of our patients (78%) with delayed presentation had a medical insurance carrier. The delay may more likely be explained by poor patient understanding of symptoms or embarrassment regarding lesion location, though lack of access to care may play a role in selected cases. Previous studies in cases of testicular cancer have shown that feelings of masculine identity are associated with normal appearing genitals and have been a source of delay.[8] It would appear that regardless of insurance status, once these patients present to a care provider their issues are addressed appropriately.

Interestingly, the patient demographics do not match our general population of patients and demonstrate a much larger percentage of patients without health insurance. It is clear that patients without health insurance are less likely to participate in screening and well-care activities. Thus, it is possible that these patients are not properly educated on healthy lifestyle practices. Unaddressed phimosis, which has been associated with penile cancer,[9] may potentially result in delay of diagnosis.

Nodal disease has long been known to be a predictor of poorer outcomes. In the series by Ravi,[10] 5 year survival in patients with 0, 1 to 3, and more than 4 positive lymph nodes were 95%, 81% and 50% respectively. Similar outcome data have also been seen in more recent series.[11-12] Eleven patients in our study had nodal disease and, of these, four (36%) did not have insurance. When examining the absolute percentage, these numbers are not striking, but when comparing this to our overall average of 4% uninsured urology patients we see a significant increase. When we looked at the pathology of these patients we found that all four of the uninsured patients with nodal disease had at least N2 disease. Among the insured patients 30% had only N1 disease. With respect to histology all of the uninsured patients had either moderate or poorly differentiated tumors. Though the data does not clearly support a delay to diagnosis, other factors related to lower socioeconomic status may apply such as poorer

hygiene, exposure to carcinogenic compounds as well as smoking.[4]

The association of alcohol consumption and the development of squamous cell carcinoma has long been established for esophageal and pharyngeal cancers.[13] The exact mechanism of carcinogenesis is as yet unknown.[14] In the current study we found that 38% of the men that reported using greater than two alcoholic drinks per day had advanced disease. In a recent Dutch analysis Madsen et al[15] found that abstinence from alcohol had a significant risk reduction of penile cancer. Though direct causal evidence is currently lacking, one can see a trend in the current literature and this study to support the notion that alcohol consumption may portend a worse prognosis in patients with penile cancer. Potential explanations would include the generalized poorer nutritional status, resultant decreased immune function, and lesser inclination towards a healthier lifestyle.

Despite associations noted previously, our series failed to identify any statistically significant factors that lead to a delay in presentation and therefore treatment. There are several limitations of the study that could explain these results. The retrospective design resulted in some unattainable data. The relatively small sample size could result in skewing data and limits the ability to find significant associations.

The debate over neonatal circumcision has been waged for decades and appears to have no end in sight with ardent supports on both sides of this issue. The relevance of this to the current study is with its regard to access to neonatal circumcision. Current series have revealed no significant differences based on public or private insurance, or tertiary or community hospitals on rates of circumcisions.[16] This trend has not always been true. With most cases of penile cancer presenting after the fifth decade, we are seeing the consequences of decisions made more than 50 years ago. Previous studies have raised questions about access to care in the past.[17] Though this study does not specifically examine this issue, given our states rural agrarian past, access to medical care could easily have been an issue for patients coming from poorer and more rural areas of the state.

Conclusions

Patients presenting to our institution with penile cancer more commonly lack health insurance when compared to our general urologic population. Additionally, patients who are heavy alcohol users or are uninsured are more likely to present with advanced disease. These factors support previous hypotheses that lower socioeconomic status and decreased utilization of healthcare appear to contribute to poorer prognosis in these patients. Future efforts to eliminate these potential detrimental variables would likely have a substantial benefit in survival rates and potentially overall incidence for penile cancer. □

References

1. Gloeckler-Ries LA, Hankey BF, Edwards BK. Cancer Statistics Review 1973-1987. Vol Institutes of Health Publication No. 90-2789. Bethesda MD: National Insitutes of Health, National Cancer Institute; 1990.
2. Narayana AS, Olney LE, Loening SA, Weimar GW, Culp DA. Carcinoma of the penis: analysis of 219 cases. *Cancer* 1982;49(10):2185-2191.
3. Agarwal P, Sharma D. Autodestruction of penis due to carcinoma. *J Eur Acad Dermatol Venereol* 2005;19(2):220-222.
4. Bleeker MC, Heideman DA, Snijders PJ, Horenblas S, Dillner J, Meijer CJ. Penile cancer: epidemiology, pathogenesis and prevention. *World J Urol* 2009;27(2):141-150.
5. Garland S, Park SN, Ngan HY et al. The need for public education on HPV and cervical cancer prevention in Asia. Opinions of experts at the AOGIN conference. *Vaccine* 2008;26(43):5435-5440.
6. DeNavas-Walt C, Proctor BD, Smith JC. Income, Poverty, and Health Insurance Coverage in the United States: 2008. In: Bureau C, ed. Washington DC: U.S. Government Printing Office; 2009.
7. Goodman MT, Hernandez BY, Shvetsov YB. Demographic and pathologic differences in the incidence of invasive penile cancer in the United States, 1995-2003. *Cancer Epidemiol Biomarkers Prev* 2007;16(9):1833-1839.
8. Gascoigne P, Mason MD, Roberts E. Factors affecting presentation and delay in patients with testicular cancer: results of a qualitative study. *Psychooncology* 1999;8(2):144-154.
9. Tsen HF, Morgenstern H, Mack T, Peters RK. Risk factors for penile cancer: results of a population-based case-control study in Los Angeles County (United States). *Cancer Causes Control* 2001;12(3):267-277.
10. Ravi R. Correlation between the extent of nodal involvement and survival following groin dissection for carcinoma of the penis. *Br J Urol* 1993;72(5 Pt 2):817-819.
11. Lopes A, Hidalgo GS, Kowalski LP, Torloni H, Rossi BM, Fonseca FP. Prognostic factors in carcinoma of the penis: multivariate analysis of 145 patients treated with amputation and lymphadenectomy. *J Urol* 1996;156(5):1637-1642.
12. Korets R, Koppie TM, Snyder ME, Russo P. Partial penectomy for patients with squamous cell carcinoma of the penis: the Memorial Sloan-Kettering experience. *Ann Surg Oncol* 2007;14(12):3614-3619.
13. Baez A. Genetic and environmental factors in head and neck cancer genesis. *J Environ Sci Health C Environ Carcinog Ecotoxicol Rev* 2008;26(2):174-200.
14. Pelucchi C, Gallus S, Garavello W, Bosetti C, La Vecchia C. Cancer risk associated with alcohol and tobacco use: focus on upper aero-digestive tract and liver. *Alcohol Res Health* 2006;29(3):193-198.
15. Madsen BS, van den Brule AJ, Jensen HL, Wohlfahrt J, Frisch M. Risk factors for squamous cell carcinoma of the penis--population-based case-control study in Denmark. *Cancer Epidemiol Biomarkers Prev* 2008;17(10):2683-2691.
16. Quayle SS, Coplen DE, Austin PF. The effect of health care coverage on circumcision rates among newborns. *J Urol* 2003;170(4 Pt 2):1533-1536; discussion 1536.
17. Schoen EJ. The status of circumcision of newborns. *N Engl J Med* 1990;322(18):1308-1312.

EDITORIAL COMMENT

Re: Penile cancer: an analysis of socioeconomic factors at a southeastern tertiary referral center

The authors are to be congratulated in tackling the relationship between socioeconomic factors and penile cancer. Several of the risk factors are already established such as lack of circumcision, smoking and HPV exposure. Alcohol consumption has been controversial, but is related to other squamous cell cancers. One hypothesis is that cirrhosis contributes to reduced resistance to carcinogens. Recognizing alcohol dependence is important for perioperative management and may impact on suitability for chemotherapy.

The size of the study may account for differences reaching statistical significance, however several trends are clear. Lack of insurance was associated with late presentation, nodal involvement at presentation. Forty five percent of patients were lost to follow up, which compares poorly with European studies, however lack of insurance did not predict for this. Also of interest is while 16% of the state residents lack insurance, only 4% of urology patients attending the institution was uninsured. Thus the most glaring comparison is between patients with penile cancer and other urology patients.

These type of studies are important as they heighten clinicians to seek out risk factors for poorer outcome and non-compliance with follow up. Cancer preventative strategies are informed by such data. Perhaps the first example of prevention of occupational acquired cancer was by the chimney sweeps' guild in Denmark, as reported in the 19th century. Their insistence on daily bathing significantly reduced the incidence of scrotal cancer among chimney sweeps when compared to nations where this was not practiced. Prevention of penile cancer is controversial. Various strategies include routine neonatal circumcision, vaccination against HPV, barrier contraception or improving hygiene.1 The lead-time between such approaches and eventual benefit is likely to be decades. Furthermore the relative rarity of this condition in North America mitigates against such projects. It may well fall to emerging economies where the incidence of penile cancer is higher to promote such strategies.

References

1. Minhas S, Manseck A, Watya S, Hegarty PK. Penile cancer - prevention and premalignant conditions. *Urology* 2010:76(2 Suppl 1);S24-S35.

Paul K. Hegarty
Consultant Urologic Surgeon
Guy's Hospital, London
United Kingdom