An unusual duo: Immunodeficiency disorder and scleroderma

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Abstract

A 45-year-old woman on treatment for HIV infection with highly active antiretroviral therapy for the past 10 years presented to us with a history of Raynaud's phenomenon and hyperpigmentation of the skin for 2 years. She was diagnosed to have pulmonary arterial hypertension 8 months ago. On examination, she had salt-and-pepper pigmentation and sclerodactyly. Her biochemical workup was normal. She had positive antinuclear antibody by indirect immunofluorescence method. Skin biopsy was consistent with systemic sclerosis. HIV has its own musculoskeletal manifestations. The paradox of autoimmunity in the background of immunodeficiency was intriguing. Treating autoimmunity in the presence of immunodeficiency was challenging. The attribution and differentiation of pulmonary hypertension were difficult. There has been a homology identified between human immunodeficiency virus 1 (HIV 1) and centromere B protein (CENP B). This case is reported because of the unusual occurrence of systemic sclerosis in an HIV patient.

Key words: Acquired immunodeficiency syndrome, centromere, immunodeficiency, infection, pulmonary hypertension, virus

Introduction

Human immunodeficiency virus (HIV) is an emerging global pandemic. There are newer emerging therapies targeting the viral replication in various stages to combat the disease. Highly active antiretroviral therapy (HAART) has now made it possible to increase the longevity of the patients with HIV infection.[1] This HAART is now turning into a double-edged sword, and we see more reports on upsurge of reactivation of infections and autoimmune diseases in these patients.[2]

The more common autoimmune states associated with HIV are the thrombocytopenia and polyclonal hypergammaglobulinemia.[3] Case reports of HIV and associated rheumatoid arthritis, systemic lupus erythematosus, Sjogren syndrome, scleroderma, and sarcoidosis are found in literature.

The combination of immune dysfunction in patients with human immunodeficiency virus (HIV) and acquired immunodeficiency (AIDS) infection and the development of autoimmune diseases is intriguing. Molecular mimicry triggered by an infection is one of the postulated mechanisms. The spectrum of reported autoimmune phenomena in these patients is increasing. The autoimmune diseases which are CD8 driven are more common in HIV. Diseases such as psoriasis and diffuse immune lymphocytic syndrome (similar to Sjogren syndrome) may present or even be the initial manifestation of AIDS.[4]

The occurrence of autoimmunity in immundeficient states also poses a challenge in terms of use of immunosuppressant therapy due to limited data and trials and the potential risk of developing opportunistic infections (OPSIs). Herein, we present a case report of HIV with systemic sclerosis and pulmonary hypertension.

Case Report

A 42-year-old female who was on HAART (tenofovir + lamivudine + dolutegravir) during the past 10 years presented with a history of Raynaud's phenomena, altered skin pigmentation, and skin tightening of 2-year duration with rapid worsening during the past 6 months. She gave a history of pulmonary tuberculosis 5 years back, which was treated with a course of antitubercular therapy.

On examination, she had poor oral hygiene, pitted scars over the tips of the fingers, sclerodactyly of Grade 2 in hands and feet, and also skin tightening of Grade 1 in the forehead and face. She had salt-and-pepper pigmentation over extensor aspect of elbows, both shins, and back of the

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neck. Respiratory system examination revealed normal breath sounds and no added sounds. Cardiac auscultation revealed a loud pulmonary second sound and an ejection systolic murmur in pulmonary area. Laboratory investigations showed normal complete blood counts, renal and liver function tests. Her immunological tests revealed 3+ positive antinuclear antibody by IIF with – anti-Cell3 centromere pattern. Immunoblot showed CENP B 3+ and anti-RO52 positivity.

High-resolution computed tomography chest was normal. Echocardiography showed severe pulmonary arterial hypertension with tricuspid annular plane systolic excursion <16 cm and a tricuspid valve pressure gradient of 68 mmHg. Upper gastrointestinal endoscopy revealed antral gastritis. Nail-fold capillaroscopy showed capillary loss and dilated capillaries but no hemorrhages. CD 4 count was 486 cells per cu mm.

Her skin biopsy showed flaky hyperkeratosis, irregular acanthosis, and increased basal pigments in epidermis and hypertrophic collagen occupying the whole of dermis. Infiltration of mononuclear cells around hair follicle and vessels were also seen. Collagen appeared to be replacing and surrounding the eccrine glands and hair follicles. Atrophic eccrine glands were noted.

Discussion

Systemic sclerosis is a chronic autoimmune disease that is typified by its pathologic triad of immune dysregulation, microangiopathy, and fibrosis. HIV induces a state of chronic immune activation, leading to immunodeficiency, subsequently dysregulation of immune system leading to the activation of autoimmunity. Other possible explanations for the autoimmunity in HIV include molecular mimicry, epitope spreading, bystander activations, superantigens, polyclonal activation, and extracellular NETosis[5]. Treating HIV with HAART allows immune modulations, immune restoration, and development of autoimmune manifestations.

Studies by Douvas and Sobelman[6] showed existence of definite homology between the HIV and CENP B with duplication identified at ten sites shared and potentially all of them were within epitopic areas.

Our patient developed scleroderma while on treatment for HIV. She was started on nifedipine SR 10 mg twice daily with bosentan 62.5 mg daily along with methotrexate. She was educated to take precautionary measures to avoid cold exposure.

Immunosuppressant drugs in this context seem to be effective, often well tolerated and not associated with new OPSIs.[3] Steroids and steroid-sparing drugs have been used sparingly in various case reports for the treatment of autoimmunity in immunosuppressed states.[3]

Various drugs such as methotrexate, azathioprine, intravenous immunoglobulin, and cyclophosphamide have been adopted from guidelines of non-HIV patients and used in HIV patients.

Management of pulmonary hypertension was challenging as pulmonary hypertension could be attributed to both HIV and limited form of systemic sclerosis. Systemic sclerosis-associated pulmonary hypertension may be associated with many autoantibodies including anti scl70, anti-centromere antibody, antiendothelial antibodies, and anti-angiotensin II antibodies. Alternatively, pulmonary hypertension can be secondary to interstitial lung disease.[7] HIV proteins can cause endothelial dysfunction, cause inflammation by releasing cytokines, bring about apoptosis of cells, and release endothelin from lung endothelium.[8] Hence, in the treatment of pulmonary hypertension, the antiretroviral therapy might be beneficial in this case.

Literature search for similar case reports was done which showed most of the published cases were of diffuse systemic sclerosis type. Association of limited cutaneous systemic sclerosis with HIV is rarely reported in the literature. Unlike female preponderance in scleroderma, studies point toward more of male preponderance of pulmonary hypertension in HIV. It is reported to occur in both early and late stages of the disease. Degree of immunosuppression does not correlate with pulmonary hypertension.[8] Treatment of pulmonary hypertension in HIV is largely derived from general considerations.

The possibility of drug interaction of indinavir and ritonavir with phosphodiesterase inhibitor increases the concentration of phosphodiesterase, and its metabolites increase the side effects. Bosentan is considered to have less interaction with antiretroviral therapy. Patients should be monitored for hepatotoxicity.[8]

In systemic sclerosis, routine anticoagulation for the treatment of pulmonary hypertension is not required and is not proven to be beneficial. Unlike other connective tissue diseases, usefulness of steroids is limited in systemic sclerosis-associated pulmonary hypertension. Use of calcium channel blockers is not favored in systemic sclerosis patients with esophageal dysmotility and reflux. They are poor candidates for lung transplantation and yet demonstrate similar survival patterns with respect to other pulmonary hypertension patients.[7]

Conclusion

Treatment of immune activation in immunodeficiency is challenging both in terms of the choices and the outcome. Although largely the treatment protocol is adapted from the general considerations, these unusual and unique situations need mention and guidelines pertaining to consideration in special situation.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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