Journal of the International Association of Providers of AIDS Care
1–3

DOI: 10.1177/2325957417711255
journals.sagepub.com/home/jia
SAGE

Human Papilloma Virus–Associated Lips Verrucous Carcinoma in HIV-Infected Male

Giuseppe Vittorio De Socio, MD, PhD[1], Olena Bidovanets, MD[1,2], Gian Marco Tomassini, MD[3], Luca Fanelli, MD[4], and Stefano Simonetti, MD[3]

Abstract

Human papillomavirus (HPV) infection, widely known as the necessary cause of cervical cancer, has been established as a major etiologic factor for head and neck cancer (HNC). HIV-infected individuals are at higher risk of HPV-associated cancers than the general population. We describe a 45-year-old man with HIV and HPV coinfection, who presented progressively enlarging verrucous neoformations of the lips. The final diagnosis of verrucous carcinoma was delayed. Early detection of HPV lesions in oral mucosa and HPV screening activities could be important in improving the diagnostic sensitivity for the HIV-infected patients with oral cancer.

Keywords

HIV, human papillomavirus, lip cancer

Introduction

Head and neck cancer (HNC) is revealed as the sixth most prevalent cancer worldwide.[1] Human papillomavirus (HPV) infection, widely known as the necessary cause of cervical cancer, has been established as a major etiologic factor for HNC. The increase of HPV-associated HNC incidence rate over the last years could be explained by generational differences in sexual behavior, increased persistence, and progression of oral HPV due to changes in cofactors, such as tobacco use, alcohol use, and immune suppression.[2]

Human papillomavirus can infect the stratified epithelia of the skin or mucous membranes of the upper gastrointestinal, respiratory, or anogenital tract, potentially leading to outcomes such as genital warts and laryngeal papillomas, as well as certain cancers. The association with cancers has led to the various types of HPV being termed as "low risk" or "high risk" depending on their known oncogenic potential. Two manifestations of HPV in the oral cavity, which may be on the rise, are HPV-associated oral warts and HPV-associated oral cancers. HIV-1-infected patients are more susceptible to developing HPV infection and squamous intraepithelial lesion (SIL). The incidence of cervical cancer is high among HIV-infected women, particularly in countries with no organized cervical cancer prevention programs.[3] Increasing survival times of HIV-positive patients may be associated with dysplasia of oral and genital mucosal epithelium. The role of HPV is well established in genital and anal cancer, but it can be relevant for oral epithelial cancer, too. HPV screening activities could be important as well for the oral cavity.

We present the case of HPV-related oral cancer in a patient with HIV and Hepatitis C Virus (HCV) infection and diabetes.

Case Description

In August 2008, a 45-year-old Caucasian male presented with a history of bilateral and symmetric progressively enlarging verrucous neoformations of the lips, indicating a clinical diagnosis of granulomatous cheilitis. The patient was HIV-1 infected prior to 1994. He had a history of asymptomatic HIV infection, stage Centers for Disease Control (CDCA2). HCV-related hepatitis, type 1 diabetes, and borderline personality disorder. The patient smoked about 20 cigarettes a day and was an active user of heroin until 2007, after which he received a formal assessment and referral to drug addiction treatment in service for drug addiction and remained on methadone therapy. The CD4 T-lymphocyte nadir was 390/mm^3. Starting from 1998, the patient is regularly receiving antiretroviral therapy (ART) with abacavir (ABC), lamivudine (3TC), and atazanavir (ATV) unboosted. At follow-up, the HIV-1 RNA results were undetectable and the CD4 count stable (from March 2008 to the last

[1] Department of Infectious Diseases, "Santa Maria della Misericordia" Hospital, University of Perugia, Perugia, Italy
[2] Department of Infectious Diseases, Epidemiology and Dermatovenerology I. Ya. Horbachevsky Ternopil State Medical University, Ternopil, Ukraine
[3] Department of Dermatology, "Santa Maria della Misericordia" Hospital, University of Perugia, Perugia, Italy
[4] Residential Care Facility, "D. Dante Savini", Perugia, Italy

Corresponding Author:
Giuseppe Vittorio De Socio, Clinica di Malattie Infettive, Azienda Ospedaliero Universitaria di Perugia, Ospedale "Santa Maria della Misericordia", Piazzale Menghini, 1, 06129 Perugia, Italy.
Email: giuseppedesocio@yahoo.it

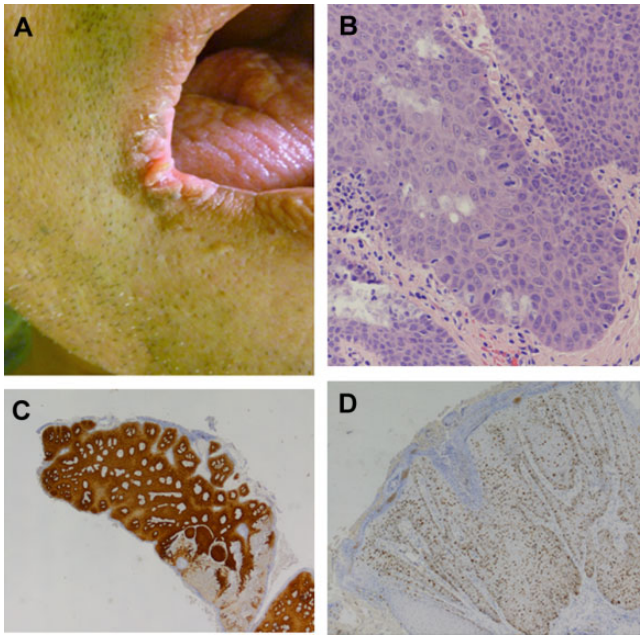

Figure 1. A, Clinical picture of the lips lesion. **B-D**, The result of histology from lip biopsy: B, Hematoxylin and eosin stain (original magnification ×40) showing several mitotic figures in the epidermidis; **C**, immunohistochemical (IHC) expression using antibody anti-CKA1/A3. **D**, IHC expression using antibody anti-Ki67/MIB1 showing about 80% of positive neoplastic cells.

check up, the CD4 count range was between 524 and 1041/mm^3).

In 2010, a biopsy of the lip lesions (lower right side of lip, including the angle of mouth) revealed squamous cell carcinoma of in situ verrucous type. At the same time, the HPV genotype 16 was identified by the HPV INNO-LiPA genotyping test (Innogenetics, Ghent, Belgium). The patient was treated with a surgical excision. Figure 1(A-D) shows the clinical appearance of verrucous carcinoma and histological findings (B-D). However, the lesion recurred 3 times in the next 4 years, requiring additional resections. Besides that, the perianal condylomatosis was found. The Papanicolaou test revealed anal low-grade SIL. Anal HPV test was positive for HPV genotype 16.

Discussion

Human papillomavirus infection accounts for approximately 5.2% of the worldwide human cancer burden including the cancer of the anus, genital tract, and oropharynx.[4]

As the HIV-positive patient's lifetime was increased due to long-term ART and HPV was revealed as the significant etiological role in carcinogenesis, aging patients with HIV/HPV coinfection was predisposed with cancer and HPV-associated oral lesions and malignancies.[5]

For HIV-positive individuals, specific routine screening recommendations are available for anal and cervical cancer, conversely the oral Papanicolaou test screening recommendations are lacking.[6] Therefore, the oral HPV lesions cannot be recognized correctly and easily, making clinical diagnosis difficult and this will cause delay in initiation of treatment.

Even after adjusting for sexual behavior and other relevant factors, HIV-positive individuals had a 2 to 3 times higher prevalence of oral HPV infection than HIV-negative individuals. Oral HPV has been suggested to clear modestly faster than anal HPV due to local mucosal immunity differences in the anatomic sites.[7]

Surgical approach or cryotherapy is the most used treatment, with cure rates for initial lesions approximating 100%.[8]

As of today, still no data are available on the efficacy of the HPV vaccines in preventing oral HPV infection (for both men and women). It was proposed to administer HPV vaccine to guard against oral infection due to the HPV types responsible for the vast majority of HPV-related HNC, opening the possibility of primary prevention of these increasingly common malignancies.[9]

Vaccination against HPV 16 during childhood and prior to HPV exposure may prevent HPV-associated cancer later in their adult lives, because the majority of HPV-associated HNC are caused by this type of HPV. Prevention strategies need to be focused by creating awareness on the harmful effects of tobacco and alcohol use, as they remain major risk factors for HNC.[1]

Early detection of HPV lesions in oral mucosa should be an important step in improving the diagnostic sensitivity of oral cancer, especially in HIV-positive patients due to their oncogenic potential. Furthermore, the HPV presence in the HIV-positive patients has to raise clinical suspicion about the possible HPV-associated malignancies at the other potential risk areas.

Authors' Note

All authors contributed to the critical revision of the article and approved the final manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. Wang CC, Palefsky JM. Human papillomavirus-related oropharyngeal cancer in the HIV-infected population. *Oral Dis*. 2016; 22(suppl 1):98–106.
2. Chaturvedi AK, Engels EA, Pfeiffer RM, Hernandez BY, Xiao W, Kim E, et al. Human papillomavirus and rising oropharyngeal cancer incidence in the United States. *J Clin Oncol*. 2011;29(32): 4294–4301.
3. Vaccarella S, Franceschi S, Zaridze D, Poljak M, Veerus P, Plummer M, Bray F. Preventable fractions of cervical cancer via effective screening in six Baltic, central, and eastern European countries

2017-40: a population-based study. *Lancet Oncol*. 2016;17(10): 1445–1452.
4. Chung CH, Bagheri A, D'Souza G. Epidemiology of oral human papillomavirus infection. *Oral Oncol*. 2014;50(5):364–369.
5. Fatahzadeh M, Schlecht NF, Chen Z, Bottalico D, McKinney Sh, Ostoloza J, et al. Oral human papillomavirus detection in older adults who have human immunodeficiency virus infection. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2013;115:505–514.
6. EACS (European AIDS Clinical Society) guidelines. http://www.eacsociety.org/files/guidelines_8.1-english.pdf. Accessed March 9, 2017.
7. Beachler DC, D'Souza G. Oral HPV infection and head and neck cancers in HIV infected individuals. *Curr Opin Oncol*. 2013;25(5): 503–510.
8. Stebbins W, Hanke CW. Lip Cancer: Not Uncommon, Often Overlooked. http://www.skincancer.org/skin-cancer-information/lip-cancer-not-uncommon. Accessed March 9, 2017.
9. Herrero R, Quint W, Hildesheim A, Gonzalez P, Struijk L, Katki HA, et al. Reduced prevalence of oral human papillomavirus (HPV) 4 years after bivalent HPV vaccination in a randomized clinical trial in Costa Rica. *PLoS One*. 2013;8(7):e68329. doi:10.1371/journal.pone.0068329.