

HPV oral infection. Case report of an HIV-positive Nigerian sex worker

Infezione orale da HPV.

Caso clinico di una prostituta nigeriana HIV positiva

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INTRODUCTION

Papillomavirus (HPV) is a DNA virus that belongs to the Papovavirus family, also called Papovaviridae family. The virus is sexually transmitted, both by direct contact, being freed from the epidermis' cells when these are scaled (above all about genital warts) and by indirect contact.

The direct contact happens by penetration of tissue infected fragments across genital micro lesions, produced by the traumatism during the sexual act. HPV penetrates initially in the cells of the basal layer of the pavement epithelium, subsequently the virions lose their protein wrap and the viral genome reaches the cell's nucleus, where it is established in episomal form. This is the latent form of infection from which then develops the subclinical form and in the end the true clinical infection (the latest two forms both productive).

Other possible way of transmission for HPV is by indirect contact; in this case the virus is transmitted by contaminated objects of common use, as towels, underwear and so on. Though it is not known how long the life of HPV is out of the organism, it is probable that this time is little and therefore a transmission by indirect contact may happen only in a reduced space of time, in which virus remains again active.

The first defence line of the organism is given by Langherans cells that play a role in the acti-

vation of the T lymphocytes; in the proclaimed HPV infection in fact there is a reduction of Langherans cells with a related depletion of the T lymphocytes and a predominance of the B lymphocytes.

It is known that:

- 1) HPV infection has a worsening during the pregnancy when there is a transitory immunodepression;
- 2) the patients with renal transplant who receive immunodepressive therapy, have more frequent HPV genital infections;
- 3) genital and anal infections are more frequent in HIV-seropositive homosexual, than in HIV-seronegative one;
- 4) HPV infection is more frequent in HIV seropositive or AIDS women;
- 5) HPV infection reactivation is very high in patients with conclamated AIDS and in HIV seropositive one.

Then the latent infection may remain such, or may become a subclinical infection or may develop a clinical infection.

Esophitic condylomas consist in an ipercheratotic proliferacion, threadlike, whitish, often with cheratotic surface, sometimes as an evident Papillomatosis. It is also possible to identify not sharp condylomas suggestive of a recent onset.

This is the most frequent type of HPV infection about the cervix.

It is often difficult to make diagnosis of the subclinical infection, about uterine cervix, vulva,

vagina and penis. Histologically the clinical and subclinical infections are related with basal layer hyperplasia, acantosis and characteristic cytopatic alterations. After the contagion the virus may disappear, defeated by the defences of the organism, or may remain latent even for long time. Persistent latent state explains the recidivisms and explains even the fluctuation in the time of the presence of HPV DNA in the tissues. The latent infection may be activated in women with immunodepression, so as during immunosoppressive treatments for neoplastic or autoimmune illnesses [1].

Women with cytologic evidences of HPV, have showed an increase 16 times greater of the risk of progression to carcinoma, than not infected women. The WHO has showed that the cervix crab has an incidence of 500.000 new cases every year in the world, of which the 45% progresses up to the death.

Young and sexually active women have greater incidence of HPV infection than elderly and monogamous women. The diffusion of the HPV reaches the maximum values among the 15 and the 25 years and greatly decreases in the old age [2]. Some possible risk factors for HPV infection are:

- 1) sexual relationships with many partners,
- 2) an infection from Herpes virus,
- 3) the smoke of cigarette,
- 4) using of oral contraceptives,
- 5) pregnancy state.

There are 20 different types of sexually transmitted HPV associated with cervix crab. This demonstration has important implications in the prevention strategy of such cancer, that includes the development of vaccine for the HPV [3, 4].

■ CLINICAL CASE

A Nigerian sex worker 35 years woman, in Italy for about 10 years, came to our ambulatory of diagnosis and therapy of the acquired immunodeficiency in March 2006 for the evaluation of her pathology.

The patient knew her HIV infection for about 5 years and from this time had begun therapy with Abacavir, Lamivudina and Zidovudina (Trizivir), assumed for 3 years. From the 2004 she had stopped the therapy and had made no other exams to control CD4 count and HIV viral load.

The patient was so evaluated at our ambulatory and we found only hepatomegaly, with-



Figure 1 - Inferior intern lip (right side).

out other clinical problems. However the examination of the oral cable showed the presence of multiple esophitic whitish lesions, with warty surface, partially confluent, like papillomatosis of little dimension, located at labial and mouth mucous membrane, without other inflammatory or neoplastic oral lesions (Figures 1, 2, 3).

The patient said that she had had these lesions since January 2006, not associated with dysphagia, odynophagia or respiratory problems; blood exams made in March 2006 did not show any pathological alterations, CD4 count was of 562 [cell]/ μ l (21%), CD4/CD8 of 0.98 and HIV load of 5269 Copies/ml.

It was therefore performed a gynecological consultation, that excluded presence of genital condilomas.

In the April 2006, for further checks, we sent our patient to the maxillo-facial surgery clinic, where it was performed a biopsy of the oral lesions with histological examination; it was diagnosed HPV infection confirmed with HPV DNA test (Hybrid Capture 2 *DIGENE*).

Blood examinations performed in June 2006 showed CD4 count of 477 cell/ μ l (20%) CD4/CD8 of 0.38.



Figure 2 - Inferior inner lip (left side).

As the patient had showed a progressive decrease of CD4+ cells and of the rate CD4/CD8 from March 2006, she began a new HAART with Lopinavir boosted with Ritonavir (Kaletra) and Tenofovir + Emtricitabine (Truvada). In January 2007 an increase of CD4+ (650 cell/uL) and of the rate (0,89) with a HIV-RNA not detectable has been observed. If the HAART therapy has determined the disappearing of HIV-RNA, it has not, on the con-



Figure 3 - Inferior inner lip.

trary, favoured the regression of oral cavity lesion

DISCUSSION

HPV infections and associated lesions have been rarely observed in body's areas different from the ano-genital one, particularly on the skin and in the oral cavity.

In HIV positive patients exists an increased risk of oral condylomas, in spite of the HAART [5, 6]. The oral HPV infections do not diminish in the HAART with increasing rates [7-8]. This phenomenon does not correspond with the reduction of the opportunistic infections in the patients under therapy [9]; the most probable reasons could be related to HPV (alteration of ecological niche of HPV, operated by the therapy) or to immune system (lack of immune reconstitution at level of the oral cable mucous membrane).

High risk HPV infections were 2, 1% in the tonsils and 6, 3% in the washings of the oral cable: the prevalence of such infections was superior in the HIV positive subject (13, 7% against 4, 5%) [10].

In the HIV negative individuals HPV oral infections increase with the age, the male sex and the HSV-2 siero-positivity, while in the HIV positive individuals with CD4 less than 200 Cells/mL, the infections increase in case of HSV-2 seropositivity, oral mucous membrane anomalies and many different sexual partners with oral sex practices in the last year. The improving of waiting of life induced by HAART and the increase of the age of the HIV positive subjects, are probably destined to favour in this population with high oncogenic risk the development of cancers with long latency.

All studies agree about the fact that HAART is not effective in the elimination of the anogenital HPV infection and that it neither decreases the persistence rate of the HPV, nor prevents the appearance of new infections in the anogenital tract [11].

After treatment with ablative therapies of the lesions, however, the patients show a free time from recidivous longer than women not treated by HAART [12. 13].

The immunotherapy with new vaccines will allow perhaps to improve the prevention and the therapy of this frequent condition.

Key words: HIV, HPV, condylomas

SUMMARY

HPV infections have become a major problem in immunocompromised patients, particularly in HIV-positive subjects. HPV lesions are observed more frequently in the ano-genital area and rarely in different body areas, such as the skin and oral cavity. However, in HIV-positive subjects there is an increased risk of oral condylomas. We describe the case of an HIV-positive Nigerian young woman, who came to our notice due to the appearance of small labial and mouth mucous membrane lesions,

related to HPV infection, as shown by a biopsy. These lesions were not evident in the genital area. After two years in which the patient no longer received therapy, there was a progressive reduction in CD4 count, associated with the development of the oral condylomas. Hence the patient began a new HAART combination, but after seven months, although a slight improvement emerged in the CD4 count with the disappearance of HIV-RNA, there has been no regression of oral condylomas.

RIASSUNTO

Le infezioni da HPV sono diventate attualmente un problema importante nei pazienti immunocompromessi, particolarmente nei soggetti sieropositivi per HIV. Le lesioni da HPV vengono osservate più frequentemente nella regione ano-genitale e raramente in differenti aree corporee, come cute e cavità orale. Nei soggetti HIV positivi, tuttavia, esiste un aumentato rischio di condilomi orali. Viene descritto il caso di una giovane donna nigeriana sieropositiva per HIV, venuta alla nostra osservazione per la comparsa, alle labbra ed alla bocca, di pic-

cole lesioni muco-membranose, correlate all'infezione da HPV, come evidenziato da una biopsia, ottenuta da esse. Tali lesioni non erano evidenti nell'area genitale. Dopo due anni in cui la paziente non ha più assunto terapia, c'è stato un progressivo declino dei CD4, associato allo sviluppo dei condilomi orali. La paziente ha, per tal motivo, iniziato una nuova combinazione HAART, ma dopo 7 mesi, malgrado si sia evidenziato un modesto incremento dei CD4, con scomparsa dell'HIV-RNA, non s'è osservata regressione dei condilomi orali.

REFERENCES

- [1] Clifford G.M., Goncalves M.A.G., Franceschi S. for the HPV and HIV Study Group. Human papillomavirus types among women infected with HIV: a meta-analysis. *AIDS* 20, 18, 2337-2344, 2006.
- [2] Holly E.A., Ralston M.L., Darragh T.M. et al. Prevalence and risk factors for anal squamous intraepithelial lesions in women. *J. Natl. Cancer Inst.* 93, 11, 843-849, 2001.
- [3] Levi J.E., Fernandes S., Tatenò A.F. et al. Presence of multiple human papillomavirus types in cervical samples from HIV infected women. *Gynecol. Oncol.* 92, 1, 225-231, 2004.
- [4] Chaturvedi A.K., Brinkman J.A., Gaffga A.M. et al. Distribution of human papillomavirus type 16 variants in human immunodeficiency virus type 1-positive and -negative women. *J. Gen. Virol.*, 85, 5, 1237-1241, 2004.
- [5] Ellerbrock T.V., Chiasson M.A., Bush T.J. et al. Incidence of cervical squamous intraepithelial lesions in HIV-infected women. *JAMA* 283, 8, 1031-1037, 2000.
- [6] Del Mistro A., Chieco Bianchi L. HPV related neoplasias in HIV-infected individuals. *Eur. J. Cancer* 37, 10, 1227-1235, 2001.
- [7] Kreimer A.R., Alberg A.J., Daniel R. et al. Oral human papillomavirus infection in adults is associated with sexual behaviour and HIV serostatus. *J. Infect. Dis.* 189, 4, 686-698, 2004.
- [8] Hagensee M.E., Cameron J.E., Leigh J.E., Clark R.A. Human papillomavirus infection and disease in HIV-infected individuals. *Am. J. Med. Sci.* 328, 1, 57-63, 2004.
- [9] Palefsky J.M., Holly E.A., Ralston M.L. et al. Effect of highly active antiretroviral therapy on the natural history of anal squamous intraepithelial lesions and an al human papillomavirus infection. *JAIDS* 28, 5, 422, 2001.
- [10] Frisch M., Biggar R.J., Goedert J.J. Human papillomavirus-associated cancers in patients with human immunodeficiency virus infection and acquired immunodeficiency syndrome. *J. Natl. Cancer Inst.* 92, 18, 1500-1510, 2000.
- [11] Massad L.S., Silverberg M.J., Springer G. et al. Effect of antiretroviral therapy on the incidence of genital warts and vulvar neoplasia among women with the human immunodeficiency virus. *Am. J. Obstet. Gynecol.* 190, 5, 1241-1248, 2004.
- [12] Heard I., Palefsky J.M., Kazatchkine M.D. The impact of HIV antiviral therapy on human papillomavirus (HPV) infections and HPV-related diseases. *Antivir. Ther.* 9, 1, 13-22, 2004.
- [13] Palefsky J.M. Cervical human papillomavirus infection and cervical intraepithelial neoplasia in women positive for human immunodeficiency virus in the era of highly active antiretroviral therapy. *Curr. Opin. Oncol.* 15, 5, 382-388, 2003.