

Clino-Pathological Correlation of Dermatological Manifestations in People Living with HIV/AIDS (PLHIV) at a Tertiary Care Hospital, Western India

Poonam Chakubhai Radadiya and Aditi Dinesh Dholakia*

Pathology Department, GMERS, Medical college, Gotri, Vadodara, India

ABSTRACT

Background: A large number of skin conditions that might present to a dermatologist ranging from infectious to benign to malignant in HIV positive patients. Many of them need detailed and time consuming investigations to confirm the clinical diagnosis. Probably skin biopsy is the most important ancillary aid to confirm the clinical diagnosis. Skin biopsies play a vital diagnostic role when different diseases present with clinically similar skin lesions. A diagnostic approach is given based on the predominant histological reaction pattern, with an emphasis on clinicopathological correlation. So, this study tries to assess the clinic-pathological correlation in dermatological manifestations in PLHIV.

Methods: Punch biopsies from the skin lesions were studied from March 2016 to April 2017 with routine histopathology examination and special stains were used as and when required. Clinical diagnosis was then correlated with histopathological examination.

Result: A total of 60 punch biopsies of PLHIV were studied. 22 (36.66%) patients had infectious lesions and 38 (63.33%) patients had non-infectious lesions. Correlation of Clinical diagnosis was done with histopathological findings, which showed 88.8% of papular lesions well correlated histopathologically. Only 33% of malignant and premalignant skin conditions were diagnosed correctly on clinical examination. Overall, 68.33% of cases including non-neoplastic and neoplastic lesions, showed clinic-pathological consistency.

Conclusion: Skin biopsy and clinicopathological correlation is clearly a worthwhile investigative procedure.

Keywords: Biopsy, Clinicopathological Correlation, Histopathology, Infectious Lesions, Skin Lesions

Introduction

HIV infection constitutes a major health problem worldwide.^[1-3] India has the third largest HIV epidemic in the world with an estimated adult prevalence of 0.26 %.^[4] Diseases of skin and mucous membranes are common clinical manifestations of acquired immunodeficiency syndrome (AIDS) causing significant morbidity among PLHIV.^[5] Dermatological lesions in PLHIV can present with a variety of manifestations.^[6,7] Moreover, dermatological manifestations may be the initial signs of immunosuppression.^[8] They affect between 80 and 95% of PLHIV occurring at any point of time during the course of infection.^[9,10] In majority of PLHIV cases, skin is often the first and only organ affected at the time of presentation as well as most of course of infection.^[9,11,12] Cutaneous disorders during HIV infection are numerous.^[13,14] Some Cutaneous disorders reflect the progression of HIV disease, but this relation is still controversial.^[14,15] Extensive HIV-related literature has focused on distinctive clinical presentations such as Kaposi's sarcoma, oral hairy leukoplakia, and oral candidiasis.^[13,15] However, the findings on careful skin examination of HIV infected patients who present for primary care have received limited attention.

In this study, we aimed to describe the dermatological manifestations of PLHIV on initial presentation and its correlation with histopathological findings.

Materials and Methods

This descriptive cross-sectional study was conducted at a tertiary care hospital (B J Medical College, Ahmedabad) from March 2016 to April 2017. Information on PLHIV were collected from ART center and from counseling center and all participants testing positive for HIV were enrolled for ongoing study. There were no specific eligibility criteria. All PLHIV who accessed care at hospital were included. Information on demographics, that is, age, sex and socioeconomic status was noted. A complete medical history and physical examination of patients were done by a dermatologist for optimal evaluation and dermatologic lesions were diagnosed on the basis of clinical appearance. Informed consent was taken from the PLHIV for skin biopsy procedure. After detailed general and local examination, the site of the biopsy was selected. All universal aseptic precautions according to National AIDS Control Organization guidelines were followed. The selected patient's written consent was taken after explaining the details of the biopsy procedure. All

skin biopsies were taken under local anesthesia. The three dimensional size and shape of the skin biopsy were assessed including the circular or elliptical shape of the biopsy for gross examination. The biopsy obtained was processed by standard formalin fixing paraffin embedding method. Serial sections and special stains were studied as and when required. We have used diagnostic technique of clinical evaluation by a dermatologist along with histopathological examination of skin biopsy for dermatological disorders in PLHIV. The obtained data was analyzed. The Clinical diagnosis obtained from dermatologist and histopathological diagnosis were correlated.

Result

Out of total 60 PLHIV included in the present study, 43 were males and 17 were female patients. In present study, Age range of the study participants was between 20 to 60 years. Among that, 20 patients (33.3%) were between 21 to 30 years of age and 25 patients (41.6%) were between 31 to 40 years. This makes 21 to 40 years of age most common age of presentation in present study.

Among 60 patients studied, most common provisional clinical diagnosis was bacterial infections 13 (21.6%) followed by papular lesions 09 (15%).(Table 1)

All the 60 cases were subjected to biopsy and histopathological examination. Out of this 60 cases, 22 (36.66%) had infectious pathology, whereas 35 (58.33%) patients had non-

infectious pathology, where as only 3 (5%) cases were fell into malignant/premalignant category. (Table 1)

Among infectious skin pathologies, variety of infections were observed such as viral, bacterial, fungal and parasitic (Arthropod) infections. Total 08 (13.3%) patients had bacterial infections, which included mainly leprosy, folliculitis, and syphilis. Total 07 (11.6%) patients showing viral pathology included Molluscum contagiosum, human papilloma virus (HPV), herpes zoster and herpes simplex virus (HSV). Total fungal infections noted were 06 (10%), which included candidiasis, dermatophytoses-tinea, cryptococcosis and histoplasmosis. Only a single (1.6%) case of parasitic infections was diagnosed as dermal leishmaniasis. Total four patients had vascular lesion and two patients had other non-specific pathology including follicular keratosis and perforating keratosis. (Table-1)

All the clinical diagnosis was correlated with histopathological diagnosis. Overall, 68.33% of cases including non-neoplastic and neoplastic, shown consistency between clinical and histopathological diagnosis. (Table-2 & 3).On correlation between both the diagnosis, it was found that 88.8% of papular lesions diagnosed clinically were well correlated histopathologically, whereas clinico-histopathological correlation was only 33% in cases of malignant and premalignant skin conditions.

Table 1: Provisional clinical diagnosis and histopathological diagnosis among PLHIV

Diagnosis	Clinical		Histopathological	
	Number (n=60)	%	Number (n=60)	%
A. Dermatitis:- Atopic Dermatitis, Ashy Dermatitis, Urticaria, Hyperpigmented patch, chronic non-specific dermatitis.	08	13.3	08	13.3
B. Papular lesion:- Pruritic papular, Psoriasis, Seborrhic Dermatitis, Eosinophilic folliculitis, Scaly lesion, Lichen planus	09	15.0	10	16.6
C. Epidermal Lesion:- Epidermoid cyst, Seborrhic keratosis	03	5.0	03	5.0
D. Viral lesions:- Warts, Condyloma Lata, Molluscum contagiosum	08	13.3	07	11.6
E. Bacterial infections:-Chanchroid, Hansens, Tuberculosis verrucosa cutis, Folliculitis, Pustular lesion, Lupus vulgaris, Syphilis, Pyoderma gangrenosum.	13	21.6	08	13.3
F. Fungal infections:- Candidiasis, Cryptococcus, Histoplasma, TineaCorporis	05	8.3	06	10
G. Parasitic &Protozoal infections:- Leishmaniasis, Scabies	-	-	01	1.6
H. Drug reaction	-	-	-	-
I. Vascular lesion:- Leukocytoclastic vasculitis, Granuloma Pyogenicum	02	3.3	04	6.6
J. Connective tissue lesion:- DLE, Granuloma Annulare	04	6.6	04	6.6
K. Malignant/Premalignant lesion:- Verrucous Carcinoma, Squamous cell carcinoma, Bowenoid papulosis	03	5.0	03	5.0
L. Vesiculobullous lesion:- Pemphigus vulgaris, Bullous pemphigoid, Bullous impetigo, ErythemaMultiforme	04	6.6	04	6.6
M. Others:- Follicular keratosis, Perforating folliculitis	01	1.6	02	3.3

Table 2: Correlation between Clinical diagnosis with Histopathological diagnosis among study participants (n=60).

Category	Total no Of cases	Cases Correlated histopathologically	Cases not correlated histopathologically
Dermatitis	08	06	02
Papular	09	08	01
Epidermal	03	02	01
Viral	08	07	01
Bacterial	13	09	04
Fungal	05	05	00
Parasitic	00	00	00
Vascular	02	02	00
Connective tissue	04	03	01
Malignant/Premalignant	03	01	02
Vesiculo-bullous	04	03	01
Other	01	01	00

Table 3; Clinico-pathological correlation of benign and malignant/premalignant category among skin lesions of study participants.

Category	Correlated histologically	Not correlated histologically	Chi-square (p -value)
Benign	40	17	0.49 (0.48)*
Malignant/premalignant	01	02	

*not significant statistically

Discussion

The dermatological manifestations including many opportunistic skin infections, are quite common in HIV infected patients.^[6,7] More than 90% of human immunodeficiency virus infected patients develop skin lesions at some point of time through the course of disease.^[16] This study was mainly focused on the dermatological manifestations of PLHIV attending a tertiary care center for treatment. All the 60 patients included in the study are already diagnosed positive for HIV infection.

The majority (90%) of the infected patients in this study belonged to rural areas and belonged to lower socioeconomic strata (79.4%). This indicates poor nutritional status, which itself can accelerate the progression of HIV infection.

In present study, age range of all the sixty patients was between 21 to 60 years. Out of these 60 patients, 25 patients (41.67%) were between 31 to 40 years of age. Similar findings have been observed in study done by Sanjay M. Chawhan et al, where maximum patients were falling in the same age range.^[16]

In the present study, we found 71.6% male patients as compared to 28.3% female patients, with 2.5: 1 male to female ratio. Similarly, male preponderance has been observed by other authors.^[16,17]

Maximum number of provisional clinical diagnosis obtained in present study, were bacterial infections, papular lesions and dermatitis.

In present study, histopathological examination of skin biopsy revealed that, maximum patients were having bacterial skin infection with Mycobacterium infections was the most common. Among these mycobacterium infections, we found 7 (11.6 %) cases of leprosy which included four cases of borderline tuberculoid and one case from each of tuberculoid leprosy, papulonecrotic tuberculid and erythema nodosum leprosum. Harminder singh et al also found leprosy as the most common dermatological disorder in HIV positive patients.^[18]

Among other skin infections, we found 07 (11.6%) patients with viral lesions, 06 (10%) patients with fungal infections and 01 (1.6%) patient with parasitic lesion diagnosed as dermal leishmaniasis. Out of total six cases of fungal cutaneous infections, there were two cases of cryptococcosis and histoplasmosis (one from each). This shows that in HIV seropositive patients, infectious agents can produce skin lesions even though the classic organs of involvement by these agents do not include the skin.

In present study, total 35 cases were diagnosed as non-neoplastic and non-infectious lesions on histopathological

diagnosis. In this category, papulo-pruritic lesions like Pruritic papular eruptions, Psoriasis, Seborrheic Dermatitis, Eosinophilic folliculitis, Scaly lesion, Lichen planus were the most prevalent; followed by dermatitis. The study done by Sanjay M. Chawhan et al. also shows papulo-pruritic eruptions as a most common non-neoplastic lesion diagnosed in PLHIV.^[16]

In present study, we found only three cases of malignant/premalignant skin lesions, which includes verrucous carcinoma, squamous cell carcinoma and bowenoid papulosis. Wiwanitkit (2004), D. N. Lanjewar (2011) and Sanjay M. Chawhan (2013) also found striking low prevalence of cutaneous and other malignancies in PLHIV.^[6,19,16] In this study, no any case of Kaposi's sarcoma or lymphoma was found.

Practicing general anatomical pathologists and dermatopathologists, especially those working in regions where HIV/AIDS is highly prevalent, must be familiar with the spectrum of cutaneous manifestations of HIV/AIDS.

The provisional clinical diagnosis of all the 60 patients were recorded and subsequently correlated with their histopathological diagnosis. The clinico-pathological consistency was found in 40 cases (68.33%) out of 60. A Study done by Jyoti Singh Rajput et al, also has clinico-pathological consistency in 75% cases.^[20] This diagnostic consistency was maximum in cases of papular lesion, where 8 out of 9 cases (88.8%) of papular lesions diagnosed clinically, were well correlated histopathologically. Whereas, in only one case of bowenoid papulosis out of three cases of malignant and premalignant category was correctly correlated with histopathological diagnoses. Thus, it is very important to subject every skin lesion to histopathological examination for confirmation of diagnosis and proper treatment plan of the patient. An erroneous clinical diagnosis and failure to perform a confirmatory skin biopsy will inevitably delay proper provision of therapy.^[21]

Many of the skin lesions in PLHIV can show atypical/unusual clinical presentations.

In present study, one patient with Histoplasmosis infection presented with multiple nodular lesions on face and upper trunk, was given provisional clinical diagnosis of seborrheic keratosis. Other diverse presentations like erythematous macules, molluscum contagiosum-like papules or nodules, a guttate psoriasis-like eruption or purpuric lesion can be found in PLHIV infected with Histoplasmosis.^[21] It is worth mentioning that, diverse clinical presentation of certain clinical conditions in HIV patients results in failure to establish proper clinical diagnosis.^[21] In such cases,

histopathological examination proves to be very essential for confirmation of diagnosis. Also it is very important on the part of a histopathologist to maintain a high index of suspicion for undiagnosed HIV/AIDS when clinical history indicates that a common dermatosis has displayed unusual/atypical clinical features.^[21]

An ulceration of overlying epidermis is not an uncommon presentation in any of infective or neoplastic dermatological conditions in PLHIV.^[21] Such ulcerative lesions need to be investigated thoroughly. In present study, one case of ulcerative lesion on genital region which was clinically diagnosed as chancroid, on histopathologically, it turned out to be non-keratinizing SCC.

Similarly, a case of dermal leishmaniasis, presented with multiple papular, erythematous, scaly lesions over face of 1and 1/2month duration and was given the provisional clinical diagnosis of Amyloidosis. On histopathological examination of biopsy, it was diagnosed as dermal leishmaniasis.

It was also observed that, submitting skin biopsy with a differential diagnosis improves chances of more corrective diagnosis.^[20] In present study, six cases were given with more than one provisional clinical diagnosis and subsequently one confirmed diagnosis on histopathological examination was given.

In present study, on histopathological examination revealed, periadnexal and perivascular inflammatory infiltrate, i.e., lymphocytic infiltration was the common finding irrespective of type of pathology. None of the lesions showed normal epidermis. Epidermal hyperplasia in the form of acanthosis, irregular parakeratosis or hyperkeratosis was seen in most of the lesions.

Conclusion

We found that the dermatological manifestations have high prevalence among HIV positive subjects; of these, papular lesions and infectious lesions are most common. Thus, patients with skin complaints should be motivated for HIV testing as dermatological manifestations can be a common clinical presentation in PLHIV patients. This also reiterates the need for thorough skin examination in HIV positive patients and provision of optimal medical care to these patients.

As with dermatopathology in general, careful clinic-pathological correlation is of paramount importance for making confirm diagnosis and proper treatment planning of patient. Histopathologists practising in regions of the world where HIV/AIDS is prevalent must be familiar with the diverse spectrum of presentation of HIV related

cutaneous pathology. There should be a high index of suspicion for HIV-related skin pathology if a biopsy is obtained from a patient whose skin disease has an atypical clinical presentation, or if that disease has failed to respond to conventional therapy. Skin biopsy material from HIV positive patients should always be carefully examined for more than one pathological process.

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*Corresponding author:

Dr. Aditi D. Dholakia, Assistant Professor, Pathology Department, GMERS, Medical college, Gotri, Vadodara, Gujarat, India

Phone: +91 0265 2681124, 9824313724

Email: dharmeshvasavada@gmail.com

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