ONCOLOGY

Vulvar cancer in young women: demographic features and outcome evaluation

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OBJECTIVE: The objective of the study was to identify prognostic and environmental factors associated with vulvar carcinoma in young women.

STUDY DESIGN: This study was a review of patients younger than 45 years who were diagnosed with vulvar squamous cell carcinoma between 1994 and 2006.

RESULTS: Fifty-six patients were identified. Median age was 38 years and median follow-up was 25.3 months. Fifty-eight percent of patients presented with stage I disease; 77% smoked tobacco. Of patients with advanced disease, 53.3% were smokers, 40% had human papillomavirus (HPV) exposure, 46.7% had a history of vulvar intraepithelial neoplasia (VIN), and 6.7% were immunocompromised. Symptoms were present for more than 12 months in 47%, but symptom duration did not correlate with stage ($P = .42$) or positive lymph nodes ($P = .28$). Disease recurred in 10.7% and 5.4% died of disease.

CONCLUSION: Young women with vulvar cancer tend to have early-stage disease, smoke, have a history of HPV, and have VIN. Many of the factors that place these patients at continuous risk are modifiable.

Key words: Demographic, outcome, vulvar cancer, young

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Vulvar cancer is a relatively uncommon malignancy, occurring at a rate of 2.2 per 100,000 women per year. The American Cancer Society estimated that 3490 women were diagnosed with vulvar cancer in 2007 and that 880 women died of their disease.[1] The incidence of invasive and in situ vulvar carcinoma has been increasing at a rate of 2.4% per year, and the National Cancer Institute has identified vulvar cancer as 1 of 12 cancers with rising incidence.[2] Although vulvar cancer typically affects women in the seventh and eighth decade with a median age of death of 79 years, Messing and Gallup[3] demonstrated the average presenting age decreased from 69 to 55 years between 1979 and 1993. Others have corroborated this increasing burden of disease in young patients.[4-6]

A recent Surveillance, Epidemiology, and End Result Program-derived data review demonstrated that over the past 28 years, the prevalence of in situ and invasive vulvar carcinoma has increased. The incidence of in situ disease increased a striking 411%, with the authors noting that the increase of in situ disease occurred predominantly in the under-65 age group, with a peak in the incidence of in situ vulvar carcinoma at 40-49 years of age.[6] Interestingly, the authors did not identify a corresponding peak in invasive disease incidence delayed 5-20 years as might be expected but rather a steady increase of invasive vulvar cancer with age, supporting a mounting body of evidence that vulvar cancer may have a different pathogenesis in younger and older women.

Owing to the evolution of the patient population, we sought to evaluate the demographic, surgicopathologic, and outcome data for women with the most common vulvar cancer, squamous cell, who present at age 45 years or younger. Our hypothesis was that in young women, vulvar cancer may be associated with different, potentially modifiable, risk factors than the traditional, elderly vulvar cancer patient.

Materials and Methods

Institutional review board-approved chart reviews were performed at the University of Oklahoma and the University of Minnesota for all patients younger than 45 years of age diagnosed with squamous cell carcinoma of the vulva between the years 1994 and 2006. We collected demographic information including: history of tobacco use, documented human papillomavirus (HPV) infection or cervical intraepithelial neoplasia, history of vulvar intraepithelial neoplasia (VIN), type of surgical intervention, adjuvant treatment, and outcome. Because the study period spanned 12 years, cervical intraepithelial neoplasia (CIN) documentation was used for earlier patients, whereas HPV testing and/or CIN abnormalities were used to classify HPV exposure. In addition, an attempt was made

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TABLE 1
Patient characteristics (n = 56)

	38 (19-45)	
Median age, y (range)	**n (%)**	
Tobacco		
Yes	43 (77)	NS[a]
No	13 (23)	
Previous HPV and CIN		
Yes	32 (57)	NS[a]
No	24 (43)	
Previous diagnosis of VIN		
Yes	35 (62)	NS[a]
No	21 (38)	
Immunocompromised state	10 (18)	NS[a]
HIV	2	
Diabetes	5	
Transplant recipient	2	
Chronic steroid use	1	
Duration of symptoms (months)	NS[a]	
No symptoms	2 (4)	
≥ 6	22 (39)	
7-12	7 (13)	
> 12	16 (28)	
Unknown	9 (16)	
Stage at diagnosis	NS[a]	
I	28 (50)	
II	13 (23)	
III	11 (20)	
IV	4 (7)	

CIN, cervical intraepithelial neoplasia; *HIV*, human immunodeficiency virus; *HPV*, human papillomavirus; *VIN*, vulvar intraepithelial neoplasia.

[a] *NS*, relationship between variables and risk of positive nodes.

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to account for immunosuppression by searching for comorbidities such as human immunodeficiency virus (HIV) infection, organ transplantation, chronic steroid use, and diabetes.

All statistical analyses were performed using SAS version 9.1 (SAS Institute, Inc, Cary, NC). Pearson's χ^2 was used for the univariate analysis of association between variables. Logistic regression was used for the multivariate analysis of covariates found to be significant in univariate analysis. Survival analysis was performed using Kaplan-Meier product limit method.

Results

Fifty-six cases of primary squamous cell carcinoma of the vulva were identified. Patient characteristics are described in Table 1. Both tobacco abuse and previous dysplasia (vulvar or cervical) were prevalent, and almost a fifth of patients had an immunosuppressive condition. The stage of distribution and associated symptoms were similar to previous reports, with the most common symptom being pruritus, but the delay from onset of symptoms to diagnosis was relatively short, with almost half of the patients reporting less than 6 months of symptoms (Table 1).

Patients with advanced disease (stage III and IV) were less likely to have had dysplasia, HPV (40%), or VIN (46.7%), and 6.7% were immunocompromised. Forty-seven percent of patients with advanced-stage disease had symptoms longer than 12 months, but there was no significant relationship between length of symptoms and stage ($P = .42$) or positive lymph node metastases ($P = .28$).

Modified radical vulvectomy with unilateral or bilateral lymph node dissection was performed in 80% of cases and 18% were noted to have positive nodes. Patients with positive lymph nodes were more likely to have had cervical dysplasia or HPV than those with negative lymph nodes ($P = .04$).

The median follow-up was 25.3 months. Overall survival and recurrence-free survival are shown in Figures 1 and 2, respectively. Six patients (10.7%) had recurrence of disease, 3 with local recurrence and 3 with distant metastases. All three patients with distant recurrences (5.4%) died of their disease.

Comment

In this largest study of young women with squamous cell carcinoma of the vulva, we found that the risk factors associated with vulvar cancer differ from those reported for the general, older vulvar cancer population. Specifically these women had more tobacco exposure, a greater risk of antecedent HPV. Given that the overall incidence of vulvar cancer is rising steadily and that premalignant lesions in young women are rising at an alarming rate, this group of women deserves directed attention.

We found, as previously reported, that there is an association between a compromised immune status and vulvar cancer.[7,8] These patients share some of the same risk factors as otherwise healthy women, such as tobacco use, multiple