Psoriasis and HIV: Rupioid psoriasis, an uncommon presentation

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Abstract

Human immunodeficiency virus infection may result in the manifestation of severe and atypical cutaneous diseases. Although psoriasis is known to result from an aberrant host immune system, reports have been published observing the presence of this disease in immune compromised patients. Psoriasis also follows an interesting pattern in relation to CD4+ T-cell counts in HIV-positive patients, likely due to a combined variety of factors. Furthermore, treatment of psoriasis in immune compromised patients can be complex, and oftentimes not effective. We present a case of an HIV-positive patient who developed a very rare clinical variant of psoriasis, rupioid psoriasis, and discuss the possible mechanisms behind the development of this autoimmune disease in the setting of immune dysregulation and outline possible treatments for this particular patient population.

ABBREVIATIONS

HIV: Human Immunodeficiency Virus; AIDS: Acquired Immunodeficiency Syndrome; HIV-AP: Human immunodeficiency virus-Associated Psoriasis; HIV-APA: Human immunodeficiency virus-Associated Psoriatic Arthritis; HAART: Highly Active Antiretroviral Therapy; NO: Nitric Oxide

INTRODUCTION

Cutaneous diseases are common manifestations of human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS), and may be indicative of the degree of immune dysfunction. Psoriasis may present for the first time with HIV infection and, when associated with HIV, has been reported as being more severe and challenging to treat. In 2012, the number of HIV-positive individuals was estimated at 35.3 million, with 9.7 million of those receiving antiretroviral therapy [1,2]. HIV-associated psoriasis (HIV-AP) and HIV-associated psoriatic arthritis (HIV-APA) have been reported with prevalence similar to, if not higher, than that of the general population. [3,4 ]

Psoriasis can be the presenting feature of HIV infection and can provide a clinical clue as to the state of the patient’s immune system, with reports identifying severe immune suppression a significant risk-factor for the development of psoriasis [5]. HIV-associated psoriasis has also been reported to present with late HIV and progressive immune dysfunction, but remission of psoriasis has been noted in the terminal stage of HIV [6]. Moreover, while immunodeficiency is associated with the development and exacerbation of psoriasis, immune reconstitution with antiretroviral therapy has been shown to have a reverse effect, with patients having resolution or improvement of their psoriasis [7].

Rupioid psoriasis, also called psoriasis rupioides, is a rare variant of psoriasis and involves cone-shaped, limpet-like lesions. To the best of the authors’ knowledge, approximately eight cases of rupioid psoriasis have been reported in the literature to date [8-15], with roughly half presenting with severe arthropathy. This type of psoriasis has been associated with Reiter’s Syndrome, a triad of inflammatory arthritis of large joints, inflammation of the eyes, and urethritis or cervicitis. We present a case of a patient with HIV-associated rupioid psoriasis with arthropathy, and discuss the possible mechanisms of immune dysregulation on psoriasis and current treatment strategies in the immune suppressed population.

CASE PRESENTATION

A 48-year old woman with a history of HIV/AIDS, highly active antiretroviral therapy (HAART) non-compliance, and asthma, presented to the emergency department with a two-month history of multiple, non-pruritic skin lesions on her extremities that continued to increase in number and size. Physical exam revealed well-demarcated, hyper pigmented, hyperkeratotic plaques that were limpet-like and cone-shaped with an exudative crust and a surrounding border of desquamation (Figure 1). The lesions had been initially treated as a fungal infection by her primary care physician. The lesions worsened and progressed...
during this treatment (Figures 2 and 3), and the patient additionally developed pain and swelling of the right leg and right hand with notable fingernail destruction. Other past medical history includes active tobacco and cocaine abuse, chronic kidney disease, and renal cancer status post right nephrectomy.

Skin biopsy confirmed psoriasis, and the patient was clinically diagnosed with rupioid psoriasis with arthropathy. Due to a low CD4 count of 111, treatment was limited to high-potency topical corticosteroids twice daily and the re-initiation of HAART therapy. No new lesions developed, and only very mild improvement was noted. The mild response may have been secondary to re-initiating HAART therapy. Subsequently, HAART therapy was discontinued due to poor renal function. The patient declined further treatment at the hospital; she was discharged to her home and lost to follow-up.

DISCUSSION

Psoriasis is thought to be a chronic papulosquamous inflammatory skin disorder of T-cell-mediated keratinocyte proliferation, classified as an autoimmune disorder. HIV is a viral infection depleting T-cell populations, leading to an immunocompromised state. As seen in our case presentation, psoriasis may present during HIV infection or other immunocompromised states. The presentation of psoriasis in the setting of HIV seems paradoxical, since psoriasis is an autoimmune disease associated with the activation of T cells, and treatments that decrease T cell counts improve psoriasis. Several hypotheses have been proposed to explain this paradox and are discussed below [16].

PATHOGENESIS

T-cell subtype imbalance

CD8+ T-cells, also known as cytotoxic T-cells, are an immune cell subtype whose function is mainly to locate and destroy virally-infected or neoplastic host cells [17]. In classic psoriasis, the number of CD8+ T cells and the memory subset of CD8+ T cells are increased in the epidermis and dermis. HIV infection characteristically targets and lowers CD4+ T-cells, or helper T-cells, whose role includes the activation and growth of cytotoxic T-cells, B-cell antibody class switching, and increasing immune cell activity against bacteria. However, with HIV infection, increased CD8+ T cell counts are seen late in the disease, and memory CD8+ T cells can comprise over 80% of the peripheral blood of patients with CD4+ T-cell counts less than 200 cells per μL [18].

Another hypothesis is that HIV infection, by depleting CD4+ T-cell counts, also depletes the T regulatory cell population. The main purpose of T regulatory cells is to modulate the host’s immune system, by activating and inhibiting a wide variety of immune cells. This important safeguard prevents excessive reactions, including unintentional ones from intolerance to self-antigens resulting in many autoimmune disorders. This reduction of regulatory cells results in unchecked pro-inflammatory pathways that may lead to psoriasis, or other autoimmune disorders. [19] This imbalance of CD8+ T-cells to CD4+ T-cells or T regulatory cells within the immune system provides a strategic environment for psoriasis development and/or exacerbation.

Direct role of HIV

Higher viral loads and progressive immunodeficiency are associated with exacerbation of psoriasis. HIV genetic material has been found in antigen-presenting dendritic cells in the skin of infected patients [20], which suggests HIV may play a larger role than simply reducing immune cell populations. HIV might directly trigger psoriasis by acting as a co-stimulatory factor
to unregulated CD8+ T-cells, generating a rampant cutaneous immune system response and psoriatic lesions. HIV may also act as an antigenic source (superantigen) to activate host CD8+ T-cells, commonly through CD4+ helper T-cells, causing a similar waterfall effect. Furthermore, when CD4+ T-cells are extremely low (as seen in terminal HIV infection), an avenue for CD8+ T-cell activation is removed, which may explain the improvement of psoriasis disease burden seen just prior to death in these patients.

Increased infections

Decreased cellular immunity often results in infections by bacteria or viruses, such as the higher colonization of the skin in immunocompromised individuals by the bacteria *Staphylococcus aureus*. Cutaneous infections have previously been reported as known triggers for psoriasis, including the bacterial species *Streptococcus* spp. [21] Though not proven, these generalized cutaneous over-colonizations may similarly elicit comparable super antigenic stimulation, leading to psoriasis. An alternative hypothesis includes the production of interleukin 17 and interferon γ, molecules known to have a significant role in the pathogenesis of psoriasis, in response to skin colonization by bacteria. [22]

Increased Nitric Oxide (NO) production

Reactive oxygen species such as NO and malondialdehyde have been found at increased concentrations in psoriasis, which may indicate oxidative stress as a causative or exacerbating factor. [23] HIV infection increases the production of NO by macrophages [24,25], theoretically to modulate the host’s immune response to viral infection. Consequently, this increase in oxidative stress during HIV infection may explain the exacerbation of psoriasis.

CLINICAL VARIANTS AND ASSOCIATIONS

All clinical variants of psoriasis may manifest in HIV-positive patients, with guttate, inverse and erythrodermic types being more common and more severe in the immunocompromised patient. [5,26] These patients often have misleading or atypical presentations, severe disease, and frequent exacerbations; therefore, it is paramount to have a high index of suspicion for HIV-associated psoriasis in HIV patients presenting with an unusual, severe cutaneous disease. A hallmark of HIV-associated psoriasis, distinct from classic psoriasis, is that a single patient may present with several coexisting morphologies. [27,28]

Rupioid psoriasis, as seen in our case presentation, is one of the rarer variants of psoriasis, and has also been reported as one manifestation of HIV-associated psoriasis. [16] This variant is described as limpet-like, cone-shaped nodules and plaques with heaped scale that is firmly fixed to underlying skin. In addition to HIV infection, these rare lesions have also been reported as unusual manifestations of Reiter’s syndrome [15, 29], malignant syphilis [30], and HIV-associated histoplasmosis. [31] In addition to our case, there have been eight case reports published on rupioid psoriasis to date, two of which are not in the English language. Rupioid psoriasis has occurred in an immunocompetent host (HIV-negative) [11], a patient with spondylarthropathy and bilateral sacroiliitis although HLA-B27 negative [15], and a patient with high anti-streptolysine-O and anti-streptokinase titers with seropositivity of HLA antigens A24, B70, B48 and Cw7. [13] Rupioid psoriasis has also been suggested as a sign of poor medication compliance [14]. Based on these reported cases, the presence of rupioid lesions may be a sign of immune dysregulation and might prompt physicians to screen for HIV infection and other autoimmune conditions.

TREATMENT

Management of HIV-associated psoriasis is challenging, as the clinical course is progressive and often refractory to conventional therapies. Many treatments used for psoriasis are immunosuppressive, which may potentially lead to further complications in HIV patients who are already highly susceptible to opportunistic infections. Furthermore, no randomized placebo-controlled trial outlining the efficacy and safety of standard psoriasis treatment regimens in HIV-positive patients has been published to date. Physicians may elect to follow the consensus presented by the National Psoriasis Foundation task force for psoriasis treatment in immunosuppressed patients [32]. These recommendations were presented in 2010 and were primarily based on published case reports and case studies.

Topical therapies, such as emollients, corticosteroids, retinoids, and vitamin D analogs, are recommended as first-line treatment for mild to moderate disease. For moderate to severe disease, phototherapy and anti retrovirals are recommended as first-line treatments in addition to topical therapies. Oral retinoids are second-line therapy if failure to respond to the above regimen is seen. For more refractory or severe disease, the use of biological therapeutic agents is cautiously recommended; these include cyclosporine, methotrexate, hydroxyurea, and tumor necrosis factor-α inhibitors [32]. This recommendation is based mainly on anecdotal and published case reports of their safety and efficacy in HIV-positive patients, although the risk of opportunistic infections while taking these medications should be carefully evaluated for each individual patient.

Phototherapy (psoralen plus UVA) [11], methotrexate with topical steroids [12], cyclosporin with topical steroids [13], topical steroids alone [14], and ustekinumab (monoclonal antibody to the IL-12/IL-23 receptor, preventing helper T-cell activation and inflammatory cytokine secretion) [15] have been used successfully in the treatment of rupioid psoriasis in published case reports.

The treatment regimen for our patient was limited by a low CD4+ T-cell count. Her therapies included topical high-potency corticosteroids and re-initiation of anti retrovirals. Her mild improvement may have resulted from reinitiation of HAART. Because her renal function deteriorated, our patient only had a few days of HAART.

CONCLUSION

HIV-associated psoriasis is a challenging disease. These patients often have misleading, atypical presentations, and the psoriatic manifestations are often severe. Recognizing psoriasis in an HIV patient may correlate to the degree of immune compromise, as psoriasis manifests in the later stages of HIV. When encountering the extremely rare rupioid psoriasis, physicians might suspect immunosuppression, such as HIV/AIDS, or other immune dysregulation. Adherence to medical
management must also be discussed.

Our patient with AIDS and a CD4+ T-cell count of 111, presented with prominent rupioid psoriasis with arthropathy. Treatment options were limited given her co morbidities. Reinitiating HAART therapy and using topical corticosteroids led to temporal mild improvement. Unfortunately the patient refused to continue to be hospitalized and was lost to follow-up.

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Conflict of Interest

The authors do not have any conflict of interests to report in the writing or publishing of this manuscript.

REFERENCES


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