A Case of Efflorescence of Cutaneous Warts as a Manifestation of Immune Reconstitution Inflammatory Syndrome in an HIV-Infected Patient

To the Editor—Instauration of HAART can cause immune reconstitution inflammatory syndrome (IRIS), especially in HIV-infected patients. We present, to our knowledge, the first case of IRIS due to cutaneous human papillomavirus (HPV) infection in a 48-year-old, HIV-positive white man who was successfully treated with topical cidofovir. Cutaneous warts should be recognized as a possible cause of cutaneous IRIS in HIV-infected patients.

Most cases of IRIS have been reported to be associated with infectious agents, such as mycobacteria, cytomegalovirus, Cryptococcus species, viral hepatitis, herpesvirus, genital warts, and, more recently, cutaneous leishmaniasis [1], as well as with noninfectious diseases, such as autoimmune thyroiditis, sarcoidosis, and Castleman disease. We present a case of IRIS due to cutaneous HPV infection that was successfully treated with topical cidofovir.

A 48-year-old, HIV-positive white man presented in February 2004 with a recent history of painful disseminated keratotic nodules located on his limbs and face (figure 1). Six weeks earlier, because several treatment regimens with antiretroviral drugs had failed, a new treatment regimen, including lopinavir, ritonavir, abacavir, zidovudine, and lamivudine, was initiated, including lopinavir, ritonavir, abacavir, zidovudine, and lamivudine, was initiated, leading to good virological control. The patient’s CD4 cell count increased from 2 cells/mm$^3$ to 31 cells/mm$^3$ over 4 weeks, and his viral load decreased from 96,000 copies/mL to <200 copies/mL. Biopsies of the skin lesions revealed typical HPV infection, with no evidence of dysplasia. Cutaneous cultures and PCR for mycobacteria, varicella-zoster virus, and herpes simplex virus had negative results. The patient was treated with occlusive topical application of cidofovir (3%) twice daily. Lesions improved dramatically within 10 days. Applications of topical cidofovir were reduced to once per day and then to alternate days over 8 months, and residual lesions were treated with CO$_2$ laser, resulting in complete clinical remission. At the latest follow-up visit (in October 2006), no clinical relapse had occurred, the patient’s viral load was undetectable, and his CD4 cell count was 187 cells/mm$^3$.

We believe that our patient’s case illustrated the rapid clinical progression of HPV skin infection that is related to good immunological response to antiretroviral therapy. IRIS characterizes inflammatory reactions related to excessive immune response to subclinical infections in severely immunosuppressed HIV-infected patients who respond to HAART. This syndrome has been reported to be associated with infectious agents (e.g., mycobacteria, cytomegalovirus, herpesviruses, and viral hepatitis) and noninfectious agents (e.g., autoimmune thyroiditis, systemic lupus erythematosus, and Castleman disease). HIV-infected patients with recalcitrant cutaneous warts that were not associated with IRIS and that completely disappeared after introduction of HAART have also been reported [2, 3]. Although HAART has lowered the incidence of opportunistic diseases, its impact on cervical squamous intraepithelial lesions is unclear [4]. However, a case of IRIS with anal Buschke-Loewenstein has been described in a HIV-infected patient who presented with anal warts before initiation of HAART, and who developed a very large peri-anal mass, despite an increase in the CD4 cell count from 50 cells/mm$^3$ to 420 cells/mm$^3$ and an undetectable viral load [5]. Another case of IRIS involving disparition of cutaneous warts has been described in a patient with common variable hypogammaglobulinemia after restoration of cell-mediated immunity [6].

In this case, we suggest that clinical lesions could perhaps be explained by the inflammatory dermal infiltrate playing a role in inducing proliferation of HPV-infected keratinocytes [7]. Administration of topical cidofovir is worth considering in this situation.

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