Clinical and histopathological aspects of lichenoid dermatitis in patients of retroviral diseases

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Aims and Objectives: The aim of this study is to study demographics, clinical, histological, and immunological profile of the HIV patients presenting with lichenoid dermatitis. Subjects and Methods: HIV patients presenting with LP such as lesions were evaluated with complete history and physical examination. Demographic profile of patients was studied with features such as age, sex, duration of disease, distribution of the lesions, CD4 count, concomitant medications, associated comorbidities, and response to the treatment. Results: Twenty-one HIV patients presenting with LP such as lesions were studied. Of these, 20 patients had LP and one patient had lichenoid drug reaction. The age of the patient ranged from 40 to 60 years with no sex predilection. The duration of lesions ranged from 15 days to 7 years. Eleven patients had simultaneous cutaneous and oral involvement, five patients had only oral involvement and four patients of LP and one patient of lichenoid drug reaction had only cutaneous lesions. All the patients were on antiretroviral therapy, mainly on lamivudine, zidovudine, and nevirapine. Almost all the patients had CD4 count of more than 250 at the time of presentation. One patient was diagnosed to have lupus erythematosus and LP overlap. Patients were treated with oral medications such as corticosteroids, methotrexate, and dapsone and topical medications such as corticosteroids and calcineurin inhibitors. Conclusions: The appearance of LP such as lesions in HIV patients is a rare occurrence with 11 cases of LP reported till date. Our case series of 20 patients will throw light on possible etiology and difficulties in the management of LP such as lesions in HIV patients.

Key words: HIV, lichen planus, lichenoid drug eruption

Introduction

Lichen planus (LP) is an idiopathic subacute or chronic inflammatory disease of the skin, mucous membranes, and nails. The exact pathogenesis of LP is still unclear, but several hypotheses have been made regarding the role of genetic, infective, psychogenic, and autoimmune factors. HIV patients suffer from numerous dermatoses. Few of these dermatoses such as psoriasis and seborrhoeic dermatitis are often found to be more severe in HIV patients.

LP has been reported in association with hepatitis B and C virus infection but its association with HIV infection is rarely reported. The occurrence of LP in HIV patients can be coincidental or it can present as lichenoid drug reaction. Lichenoid dermatitis as a result of adverse cutaneous drug reaction has been reported with antiretroviral therapy (ART) drugs, especially with zidovudine and tenofovir. Other concomitant medications given to HIV patients such as cotrimoxazole and nonsteroidal anti-inflammatory drugs can cause similar adverse effects. The occurrence of classical LP and its variant is quite possible in HIV patients. The exact association between these two diseases needs detailed study which cannot be conducted as there are only 11 cases reported.

Subjects and Methods

This is a retrospective observational study of HIV patients presenting with LP such as lesions. Patients with details of complete history, clinical examination, and skin biopsy were studied. The features such as age, sex predilection, and clinical and histopathological aspects of lichenoid dermatitis in patients of retroviral diseases. Indian J Sex Transm Dis 2022;43:59-63.

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duration of LP and HIV, distribution and morphology of the lesions, histopathology findings, CD4 count, concomitant medications, ART regimen, associated comorbidities, and response to treatment were studied.

Results

We found 21 HIV patients presenting with LP like lesions over the last few years in our outpatient department. Ten patients in our study were in the fifth decade with a male:female ratio of 1.1:1. The duration of LP like lesions ranged from 15 days to 7 years with maximum patients having duration of <1 year. The duration of seropositive status ranged from 1 month to 23 years with 8 of 21 patients having duration of 6–10 years. Aggravating factor like photosensitivity was seen in two patients. Addiction to tobacco and smoking was seen in six patients with oral lichenoid lesions. Medication as an aggravating factor was seen in only one patient. Of the 21 patients, 11 patients had simultaneous cutaneous and oral involvement; five patients had only oral involvement while four patients of LP and one patient of lichenoid drug reaction had only cutaneous lesions.

The distribution of cutaneous lesions was almost generalized in seven patients of LP and one patient of lichenoid drug reaction. Two patients had actinic LP localized to the face, neck, and lower lips. Four patients had hypertrophic lesions of LP on the lower extremities. One patient had hypertrophic lesion on photo-exposed distribution [Figure 1a-c] while one patient had violaceous and hyperpigmented patches on the face and neck suggestive of LP pigmentosus [Figure 1d-f]. Majority of cutaneous lesions had classical morphology of LP except for one patient of lichenoid drug eruption showing larger scaly lichenoid plaques with severe involvement of photo-exposed areas [Figure 2a-c]. Another patient with hypertrophic LP had scaly fissured annular plaques on soles [Figure 2d].

Of the 16 patients of LP with mucosal involvement, the buccal mucosa was most commonly affected in all 16 patients. Tongue, hard palate, and lower lip were the other affected areas. Genital mucosal involvement was seen in one male and two female patients. In the morphology of oral lesions reticular or lacy pattern was the most common (seen in 8 of 15 patients) followed by erosive LP (seen in 7 of 15) and plaque like form (seen in 3 of 15) patients. The combination of these patterns was seen in few patients simultaneously [Figure 3].

One patient of LP with the duration of 4 years, later developed changes in the morphology of lesions as depigmented hypertrophic plaques and erosive and reticulate lesion on the buccal mucosa suggestive of discoid lupus erythematosus.

Nail involvement was seen in 6 of 21 patients. The common clinical features observed were longitudinal ridging and pitting. Pterygium of the nail was seen in only one patient.

On histopathology, 18 patients showed the features of LP. One patient was diagnosed as LP pigmentosus, one patient was diagnosed with lichenoid drug eruption and one patient showed features of LP-lupus erythematosus overlap [Figure 4].

Direct immunofluorescence was done in only one patient of LP-lupus erythematosus overlap which showed granular band with IgM and C3 at the basement membrane zone with colloid bodies in the papillary dermis, staining with IgM, IgA, and C3. Diffuse nuclear staining in epidermal cells with IgG (ANA in vivo) suggesting the diagnosis of LP lupus erythematosus overlap. Patient’s ANA was positive in the speckled pattern with titer of 1:1000.

All patients were screened for hepatitis B, hepatitis C virus infection, and syphilis with hepatitis B antigen (HbsAg) anti-HCV antibodies and Venereal disease research laboratory (VDRL). All three tests were nonreactive in all the patients.

Of these 21 HIV patients with LP like lesion, CD4 count at the time of presentation was available in 20 patients [Table 1]. Baseline CD4 count and CD4 count at the time of presentation was available in 16 patients.
Except for one patient, majority of them had CD4 count more than 250 at the time of presentation with lichenoid lesions. Comparison of baseline CD4 count and CD4 count at the time of presentation revealed that except for two patients there was significant increase in CD4 count at the time of presentation with LP like lesions. Lamivudine was the most common ART medication taken by all 21 patients in our study. Fifteen patients were on zidovudine, 11 patients were on nevirapine, 8 patients were on efavirenz, 5 patients were receiving tenofovir and 2 patients were on protease inhibitors like indinavir and combination of atazanavir and ritonavir. In 1 patient of lichenoid drug reaction non-steroidal anti-inflammatory medication was the causative drug.

![Figure 3: (a-f) Multiple erosive lacy-white lesions on oral mucosa and plaques on lips](image)

**Table 1: CD4 count and antiretroviral therapy details of all the patients**

| Patient number | CD4 count before initiation of ART | CD4 count at the time of presentation of lichen planus | ART regimen | Duration of ART |
|----------------|-----------------------------------|------------------------------------------------------|-------------|----------------|
| 1              | 200                               | 1164                                                 | ZLN         | 12 years       |
| 2              | 154                               | 415                                                  | ZLN         | 7 years        |
| 3              | 12                                | 370                                                  | ZLN         | 10 years       |
| 4              | 156                               | 489                                                  | ZLE         | 7 years        |
| 5              | NA                                | NA                                                   | ZLN         | 1 year         |
| 6              | 234                               | 568                                                  | ZLE         | 4 years        |
| 7              | NA                                | 822                                                  | ZL + Indinavir | 10 years      |
| 8              | 191                               | 1189                                                 | TL + ATZ/Rv | 23 years       |
| 9              | 273                               | 511                                                  | TLE         | 10 years       |
| 10             | 253                               | 459                                                  | TLE         | 7 months       |
| 11             | 261                               | 1011                                                 | ZLN         | 5 years        |
| 12             | 311                               | 441                                                  | ZLN         | 10 years       |
| 13             | 241                               | 405                                                  | ZLN         | 7 years        |
| 14             | NA                                | 109                                                  | ZLN         | 3 years        |
| 15             | 267                               | 252                                                  | ZLN         | 3 years        |
| 16             | 64                                | 632                                                  | ZLN         | 8 years        |
| 17             | 285                               | 663                                                  | TLE         | 4 months       |
| 18             | 340                               | 330                                                  | ZLN         | 4 years        |
| 19             | NA                                | 686                                                  | ZLN         | 9 years        |
| 20             | NA                                | 294                                                  | TLE         | 8 years        |
| 21             | 314                               | 974                                                  | ZLN         | 7 years        |

Z=Zidovudin; L=Lamivudin; N= Nevirapine; E=Efavirenz; T=Tenofovir; ATZ= Atazanavir; Rv=Ritonavir; NA=Not available; ART=Antiretroviral therapy

**Table 2: Inflammatory skin diseases in human immunodeficiency virus**

| Inflammatory diseases in HIV | Clinical presentation |
|-----------------------------|-----------------------|
| Seborrheic dermatitis       | Seborrheic dermatitis can affect up to 85% of the HIV-positive population. Presence of SD could indicate rapid progression of HIV. It may occur at any CD4 cell count, (>500 cells/mm³) but usually becomes extensive and refractory as CD4 cell counts decline (<100 cells/mm³). Progression to erythema is known in HIV-positive patients. HAART therapy can lead to significant improvement in the severity of disease. |
| Psoriasis                   | Psoriasis affects up to 2% of the HIV population. It can also present as IRIS. |
| Reiter’s syndrome           | Clinical severity, including increased incidence of incapacitating arthritis pose special problems in therapeutic management of Reiter’s disease. Only one-third of RS in AIDS patients presented with prior genital or enteric infection. |
| PPE of HIV                  | One of the earliest manifestations of HIV seen in 25%-50% of patients. PPE is regarded as a cutaneous marker of advanced HIV (CD4 <50/mm³). It can also present as IRIS. |
| EF                          | EF is seen in the late stage of HIV commonly at CD4 cell count below 250 cells/mm³, thus it may be considered as an important marker of HIV. |

HIV=Human immunodeficiency virus; HAART=Highly active antiretroviral therapy; PPE=Pruritic papular eruption; EF=Eosinophilic folliculitis; IgE=Immunoglobulin E; RS=Reiter’s syndrome; SD=Seborrheic dermatitis; IRIS=Immune reconstitution inflammatory syndrome

Associated comorbidities in these patients were vitiligo vulgaris, recurrent herpes genitalis, perianal warts and pulmonary tuberculosis.

All the patients were treated with emollients, oral antihistamines. Topical steroids and tacrolimus 0.1% ointment were preferred topical agents for cutaneous lesions. For oral involvement topical triamcinolone acetonide paste and tacrolimus ointment 0.03% was preferred. Patients with extensive involvement and those not responding to topical treatments were considered for
systemic therapy. Six patients received treatment with oral prednisolone, four patients received oral dapsone, and two patients of actinic LP responded very well to oral antimalarial agents while one patient of widespread LP and one patient of LP and one patient of LE-LP overlap syndrome received oral methotrexate with regular monitoring of CD4 count. As stated earlier, majority of these patients had CD4 count more than 250 at the time of presentation. Patients on oral immunosuppressive therapy were monitored regularly for CD4 counts and other concomitant infections. All the patients showed excellent response to the treatment with discontinuation of systemic immunosuppressive medications after improvement and maintenance on topical steroids and tacrolimus ointment.

**Discussion**

IP is a chronic inflammatory papulosquamous skin disorder. It may occur in immunocompromised hosts such as patients with graft versus host disease and those with tumor-induced immunodeficiency, abnormal humoral immunity. However, there are a few case reports of LP, especially a severely hypertrophic form, occurring as an associated feature of HIV infection.[3-5]

Rippis et al.[3] have reported the three cases of hypertrophic LP in HIV-positive patients, in which they have studied alteration in the immune status in HIV-positive hosts by proportion of T-helper and T-suppressor cells in the inflammatory infiltrate. They found majority of the infiltrating lymphocytes in the dermis were of the T-helper phenotype and epidermal lymphocytes were of the T-suppressor phenotype.

The depletion of CD4+ T-cells and the associated disruptions of immune homeostasis result in greatly elevated susceptibility to numerous pathologies in HIV-positive persons. Infected persons also suffer from elevated incidence and severity of dermatophytes, seborrheic dermatitis, herpes simplex, Ofuji disease, psoriasis, molluscum contagiosum, and other dermatoses and infections.[6]
Inflammatory skin disease in HIV infected can have different clinical presentation compared to non-HIV patients⁷ [Table 2]. There is a paucity of literature on the occurrence of LP in HIV with only 11 cases of LP reported in HIV patients. These cases are summarized in Table 3,[3‑5,8‑13]

We have compared the findings in our study with reported cases of LP.

Most of the patients of LP-HIV reported in the literature and cases in our study were in the fifth decade. In literature, cases of LP-HIV showed male preponderance, while in our study, no sex preponderance was seen. The duration of the LP in our study ranged from 15 days to 7 years, whereas the duration of LP in reported literature ranged from 15 days to 5 years.

Higher number of patients in our study showed generalized distribution of the disease, actinic and hypertrophic lesions compared to available literature.

Mucosal involvement was predominantly seen in our patients compared to cases reported in literature.[3‑5,8‑13] Buccal mucosa was the most commonly affected mucosa, and reticulate type of LP was the most common.

In reported literature, almost 50% of LP patients had CD4 count <250 cells/mm³. This finding was not seen in our study.

In reported cases, majority of patients were treated conservatively with topical steroids and antihistamines while two patients with extensive involvement were treated with oral etretinate and oral methotrexate. Higher number of patients in our study had generalized distribution requiring treatment with systemic agents such as prednisolone, dapsone, antimalarial drugs, and methotrexate along with topical steroids and calcineurin inhibitors.

In HIV-positive patients, zidovudine[2,15] and tenofovir,[2,15] cotrimoxazole, NSAIDs, dapsone and ketoconazole are reported to cause lichenoid drug reaction. Zidovudine can cause oral lichenoid reactions while tenofovir-induced lichenoid reactions were generalized in distribution.[2,15,16] In our study, only one patient had lichenoid drug eruption secondary to NSAIDs.

Eruptions resembling LP are commonly encountered as a sequel of graft-versus-host disease in persons receiving bone marrow transplantation or blood transfusions. The lichenoid phase of graft-versus-host disease may be clinically and histologically identical to LP and both diseases are thought to result from the destruction of basal cells by activated lymphocytes. Disease similar to that seen in persons who have received transplants or transfusions may result from infection of lymphocytes with human immunodeficiency virus. It is typically a generalized eruption.

Adverse cutaneous drug reactions occur far more often in HIV-infected persons than in the general population.[16] After reviewing the literature, there are more reports of lichenoid drug reactions in HIV patients than LP. The feature of photo-distribution of the lesions, especially in darkly pigmented patients indicates a need for more studies to know the relevance of this observation.

**Summary**

Occurrence of LP in patients of HIV can be coincidental or could be part of changed immunological profile of the patients which has also been seen in patients of psoriasis and seborrhoeic dermatitis. Other differentials such as lichenoid drug eruption should be ruled out by detailed clinical history and histopathological examination. Our study of 19 patients of LP and one patient of lichenoid drug eruption is the largest series of LP reported in HIV patients.

**Limitations**

The small number of patients in our retrospective study could be attributed to the rare occurrence of these diseases in patients on antiretroviral drugs.

**Declaration of patient consent**

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

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**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Ficarra G, Flaitz CM, Gaggioli D, Piluso S, Milo D, Adler-Storzh K, et al. White lichenoid lesions of the buccal mucosa in patients with HIV infection. Oral Surg Oral Med Oral Pathol 1993;76:460‑6.

2. Gupta M, Gupta H, Gupta A. Tenofovir induced lichenoid drug eruption. Avicenna J Med 2015;5:95‑7.

3. Rippis GE, Becker B, Scott G. Hypertrophic lichen planus in three HIV-positive patients: A histologic and immunological study. J Cutan Pathol 1994;21:52‑8.

4. Fitzgerald E, Purcell SM, Goldman HM. Photodistributed hypertrophic lichen planus in association with acquired immunodeficiency syndrome: A distinct entity. Cutis 1995;55:109‑11.

5. Parido RJ, Kerdel FA. Hypertrophic lichen planus and light sensitivity in an HIV-positive patient. Int J Dermatol 1988;27:642‑4.

6. Sadick NS, McNutt NS, Kaplan MH. Papulosquamous dermatoses of AIDS. J Am Acad Dermatol 1990;22:1270‑4.

7. Betkerur JB, Ashwini PK, Ranugha PS, Sachdev A. Mucocutaneous manifestations of HIV/AIDS. In: Sacchidanand S, Oberai C, Inamdar A, editors. IADVL Textbook of Dermatology. 4th ed. Mumbai: Bhulani Publishing House; 2015. p. 2962‑96.

8. Ruiz Villaverde R, Blasco Melguizo J, Naranjo Sintes R, Serrano Ortega S, Dulantı Campos MC. Multiple linear lichen planus in HIV patient. J Eur Acad Dermatol Venereol 2002;16:412‑4.

9. Kumari R, Singh N, Thappa DM. Hypertrophic lichen planus as a presenting feature of human immunodeficiency virus infection. Indian J Dermatol 2009;54, S1:8‑10.

10. Emadi SN, Akhavan-Mogaddam J, Yousefi M, Sobhani B, Moshikforoush A, Emadi SE. Extensive hypertrophic lichen planus in an HIV positive patient. Dermatol Online J 2010;16;8.

11. Patil P, Nayak C, Tambe S, Das D. Lupus erythematosus‑lichen planus overlap syndrome in an HIV-infected individual. Int J STD AIDS 2016;27:1117‑22.

12. Wilson S, Pollinger T, Turiansky G. An atypical presentation of unilateral, linear, hypertrophic lichen planus in a patient with HIV. Pract Dermatol 2016;24‑6.

13. Shah PM, Dhakre VW. The rare occurrence of cutaneous and mucosal lichen planus in HIV infection. BMJ Case Rep 2017;2017:bcr2017222625.

14. Arirachakaran P, Hanvanich M, Kuyasakorn P, Thongprasom K. Antiretroviral drug-associated oral lichenoid reaction in HIV patient: A case report. Int J Dent 2010;2010:291072.

15. Woolley UJ, Veitch AJ, Harangozo CS, Moyle M, Korman TM. Lichenoid drug eruption to tenofovir in an HIV/hepatitis B virus co‑infected patient. AIDS 2004;18:1587‑8.

16. Bigby M, Jick S, Jick H, Arndt K. Drug-induced cutaneous reactions. A report from the Boston Collaborative Drug Surveillance Program on 15,438 consecutive inpatients, 1975 to 1982. JAMA 1986;256:3358‑63.