Clinical presentation of verruca vulgaris in HIV

J Leavens MD, PM Young MD, M Mert MS, D Sawcer MD PhD, I Ahronowitz MD

Affiliations: Department of Dermatology, Keck School of Medicine, University of Southern California, Los Angeles, California, USA

Corresponding Author: Paulina M Young MD, Department of Dermatology, Keck School of Medicine, University of Southern California, 1975 Zonal Avenue, Los Angeles, CA 90089, Tel: 949-300-1840, Email: paulina108@gmail.com

Abstract

Background: Immunocompromised patients, including those with human immunodeficiency virus (HIV), have been observed to have verrucae that are more extensive and treatment-resistant compared to those in immunocompetent patients. However, there is a critical lack of data in the current literature on the characteristics of verruca vulgaris in individuals with HIV.

Methods: This retrospective chart review included a cohort of HIV-positive individuals and a control group of immunocompetent individuals presenting to an outpatient, county hospital-based dermatology clinic for evaluation of verruca vulgaris between the years of 2016 and 2018. Clinical characteristics, including gender, age, last CD4 count, viral load, antiretroviral therapy adherence, and total number and location of lesions were recorded.

Results: A total of 66 patients (33 HIV-positive, 33 immunocompetent) were included in the study. HIV-positive status was significantly associated with a higher total number of lesions (42% of immunocompromised patients versus 21% of immunocompetent patients presented with four or more lesions, P=0.04) as well as location of lesions on the face, scalp, and neck (51.5% versus 9.1%, P<0.001).

Conclusions: HIV-positive status may be associated not only with a higher burden of verruca vuwlgaris lesions but also a higher number of lesions in locations at or above the neck.

Keywords: HIV, human papillomavirus, verruca vulgaris,

Introduction

Verruca vulgaris (common warts) that are more extensive and resistant to therapy have been observed in immunocompromised individuals, including those with human immunodeficiency virus (HIV), [1-3]. It is known that individuals with inherited immunodeficiencies, autoimmune disorders, organ transplantation, and HIV infection are at increased risk of infection with both low- and high-risk human papillomavirus (HPV) types. Immune compromise creates an environment for persistent HPV infection and a subsequent increased risk of malignant transformation [4-6].

The incidence of HPV-related cancers has increased among the HIV-infected population compared with the general population [6] and high rates of HPV infection and HPV-associated diseases have been detected at various body sites, including the cervix, anus, and mouth [1]. A comparative study of HIV-positive and HIV-negative men who have sex with men showed that HPV-positive individuals were more likely to have oral HPV infection and to be infected with high-risk HPV types and with multiple HPV types [2]. Furthermore, oral HPV infection in HIV-infected individuals was found to be related to low CD4 cell counts (<200 cells/ml) and more than one oral sex partner within the previous year [2].

In addition to recent medical literature showing high rates of anogenital, cervical, and oral HPV in HIV-positive individuals, previous studies have demonstrated that plantar warts tend to have a more aggressive course in HIV-infected individuals. A study found that HIV-positive individuals presented with a significantly greater number and total area of plantar verrucae than did HIV-negative patients and had a greater frequency of lesion recurrence following treatment with surgical curettage [3]. Similarly, Meberg et al. found that HIV-positive individuals presented with significantly larger and

more numerous plantar verrucae, and also with a greater number of mosaic-type lesions, than did those who were HIV-negative [7]. These three characteristics did not correlate with CD4 cell counts [7].

In our county hospital-based HIV dermatology clinic, we have observed clinically that HIV-positive patients tended to present with a greater total number of verrucae and with lesions in less classic locations, such as the head and neck area. The purpose of this study is to further evaluate the clinical features of verruca vulgaris in patients with HIV/AIDS compared to immunocompetent individuals through a retrospective chart review.

Methods

Patients

This retrospective study included two groups of patients who were diagnosed with, and treated for verruca vulgaris at Los Angeles County (LAC) and University of Southern California's ambulatory dermatology clinic from 2016 to 2018. The first was a group of 33 individuals with HIV/AIDS and no comorbid immune compromising conditions and the second was a group of 33 immunocompetent individuals. Excluded from the second group were any patients taking immunosuppressive medications or having a history of solid organ or hematopoietic transplant, malignancy, autoimmune conditions, or inflammatory disorders. The diagnosis of verruca vulgaris was made through clinical history and examination, although a biopsy was performed in one case in which the diagnosis was questionable. Individuals with condyloma acuminata were excluded from the study.

Clinical profiles

The following clinical characteristics were recorded for the group of HIV-positive individuals: gender, age at presentation to clinic, race; number of years between HIV/AIDS diagnosis and initial clinical encounter, antiretroviral therapy status (adherent versus non-adherent, determined through chart review of documentation by primary care physician), last CD4 count and viral load prior to diagnosis, history of AIDS-defining illness, the total number and location of verruca vulgaris lesions on initial clinical encounter, and any reported associated symptoms. The same data was recorded for the group of immunocompetent patients with the exception of that related to HIV-infection. Of note, due to the protected nature of HIV-related health information, the data collection was performed anonymously without extraction of individual protected health information, allowing exempt designation by our Institutional Review Board.

Statistical methods

Descriptive statistics were reported as mean (standard deviation [SD]) for continuous variables and as frequency and percentage for categorical variables. Differences in patient characteristics and lesion location were tested by Student's t-test or Fisher's exact test, as appropriate. Differences in the number of lesions by HIV status were tested by the Cochran-Armitrage test for trend. In a subgroup of patients where symptoms were reported in clinic notes, differences in whether or not pruritus or pain-related symptoms were reported were tested by Fisher's exact test. Significance was evaluated using 0.05-level 2-sided tests. All statistical analyses were performed using SAS 9.4.

Results

A total of 66 individuals (33 HIV-positive, 33 immunocompetent) were included in the study. **Table 1** displays the baseline characteristics of the two study populations, which showed no significant differences in age and ethnicity, although the immunocompetent group included a higher (though insignificant) proportion of females than did the HIV-infected group. The average age at presentation was 47.6 for the HIV-positive group and 45 for the immunocompetent group. The majority of patients in both groups were Hispanic. Most (78.8%) of the HIV-positive individuals were taking highly active antiretroviral therapy (HAART) consistently, as determined by documentation from primary care physician. In addition, 6 patients had a history of AIDS-defining illnesses (including esophageal candidiasis, extrapulmonary cryptococcus, Kaposi sarcoma, and *Pneumocystis jiroveci* pneumonia).

Table 1. *Patient demographics and disease characteristics by HIV status (N=66).*

Characteristic	HIV		P value
	Yes (n=33)	No (n=33)	
Age, years	47.6 (8.7)	45.0 (13.5)	0.36
Gender			
Female	8 (24.2%)	15 (45.5%)	0.12
Male	25 (75.8%)	18 (54.5%)	
Race/Ethnicity			
Black	2 (6.1%)	2 (6.0%)	0.41
Hispanic	23 (69.7%)	22 (66.7%)	
White	8 (24.2%)	6 (18.2%)	
Asian	0	3 (9.1%)	
Time since diagnosis, years		-	-
<1	2 (6.1%)		
1-3	5 (15.2%)		
4-6	1 (3.0%)		
7-10	6 (18.2%)		
>10	8 (24.2%)		
Unknown	11 (33.3%)		
Treatment			
ART with consistent adherence	26 (78.8%)	-	-
ART with inconsistent adherence	7 (21.2%)		
History of AIDS-defining illness	6 (18.2%)	-	-

Results are reported as N (%) or mean (SD).

Table 2 shows the number and location of lesions by HIV-status. HIV-positive status was significantly associated with a higher total number of lesions at initial presentation (Cochran-Armitage P value=0.04).

Table 3 and **Figure 1** demonstrate the location of verrucous lesions for each group at initial presentation to clinic. **Table 3** shows the total number of individuals in each group that presented

Table 2. *Number of lesions by HIV status (N=66).*

Characteristic	HIV		P value
	Yes (n=33)	No (n=33)	
Number of lesions			
1	8 (24.2%)	15 (45.5%)	0.04*
2	6 (18.2%)	7 (21.2%)	
3	5 (15.2%)	4 (12.1%)	
4+	14 (42.4%)	7 (21.2%)	

Results are reported as N (%) per group.
*By the Cochran-Armitrage trend test.

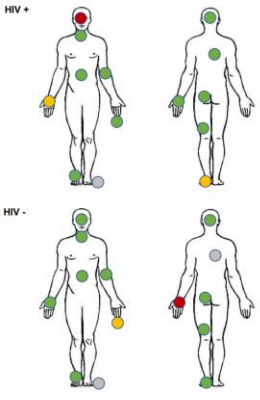
Table 3. *Location of lesions by HIV status (N=66).*

Characteristic	HIV		P value
	Yes (n=33)	No (n=33)	
Lesion location			
Scalp, face, and/or neck	17 (51.5%)	3 (9.1%)	<0.001
Hands and/or feet (dorsal and palmar)	16 (48.5%)	28 (84.9%)	0.004*

Results are reported as N (%) per group.
*By Fisher's exact test

with lesions on the scalp, face, and/or neck area, in addition to the hands and/or feet. In the immunocompetent group, only three individuals presented with lesions affecting the scalp, face, and neck areas, whereas 28 of 33 had involvement of the hands and feet. HIV-infected individuals were significantly more likely to present initially with lesions on the face, scalp, and neck (51.5% versus 9.1%, P<0.001) and less likely to present initially with lesions on the hands and feet (48.5% versus 84.9%, P=0.004). **Figure 1** provides the number of patients in each group that presented with one or more lesions in a particular location of the body. Patients who presented with lesions in multiple locations were counted more than once. Of note, 15 of 33 patients in the HIV-positive group presented with one or more lesions on the face.

Within the HIV-positive group, no significant correlations were observed between CD4 count and the number of lesions at initial presentation or between the median CD4 count in patients presenting with or without lesions of the face and scalp.



Lesion Location	HIV	
	Yes (n=33)	No (n=33)
Face (including ears)	15 (45.5%)	1 (3.0%)
Scalp	3 (9.1%)	1 (3.0%)
Neck	4 (12.1%)	1 (3.0%)
Arm including shoulder	5 (15.2%)	1 (3.0%)
Dorsal hand	5 (15.2%)	20 (60.6%)
Palmar hand	9 (27.3%)	4 (12.1%)
Periungual hand	2 (6.1%)	8 (24.2%)
Dorsal foot	1 (3.0%)	1 (3.0%)
Plantar foot	6 (18.2%)	1 (3.0%)
Periungual foot	0	0
Buttocks	1 (3.0%)	1 (3.0%)
Leg	3 (9.1%)	2 (6.1%)
Abdomen	1 (3.0%)	1 (3.0%)
Back	1 (3.0%	0

Lesion Legend			
0	1-5	6-10	>10

Figure 1. *Lesion locations by HIV status (N=66).*

Patients without documentation of symptomatology were excluded from the sub-analysis of symptoms. Symptoms, which included pain and pruritus, were present in approximately 40% of individuals and did not differ significantly based on HIV status.

Discussion

Individuals with HIV infection and other immunocompromising conditions, such as organ transplant, have been reported to develop HPV infections that are more severe, persistent, and in certain sites likely to progress to intraepithelial neoplasia [8,9]. Similarly, in this study we found that infection with HIV was significantly associated with a higher number of cutaneous warts at initial presentation (P=0.04). Interestingly, our study also found that HIV infection may impact the distribution of warts, as we observed that HIV-positive individuals were significantly more likely to present with lesions on the face, scalp, and neck (51.5% versus 9.1%, P<0.001) than those who were HIV-negative. The reason for this apparent difference in distribution is not clear and warrants further investigation in future studies. Interestingly, although previous studies have noted that more severe HPV infection is associated with lower CD4 counts [1,2,6], we did not find a significant correlation between CD4 count and the number of lesions at initial presentation.

The exact mechanisms by which HIV infection increases the prevalence and severity of HPV infection is not fully understood. Increased risk of HPV infection in HIV patients has previously been associated with impaired immune response in HIV, antiretroviral therapy, aging of HIV-infected patients, and direct interaction between the two viruses [1]. Although the data is sparse, it is believed that there may be direct interaction between HIV and HPV proteins; specifically, HIV may increase the expression of E6 and E7 oncoproteins and thereby enhance the proliferative capacity of HPV-infected cells [1].

Additionally, it is known that certain HPV types are more prevalent in immunocompromised individuals. For instance, multiple studies have demonstrated that HPV-32 is more prevalent in HIV-infected individuals with oral HPV infections than in the general population [1,10]. Additionally, high levels of β HPV types are present in both skin tumors and non-lesional skin of individuals with epidermodysplasia verruciformis, a rare condition that classically manifests as widespread verrucae resembling flat warts in immunocompromised individuals [11]. The role of ultraviolet exposure as a possible cofactor in wart pathogenesis, as has been described in epidermodysplasia verruciformis, could play a role in the higher prevalence of warts in head and neck areas in HIV patients; this, also warrants further investigation [12].

This study was limited by its retrospective nature and small sample size. Because the data were gathered through retrospective anonymous chart review, we were unable to include and analyze other potentially important variables that were not consistently recorded, such as patterns of tobacco and alcohol use and more precise information about antiretroviral therapy adherence patterns.

Conclusion

Considering our findings that HIV infection was significantly associated with a higher total number of verrucous lesions on initial presentation and more lesions on the face, scalp, and neck in comparison with immunocompetent individuals, providers should have a lower threshold to risk stratify and test for HIV when evaluating patients presenting with these patterns.

Potential conflicts of interest

Authors declare no conflicts of interest.

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