HIV has been linked to several autoimmune disorders since its emergence in the 1980s. By affecting different cells and pathways in the immune system, HIV induces the development of certain autoimmune diseases while prohibiting the emergence of others. Dermatomyositis has been rarely described in patients with HIV. We present a case of dermatomyositis in a patient with HIV and explore the pathogenesis of autoimmune disorders in HIV focusing on dermatomyositis.

Keywords: dermatomyositis; HIV; autoimmunity; inflammatory myopathy; immune dysfunction

Dermatomyositis is one of the idiopathic inflammatory myopathies that share immune-mediated muscle injury as their pathogenesis. The combined annual incidence of dermatomyositis and polymyositis is estimated to be 1.8 per 100,000 patient-years (1). It affects females twice as often as males, and the peak incidence is between the ages of 40 and 50 (2, 3). Since its emergence in the 1980s, human immunodeficiency virus (HIV) infection has been associated with several autoimmune diseases, with up to 70% of HIV patients developing some form of rheumatologic disorder (4). Despite this association, thus far only six cases (5–10) of HIV patients developing dermatomyositis have been reported. We present a rare case of dermatomyositis in a young male with HIV infection.

**Case report**

A 19-year-old male presented to our medical clinic in mid-2009 with complaints of acne, hair loss, and difficulty in getting up from sitting position with evidence of proximal muscle weakness. He had been recently diagnosed with dermatomyositis based on his clinical features of elevated creatine kinase levels, typical skin changes, and electromyography (EMG) pattern consistent with dermatomyositis. His medications at the time included prednisone, methotrexate, folate, and vitamin D. He was sexually active with both male and female partners with inconsistent use of condoms. Subsequently, he had multiple clinic visits between 2010 and 2011 for complaints of sore throat, fever, chills, anal pain, anal itching, and anal discharge. During this time, he was treated for oral candidiasis, scabies infestation, syphilis, and condyloma acuminata. He refused HIV testing, claiming that he was tested negative elsewhere. In early 2012, he consented for HIV testing. HIV ELISA and western blot were positive, with a CD4 count of 182 cells/µL and HIV RNA copies of 1,337,310 copies/mL on diagnosis. He was started on highly active antiretroviral therapy (HAART). After initiation of HAART his CD4 count gradually increased to 346 cells/µL and HIV-1 RNA copies decreased to 462 copies/mL within 2 months. At this time, he started having frequent flares of dermatomyositis. His dermatomyositis had been fairly well controlled on prednisone and methotrexate before initiation of HAART. He was switched to a combination of prednisone and azathioprine, then with mycophenolate mofetil, all with poor response. In June 2013, he was started on monthly intravenous immunoglobulins (IVIG), to which he initially had a fair response but ultimately required reintroduction of methotrexate and increased doses of prednisone to control the dermatomyositis flares. Despite this regimen, he had another dermatomyositis flare in 2014. In mid-2015, he presented to the emergency department with complains of diffuse muscle pain, chest pain, and shortness of breath on exertion. His last dose of IVIG was a week before presentation. His active medications were prednisone 60 mg daily, methotrexate 40 mg once a week, IVIG once a month, and Atripla.
On physical examination, he had mild heliotrope rash on eyes, chest wall tenderness, neck, and proximal muscle weakness on both upper and lower limbs. Critical laboratory findings included creatine kinase of 1,145 IU/L, aspartate transaminase of 400 IU/L, and alanine transaminase of 220 IU/L. Because of the refractoriness of therapy, a muscle biopsy was done which confirmed the clinical diagnosis of dermatomyositis (Fig. 1a and 1b). He was treated with intravenous methylprednisolone at stress doses with prompt improvement in overall muscle strength. He was discharged to follow up as an outpatient for rituximab therapy. He continues to take HAART and follows up in Infectious disease clinic. At the time of this report, the patient’s latest helper CD4 counts was 320 cells/mcL and HIV-1 ultrasensitive RNA < 20 copies/mL 02/8/2016. The patient is yet to follow up at the rheumatology clinic.

Discussion
HIV initially infects dendritic cells, monocytes, and macrophages. It then infects the CD4+ T cells leading to their apoptosis and thus uncoupling of CD8+ T cells (CTLs) activation through the Type 1 T helper cells (TH1) pathway (11). It infects CTLs directly as well and alters the function of the memory and effector CTLs, which is a critical blow to the antiviral defense mechanism of the body. Despite this, the host is usually able to mount a seemingly effective immune response to HIV infection as is seen with the clearance of viremia and partial recovery of the CD4 T cell numbers. However, HIV is not completely eradicated as its reservoir has already been established in the monocyte/macrophage cell lines (11). As viral replication occurs at this stage, CD4 counts begin to drop again and there is an inversion of the CD4:CD8 ratio. The differentiation of the remaining CD4 cells is persistently moved from the strong antiviral TH1 arm to the B-cell activating TH2 arm (11). This explains the hypergamma-globulinemia that is observed in HIV patients. In addition, there exists the homology between some HIV-1 epitopes and some regions on T and B lymphocytes which may induce molecular mimicry. As a result of this mimicry, the immune system becomes target of autoimmunity (4, 12). HIV also targets the regulatory T cells (Treg) that are critical in peripheral tolerance of naive T cells and prevent autoimmunity. B cell activation through the TH2 pathway and dysfunction of Treg provides the perfect milieu for the development of autoimmune diseases. This could be the reason why TH1 response-mediated autoimmune diseases such as rheumatoid arthritis are seen infrequently and undergo remission/stabilization in HIV infection, while immune complex-mediated illnesses such as vasculitis and CD8 cell-mediated illnesses such as diffuse infiltrative lymphocytic syndrome or reactive arthritis are seen much more frequently in HIV patients (13). With progression of HIV infection, both CD4 and CD8 numbers drop and there is profound immunodeficiency that would preclude emergence of any autoimmune diseases. Ultimately, with restoration of immunity from HAART, a resurgence of autoimmune diseases is seen in the subsequent period. The different stages of autoimmune diseases as a function of natural history of HIV infection has been proposed by Zandman-Goddard and Shoenfeld, as in Table 1 (12).

There are three phases in the pathogenesis of dermatomyositis. Initial injury is from autoantibodies directed at vascular endothelial components in the endomysium. There are also blue discolored degeneration/regeneration fibers scattered throughout the biopsy. Paraffin embedded section, H&E, ×175. (b) A distorted frozen section shows small round mononuclear inflammatory cells in the upper right quadrant of the picture. H&E ×175.
Table 1. Stages of autoimmune diseases as a function of the natural history of HIV infection.

| Stage | CD4+ count | Autoimmunity |
|-------|------------|--------------|
| I     | High (>500) | Initial presentation of some autoimmune diseases |
| II    | Normal/low (200–499) | Immune complex formation, vasculitis |
| III   | Low (<200) | CD8+ cell predominant rheumatologic illnesses |
| IV    | High (>500) | Resurgence of once quiescent disease |

dermatomyositis. presume the pathogenetic association between HIV and potentiate formation of autoantibodies. It’s reasonable to HIV can also have direct cytotoxic effect on the endothelial components of endomyial blood vessels and capillaries (14). Products of complement activation have been detected in the plasma of adult HIV patients, suggesting the presence of chronic low-grade complement activation. HIV can also have direct cytotoxic effect on the endothelial wall, which through molecular mimicry could lead potentiate formation of autoantibodies. It’s reasonable to presume the pathogenic association between HIV and dermatomyositis.

Although our patient’s HIV diagnosis was confirmed 3 years after the clinical diagnosis of dermatomyositis, he had sexual risk factors and multiple opportunistic and syphilis infection during this time, which suggests that he likely was already infected with HIV before his dermatomyositis symptoms manifested. If indeed our patient tested negative for HIV as he claimed in 2009, it is not far-fetched to wonder if he developed dermatomyositis during the seroconversion phase of his HIV illness. One case report has described a similar scenario (11).

Our case highlights an important consideration in treatment of HIV patients with autoimmune diseases. HAART leads to immune reconstitution in HIV and has changed HIV from a rapidly fatal illness to a chronic medical condition. At the same time, immune reconstitution may produce emergence and flare of new autoimmune phenomenon in these patients with HIV. The autoimmune conditions in HIV patients on HAART are often refractory to treatment and management is fraught with multiple relapses as seen in our patient.

First-line treatment of dermatomyositis flares is usually with stress doses of glucocorticoids. However, there exists a risk of opportunistic infection at these doses of steroids, more so in patients with HIV and low CD4 counts. As a precaution, we started our patient on Pneumocystis jiroveci pneumonia (PJP) prophylaxis despite his CD4 counts being > 200 cells/mcL (260 cells/mcL on 05/21/15). Because our patient was refractory to steroids and immunosuppressants, he was advised to follow up for rituximab therapy.

Physicians should be aware of the possibility of an underlying HIV infection precipitating an autoimmune phenomenon such as dermatomyositis, especially in patient with risk factors for HIV. Treatment remains a huge challenge, as immune reconstitution can potentially worsen the course of autoimmune phenomenon.

Roles of authors
M.C.: Conception and design, analysis and interpretation of Literature, involved in drafting the manuscript and revising it critically for important intellectual content. Also gave the final approval of the version to be published.
A.N.: Conception and design, analysis and interpretation of literature, involved in drafting the manuscript and revising it critically for important intellectual content. Also gave the final approval of the version to be published.
K.S.: Analysis and interpretation of literature, involved in drafting the manuscript and revising it critically for important intellectual content. Also gave the final approval of the version to be published.

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