Pemphigus vulgaris in association with human immunodeficiency virus infection: A management dilemma

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Abstract

The association of immunobullous disorders with human immunodeficiency virus (HIV) infection is rare. Concurrence of these two conditions poses a therapeutic challenge as both cause immune dysregulation. We report pemphigus vulgaris in association with HIV infection in a 50-year-old woman who died of sepsis after receiving high-dose corticosteroids for the treatment of pemphigus vulgaris.

Key words: Human immunodeficiency virus, management, pemphigus vulgaris

Introduction

Pemphigus vulgaris is an intraepidermal immunobullous disorder resulting in suprabasal blisters and erosions over the body. The occurrence of pemphigus in a patient of human immunodeficiency virus (HIV) is rare.[1] The interplay of two immune-mediated processes in one patient not only offers an opportunity to evaluate the different immunologic mechanisms operating in the patient but also poses a management dilemma.[2] We report the case of pemphigus vulgaris in a 50-year-old woman who was diagnosed case of HIV infection and was on antiretroviral therapy (ART) since 2014. However, the administration of high-dose corticosteroids in her for control of her disease led to sepsis and death. This case report highlights the need to understand the complex relationship between HIV infection and pemphigus vulgaris to guide effective therapeutic management of two immunologically mediated diseases (pemphigus vulgaris and HIV infection).

Case Report

A 50-year-old female presented to the dermatology outpatient department with erosiocrustive plaques over the scalp, face, trunk, and extremities for the past 1½ months. The patient gave a history of formation of clear fluid-filled flaccid blisters which ruptured spontaneously to leave behind erosions. There was no history of mucosal erosions in the patient and she denied any family history of autoimmune blistering disorders. She was a known case of HIV infection and was taking ART for the past 9 years and 2 months. She took tenofovir 300 mg, lamivudine 300 mg, and efavirenz 600 mg from August 2014 and shifted to tenofovir 300 mg, lamivudine 300 mg, and dolutegravir 50 mg in January 2021.

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On dermatological examination, no intact blisters were noted. There were multiple discrete to coalescing erosiocrustive plaques over the scalp, face, trunk, and extremities. Both direct as well as indirect Nikolsky signs were positive in the patient. Tzank smear made from the fresh erosions revealed the presence of acantholytic cells [Figure 1]. Biopsy showed mild perivascular infiltrate with neutrophils and lymphocytes. Direct immunofluorescence showed immunoglobulin G (IgG) and C3 deposits in intercellular spaces of the epidermis [Figure 2]. Her CD4 count was

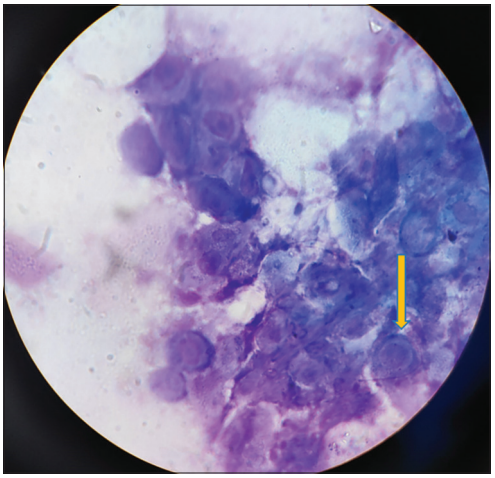

Figure 1: Arrow highlights a single acantholytic cell in the smear

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611 cells/mm^3 (October 2023). Based on the clinical history, examination, and laboratory tests, a diagnosis of pemphigus vulgaris was made. In view of her HIV-positive status, she was treated with dapsone 100 mg once daily and apremilast 30 mg twice daily orally along with injection linezolid in view of the superimposed secondary infection. The disease activity was brought under control and the appearance of new lesions was arrested. However, she discontinued all medication after discharge and shifted to homeopathic treatment. The patient presented 20 days later with extensive erosiocrustive plaques involving more than 90% of the body surface area predominantly involving the face (periocular and perioral area), neck, chest, groin, and buttocks [Figure 3a and b]. Pemphigus disease area index was 65. Her hemoglobin was 7.2 and total leucocyte count was 17,500. Blood urea was showing increasing trend and was 103 mg/dl on the day of second admission. Liver enzymes were raised (aspartate transaminase and alanine transaminase were 400 units/L and 197 units/L, respectively). Blood culture report showed *Enterococcus faecalis* growth. C-reactive protein was 136 mg/dl, erythrocyte sedimentation rate was 22 mm/h, and procalcitonin was 25.5 ng/ml. She was started on intravenous linezolid, meropenem, co-trimaxozole, and piperacillin–tazoactam combination, along with intravenous dexamethasone and intravenous fluids.

Unfortunately, 5 days later, the patient expired due to sepsis, metabolic acidosis, and prerenal failure, followed by sudden cardiac arrest.

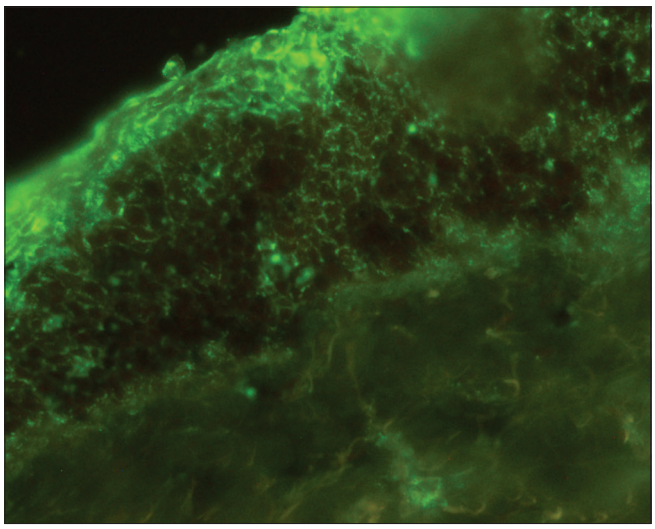

Figure 2: Direct immunofluorescence showing immunoglobulin G and C3 deposits in intercellular spaces of epidermis

Discussion

Pemphigus vulgaris is an immunobullous skin disorder characterized by IgG antibody formation against desmoglein-3 antigens resulting in the formation of suprabasal blisters in the skin and mucosae. Many mechanisms have been proposed to explain the concurrence of autoimmune blistering disorders in HIV-infected individuals. One such mechanism is the production of interleukin (IL)-1 and IL-6 by HIV-infected macrophages. This causes B-cell stimulation, which may activate autoantigen clones and produce autoantibodies leading to autoimmune sequelae. Another concept is that people with certain human lymphocyte antigens who are predisposed to HIV have certain clones of cytotoxic T cells that can recognize HIV antigens. HIV-infected macrophages get covered in viral antigens after becoming infected. When they move to other tissues and organs, they are recognized and killed by cytotoxic T cells. Unaffected healthy cells in the vicinity could also be destroyed in the process. Molecular mimicry of the HIV virion is also a proposed mechanism in the development of autoimmune diseases.[3]

Clinically, the patient presents with flaccid blisters which spontaneously rupture to form erosions. Intact blisters may sometimes not be seen due to their superficial location and consecutive rupture. These lesions may extend, coalesce, and progress to exfoliative erythroderma. The occurrence

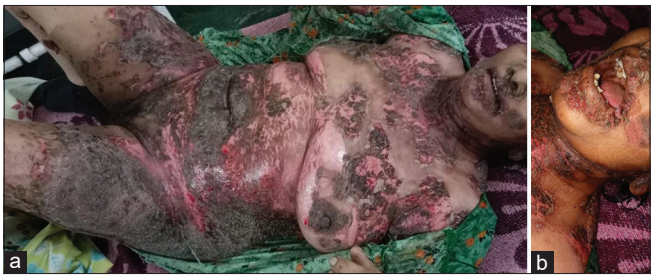

Figure 3: (a and b) Erosio-crusted plaques coalesced to involve more than 90% of body surface area

Table 1: Review of case reports of autoimmune bullous disorders with human immunodeficiency virus

Author	Age/sex (years)	Disease	Treatment given	Comment
Polansky *et al.*[5]	54/male	Pemphigus vulgaris	Systemic steroids, mycophenolate mofetil, azathioprine, and rituximab	Disease persistence and progression were seen with steroids, azathioprine, and mycophenolate mofetil. Remission was seen with rituximab
Chaudhry *et al.*[6]	50y/male	Linear IgA bullous dermatosis	Dapsone	Remission was seen
De *et al.*[7]	30/male	Bullous pemphigoid	Systemic steroids and ART were discontinued	After remission with steroids, ART was reintroduced
Marfatia *et al.*[4]	30/male	Pemphigus vulgaris	Systemic steroids (dexamethasone)	Patient responded to systemic steroids
Mignogna *et al.*[8]	29/male	Pemphigus vulgaris	Oral cyclosporine and oral steroids	Initially was started on cyclosporine but led to acute renal dysfunction so was shifted to oral steroids which led to remission
Hodgson *et al.*[1]	29/male	Pemphigus vulgaris	Oral cyclosporine	Initially patient was treated with oral steroids and azathioprine but it led to relapses. Cyclosporine was introduced and it led to remission
Splaver *et al.*[9]	30/female	Pemphigus vulgaris	Systemic steroids and azathioprine	Led to remission
Capizzi *et al.*[10]	59/male	Pemphigus vulgaris	Systemic steroids and cyclophosphamide	Remission present but led to the development of *Staphylococcus aureus* septicemia and decrease in CD4 count

ART=Antiretroviral therapy; IgA=Immunoglobulin A

of pemphigus in an HIV-infected individual is rare. The impact of each disease on the course of the other is not well understood.[1] Few cases of autoimmune blistering diseases in HIV-infected patients that have been reported are summarized in Table 1.

In this patient, the fatal flare of pemphigus vulgaris following discontinuation of therapy could be due to various reasons. First, the abrupt discontinuation of immunomodulatory drugs which initially helped achieve disease control appears to be the primary reason. Second, immunocompromised status can lead to flare of autoimmune diseases such as pemphigus. Finally, the use of unknown indigenous medications could have also contributed to the flare.

Concurrence of pemphigus vulgaris with HIV poses a therapeutic challenge.[4] Various systemic immunosuppressive therapies have been tried, including systemic corticosteroids, cyclosporine, mycophenolate mofetil, azathioprine, and rituximab.[2] Cyclosporine has shown to have *in vitro* antiretroviral activity and can be considered a possible treatment option for individuals with pemphigus vulgaris and HIV infection. Renal functions should be monitored in an HIV patient on cyclosporine as renal toxicity can be amplified through interactions with ART medications.[1] ART should be continued along with immunosuppressive therapy.

Conclusion

In summary, HIV-infected individuals presenting with autoimmune blistering disorders require careful evaluation and therapeutic management as the use of immunosuppressives may lead to serious complications such as septicemia and HIV disease progression.

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 her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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