
Case report

Allergen immunotherapy in a patient with human immunodeficiency virus: effect on T-cell activation and viral replication

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Background: Allergen immunotherapy is a major therapeutic modality in the treatment of allergic rhinitis. However, with T-cell activation potential, its role in patients with human immunodeficiency virus (HIV) was theoretically limited.

Objective: To report the results of allergen immunotherapy in a patient with HIV treated with highly active antiretroviral therapy (HAART).

Methods: A 44-year-old man with a history of HIV did not respond to medical therapy for allergic rhinitis. His HIV status was well controlled with HAART. Owing to the severity of his allergic rhinitis symptoms, he accepted the risk of allergy immunotherapy despite the unknown effect of immunotherapy in patients with HIV.

Results: After 6 weeks of weekly immunotherapy injections, his viral load remained undetectable and his CD4 cell count changed from 540 to 570 cells/ μ L. After 16 weeks of weekly immunotherapy, his viral load increased to 10,900 copies/mL, and his CD4 cell count increased to 665 cells/ μ L. After 24 weeks of weekly immunotherapy, his viral load returned to an undetectable level, and his CD4 cell count stabilized at 356 cells/ μ L. Despite his notable change in HIV status, he continues to receive the same HAART. He currently continues en route to maintenance immunotherapy.

Conclusions: The effect of allergen immunotherapy on HIV infection has not been previously reported. A concern remains that any form of immunotherapy may negatively affect HIV disease progression. This case illustrates that weekly allergen immunotherapy may have induced limited T-cell proliferation and a modest increase in RNA viral load, which resolved with continuation of HAART.

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INTRODUCTION

In the new age of improved human immunodeficiency virus (HIV) therapy, patients are living decades after HIV diagnosis. This patient population poses a unique challenge in the medical management of concomitant chronic disease. The primary concerns of treating patients with HIV for other comorbid conditions are antiretroviral drug interactions and the effects of treatment on T-cell activation, viral suppression, and T-cell survival. We report the early clinical results of initiating allergen immunotherapy for treatment of chronic allergic rhinitis in a patient with HIV receiving highly active antiretroviral therapy (HAART).

CASE REPORT

A 44-year-old man with a history of hepatitis C, papillary thyroid cancer status after thyroidectomy in remission since the age of 36 years, and HIV diagnosed at the age of 23 years was evaluated at the UCLA West Los Angeles VA Medical

Center for allergic rhinitis. With a history of childhood allergic rhinitis, he was evaluated for persistent perennial rhinitis symptoms. He did not respond to trials of oral antihistamine and intranasal corticosteroid therapy. Skin testing revealed positive results to mixed grass pollens, trees, molds, dust mites, cat dander, dog dander, and cockroach antigen. His initial total IgE level was elevated at 191 IU/mL. His HIV status was well controlled, with no history of acquired immunodeficiency syndrome–defining illnesses. The HIV treatment included HAART with emtricitabine and lopinavir-ritonavir. His CD4 cell count ranged from 262 to 600 cells/ μ L, and his RNA viral load was less than 10,000 copies/mL to undetectable for nearly 5 years. He was compliant with HAART, and these ranges of HIV disease markers were within normal variation according to his infectious disease physicians.

Owing to the severity of his allergic rhinitis symptoms and his poor response to medications, the patient accepted the risk of allergy immunotherapy despite the unknown effect of immunotherapy in patients with HIV. His allergen immunotherapy was prepared in a standard manner through Greer Pharmaceuticals (Lenoir, NC). His immunotherapy consisted of 4 vaccinations separated into tree pollens, weed pollens,

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and grass pollens positive on prick testing. The fourth vaccination consisted of mites mix, feather mix, *Hormodendrum*, and *Penicillium* antigen. The antigen was diluted with standard diluent consisting of 0.9% sodium chloride, human albumin, and phenol. Vials with small surface area and storage at 4°C maintained preservation of antigens.

After 6 weeks of weekly immunotherapy injections his viral load remained undetectable, and his CD4 cell count changed from 540 to 570 cells/ μ L. After 16 weeks of weekly immunotherapy, his viral load increased to 10,900 copies/mL, and his CD4 cell count increased to 665 cells/ μ L. Four weeks after this increase in viral load, he developed community-acquired pneumonia, which required hospitalization and intravenous antibiotic drug treatment. His viral load during hospitalization was undetectable, and his CD4 cell count was 425 cells/ μ L. Weekly immunotherapy was continued during his 3-day hospitalization. After 24 weeks of weekly immunotherapy, his viral load remained at an undetectable level, with a CD4 cell count of 356 cells/ μ L. During 6 months of immunotherapy, absolute CD8 cell counts did not fluctuate significantly (1,408–1,528 cells/ μ L). His 6-month IgE level was 206 IU/mL. Despite his notable change in HIV status, he has continued to receive the same HAART. He had typical local reactions to immunotherapy, which has slowed his ability to achieve maintenance dosing. He had no systemic or delayed reactions. He currently continues toward maintenance immunotherapy.

DISCUSSION

With a 25% prevalence in the general population, allergic rhinitis occurs with equal or increased frequency in patients with HIV.¹ The effect of allergen immunotherapy on HIV infection is as yet unknown. A concern remains that immunotherapy in any form, particularly vaccine based, may enhance HIV replication, activate T cells, and negatively affect disease progression. However, vaccine immunotherapy has been studied extensively in the HIV population.² T-cell activation via specific vaccine immunotherapy, such as influenza vaccine, produces moderate immunogenicity in adult and pediatric patients with HIV infection receiving HAART. The vaccine immunotherapy has minimal effects on HIV infection markers, such as CD4 cell count and RNA viral load, despite an increase in serum markers of T-cell activation.^{3,4} Hence, the Advisory Committee on Immunization Practices⁵ recommends the administration of influenza vaccination to patients with HIV infection receiving HAART.

Other immune-based therapies that potentially activate T cells and other branches of the immune system in patients with HIV have been published. To increase the depleted T-cell population in patients with HIV, one analysis⁶ of T-cell stimulation with interleukin 2 (IL-2) administration in HIV-positive adult patients receiving HAART showed a statistically significant increase in RNA viral load and a statistically significant decrease in CD4 cell counts during the initial phase of therapy. However, in all 6 studies analyzed, the duration of these effects was brief because CD4 cell counts

rebounded beyond pretreatment baseline levels, and prolonged elevation of RNA viral load was not observed. This pooled analysis of nonintermittent therapy during as long as 44 months of treatment would most closely mimic the duration and frequency of T-cell stimulation by allergen immunotherapy.⁶ Similar results of minimal increase in RNA viral loads and stabilization of CD4 cell counts were also observed in studies^{7–9} using granulocyte-macrophage colony-stimulating factor, granulocyte colony-stimulating factor, and IL-15 therapy. Alternatively, IL-7-stimulated T-cell renewal has been successfully used without increasing viral replication in simian immunodeficiency virus-infected macaques.¹⁰ Recently, IL-2 was also shown to reconstitute defective HIV- and cytomegalovirus-specific CD8 with or without T-cell proliferation in HIV infection in vitro.¹¹ It seems that immunomodulating therapies in patients with HIV exhibit the potential to reconstitute T-cell numbers and function with only marginal therapy-induced fluctuations in the CD4 cell count and viral load. Whether these fluctuations are clinically relevant remains to be determined.

Previously, immune-based therapeutic interventions have been used with extreme caution in the HIV population. However, with HAART and HIV control bestowing longer life expectancies, chronic medical illnesses such as allergic rhinitis may now be reassessed in patients with HIV. The present case report did not directly monitor serum markers of T-cell activation, such as C-reactive protein, CD25 cell counts, or levels of soluble IL-2 receptor. Nevertheless, this case illustrates that weekly allergen immunotherapy may have induced some T-cell proliferation and a relatively modest increase in RNA viral load, which resolved with continuation of HAART. The community-acquired pneumonia seen in this patient was diagnosed 1 month after an increase in viral load. However, during hospitalization the viral load was undetectable. A direct correlation of these events is concerning but not entirely conclusive.

Other questions remain about the use of allergen immunotherapy in patients with HIV. Unlike vaccine immunotherapy, allergen immunotherapy requires weekly T-cell modulation followed by monthly maintenance therapy for 3 to 5 years. Hence, it is unclear whether this patient's HIV status will remain under control as the patient achieves increasingly immunogenic maintenance doses of immunotherapy for longer periods, but the initial results are encouraging.

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