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Persistent Prurigo Nodularis Responsive to Initiation of Combination Therapy With Raltegravir

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Prurigo nodularis (PN) presents with excoriated nodules on the extensor surfaces of limbs and trunk. It is commonly seen in persons infected with human immunodeficiency virus (HIV) and with low CD4 counts.¹ The pathogenesis of PN is not well understood, but it may be related to inflammatory mediators.^{2–4} Interestingly, combination therapy that includes raltegravir, an integrase inhibitor that prevents viral DNA insertion into host cell DNA, has been noted to rapidly reduce viral load to levels comparable to or lower than other HIV antiretroviral therapies (ARTs).^{5,6} We report 2 cases of PN that dramatically improved within 2 weeks of initiating twice daily oral dosing with raltegravir, 400 mg.

Report of Cases

Case 1

A 47-year-old HIV-positive man with a CD4 cell count of 19/ μ L, viral load of 28 771 copies/mL, and CD4 nadir of 7/ μ L had longer than a 5-year history of biopsy-proven PN distributed over both arms (Figure 1) and legs. His PN persisted in spite of various treatments, including clobetasol ointment, diphenhydramine, hydroxyzine, and HIV ART including Combivir (GlaxoSmithKline, Research Triangle Park, North Carolina) (combination of lamivudine and zidovudine), enfuvirtide, lopinavir, tenofovir, tipranavir, darunavir, ritonavir, and atazanavir. Within 2 weeks of adding raltegravir to his ART, he experienced lesion recession and a dramatic decrease in pruritus, an improvement maintained at 6-month follow-up (Figure 2). His previous 5-year CD4 cell counts ranged from 7 to 113/ μ L (median, 22/ μ L) with viral loads lower than 75 copies/mL in the 6 months after commencement of combination raltegravir therapy.

Case 2

A 53-year-old HIV-positive man with a CD4 cell count of 218/ μ L, viral load of 3095 copies/mL, and CD4 nadir of 4/ μ L had longer than a 5-year history of biopsy-proven PN distributed bilaterally over his extremities. His PN persisted despite various treatments, including ongoing ART, clobetasol ointment, hydroxyzine, thalidomide, intralesional triamcinolone, and phototherapy. However, within 2 weeks of changing HIV ART from stavudine, lamivudine, and efavirenz to raltegravir, ritonavir, atazanavir, and emtricitabine-

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tenofovir (Truvada; Gilead, Foster City, California), he experienced lesion recession and a dramatic decrease in pruritus, an improvement maintained at 6-month follow-up. In the preceding 5 years, his ART remained unchanged, aside from switching nevirapine to efavirenz 2 years prior. Previous 5-year CD4 cell counts and viral loads ranged from 4 to 190/ μ L (median, 79/ μ L) and from less than 75 to 177 952 copies/mL. Notably, CD4 cell counts from the previous 2 years ranged from 76 to 218/ μ L with a maximum viral load of 13 374 copies/mL and a viral load of lower than 75 copies/mL in the 8 months after commencement of combination raltegravir therapy.

Comment

The response of both of our patients to HIV ART that includes raltegravir is notable given the persistent prior disease course and the rapidity of the therapeutic response. The 2-week response time indicates that effects due to reduction of viremia may play a significant role in initial recession of PN rather than immune recovery associated with increased CD4 cell counts. Antiretroviral therapy that includes raltegravir has been documented to reduce viremia to levels lower than those achieved by other ART combinations.^{5,6} It is also conceivable that raltegravir may have a direct effect on the cytokine milieu regardless of its potent antiviral properties. In addition to suggesting inflammation as a mediator of PN, this response to raltegravir offers practitioners another consideration when tailoring ART. While there exists a report of occasional raltegravir-associated pruritus in a phase 2 trial,⁷ this association was not reproduced in more recent and larger investigations,⁸ and there are no reports of prurigo nodularis associated with raltegravir therapy.

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Figure 1.
Case 1. Dorsal surface of the left hand prior to commencement of raltegravir therapy.

Figure 2.
Case 1. Dorsal surface of the left hand after commencement of raltegravir therapy.