Original Research Article

Clinico pathological study of cutaneous lesions in HIV positive patients

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Abstract

Background: AIDS is a fatal illness caused by human immunodeficiency virus. About 90% ofthe HIV infected individuals sufferfrom one ormore skin lesions.The proportion of skincomplications and severity of several common cutaneous diseases are increased in HIV infected patients. **Aim:** 1. To study the histopathology of different cutaneous lesions present in HIV positive patients.2To correlate histopathological diagnosis with clinical diagnosis of skin lesions in HIV positive patients. **Materials and Methods:** Clinico pathological study of 65 skin biopsy specimens from HIVseropositive patients with cutaneous manifestations was carried out. Laboratory findings carriedout for the patients like routine haematological tests, serology test for HIV and CD4 and CD8 T cell count were noted and included in the study. **Results:** A total of 31 skin lesions were identified from 65patients. Specific microscopic findings were seen in all these cases. The infectious etiology was seen in 26 cases (40%), non infectious skin lesions in 23 cases (35.38%) and neoplastic lesions in 3 cases (4.61%). The spectrum of histopathological findings was correlated with clinical diagnosis. Clinico-histopathological discrepancies were observed in 5cases(7.66%). **Conclusion:** Cutaneous biopsy confirmed the diagnosisin many cases andin few cases it revealed clinically unsuspected diagnosis which reiterates the necessity of histopathologic investigations of cutaneous lesions in HIV/AIDS patients.

Keywords: AIDS, clinicopathology, cutaneous lesions, HIV.

Introduction

The infection with HIV (Human Immunodeficiency Virus) is distinct in that it is a disease with no cure in the current times and it results in a slowly progressive systemic disease with specific targets and sequelae; characterized by the gradual depletion of CD4 bearing T-cells, opportunistic infections, neoplasms and degenerative neurological diseases resulting in a finals tageter med the 'AIDS'(Acquired Immuno deficiency Syndrome).

HIV infection does not affect one organ or one system, but practically affects all the tissues andorgans of the human body.Skin is the mostc ommonly affected organ (90%)[1]. Theincidenceand severity of several common cutaneous diseases are increased in patients with HIV and thiscorrelates in many instances with the absolute number of CD4 T-helper cells[2]. The cutaneouslesions of HIVinfection have been the subjectof intense scrutiny as the skinis themostcommonly affected organ in HIV infected indivisuals[3]. The spectrum of skin disease in HIV infected individuals continues to change with the advent of HAART[4,5] and the morphology of HIV induced skin lesions is often unusual and clinically non diagnostic. Histopathological appraisal is therefore pivotal in the accurate diagnosis of many HIV induced skin diseases[5]. Anerroneous clinical diagnosis and failure to perform a confirmatory skin biopsy will inevitably result in delayed treatment. Hence skin biopsy and histopathological study help forcorrectdiagnosis and institution of appropriate treatment at the earliest[6]. A skin biopsy may provide the first opportunity to diagnose an unsuspected and potentially life threatening opportunistic infections[8].

The spectrum of HIV associated skin diseases encompasses a broad range of non infective dermatoses, infective dermatoses, that may be specific to HIV infections, inflammatory lesions, neoplastic proliferations, hyperpigmented conditions[6,7,8], and drug reactions which can be disabling or disfiguring and may require discontinuation of essential drugs[9]. A diagnostic approach is given based on the pre dominan this to pathological pattern with an emphasis on clinic pathological condition[6].

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Materials and methods

The present prospective study was carried out in the Department of Pathology, Tagore MedicalCollege and Hospital, Rathinamangalam, Melakottaiyur, Chennai, Tamil Nadu during the period:January 2020 to December 2020 (1 year). Patients who are attending to Skin and STD OPDTagore Medical College and Hospital and those who undergo skin biopsy form the source ofstudy and material. Histopathological study of 65 skin biopsy specimens from HIV seropositive patients with cutaneous manifestations was performed.

Inclusion criteria

All the skin biopsy specimens of HIV infected individuals with cutaneous manifestations sent to the Department of Pathology are included in the study.

Exclusion criteria

Lesions present over mucous membrane and mucocutaneous junction are excluded

History taking, Examination and Collection of sample

Detailed clinical history and examination findings of the patients were noted. Findings were recorded on proforma (Annexure). The skin biopsy specimen is obtained either by punch biopsy, incisional biopsy or excisional biopsy. In majority of cases punch biopsy was performed using'Easy punch' with size ranging from 3mm to 5mm as per the guidance of the dermatologist. Allthe biopsy specimens were received along with requisition for histopathological study containingclinical history, signs and symptoms of skin lesions and probable clinical diagnosis. Cases were selected regardless of age, sex, race, religion, occupation and socio economic status.

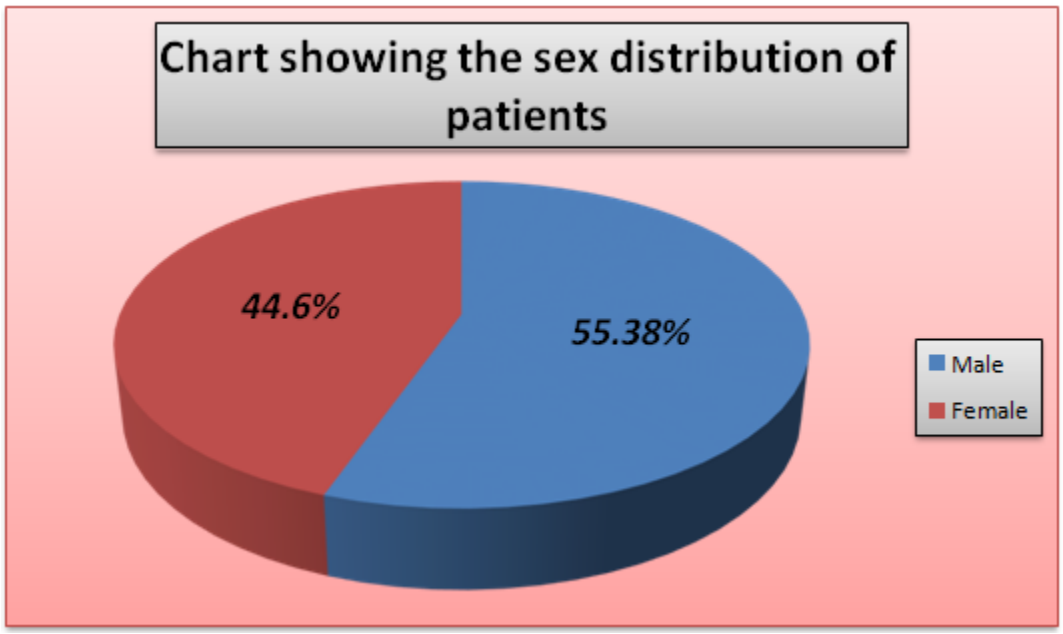
Laboratory findings carried out for the patients like routine haematological tests, serology test forHIV and CD4 and CD8 T cell count were noted and included in the study. Biopsy specimenswere

fixed in 10% formalin for 12 to 24 hrs. After recording the gross morphological features the specimens were routinely processed, embedded in paraffin wax and sections were cutat 3 to5µm thickness using rotatory microtome. Sections were stained routinely with Hematoxylin and Eosin. Special stains like Periodic Acid Schiff (PAS), Ziehl-Neelsen (ZN) and Gram's stain wereemployed wherever necessary. The stained sections were studied by light microscopy. Patients'clinical details were properly reviewed and were examined when ever needed.

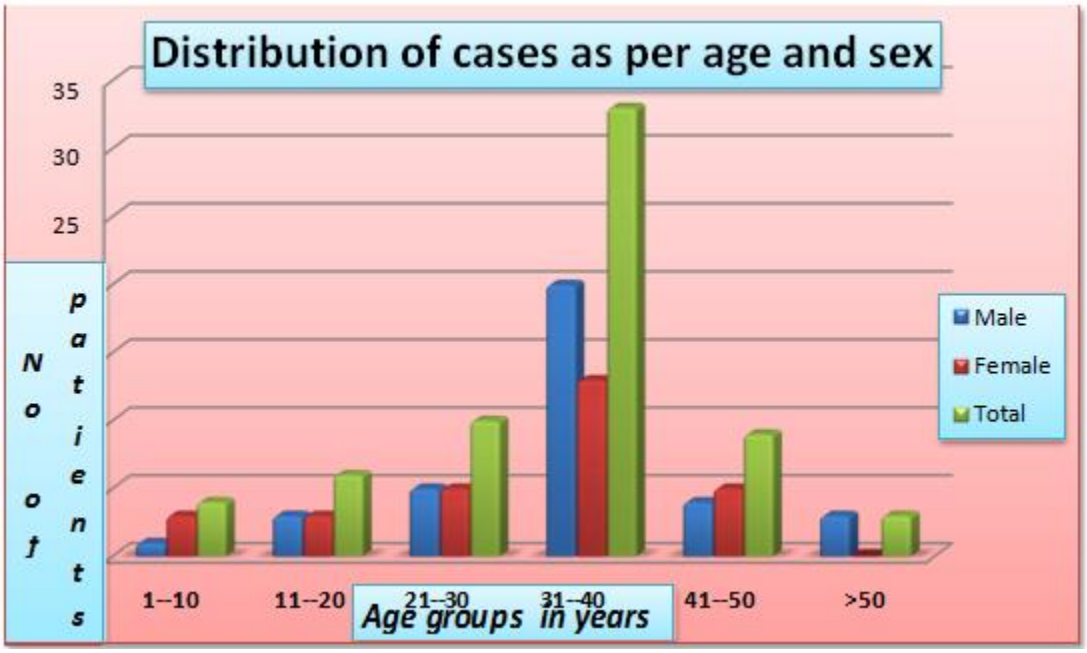
The diagnosis of skin lesions in HIV infected individuals were made on the basis of clinical findings and histopathological features.

Results

The total number of patients studied during the course of present study was 65 i.e. from January2009 to December 2009. This includes infectious and non-infectious inflammatory dermatoses, adverse drug reaction and pigmentary disorders, neoplastic conditions and miscellaneous conditions.



Demographic details and incidence of disease of various categories encountered during the course of study are listed below-



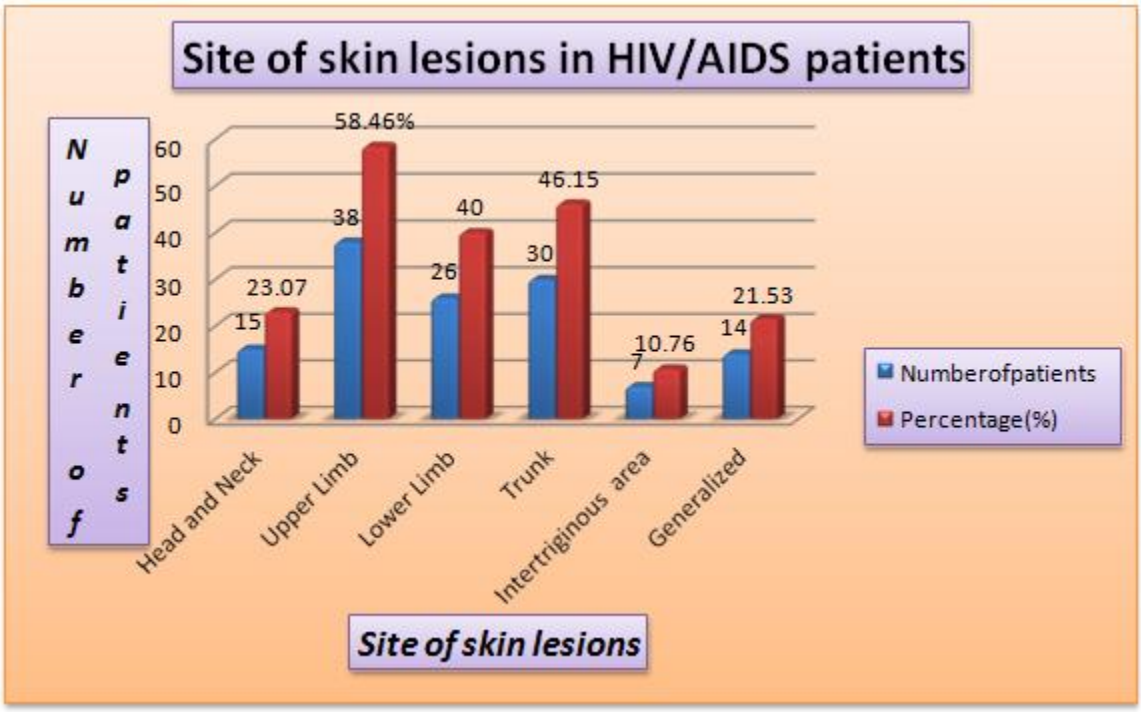
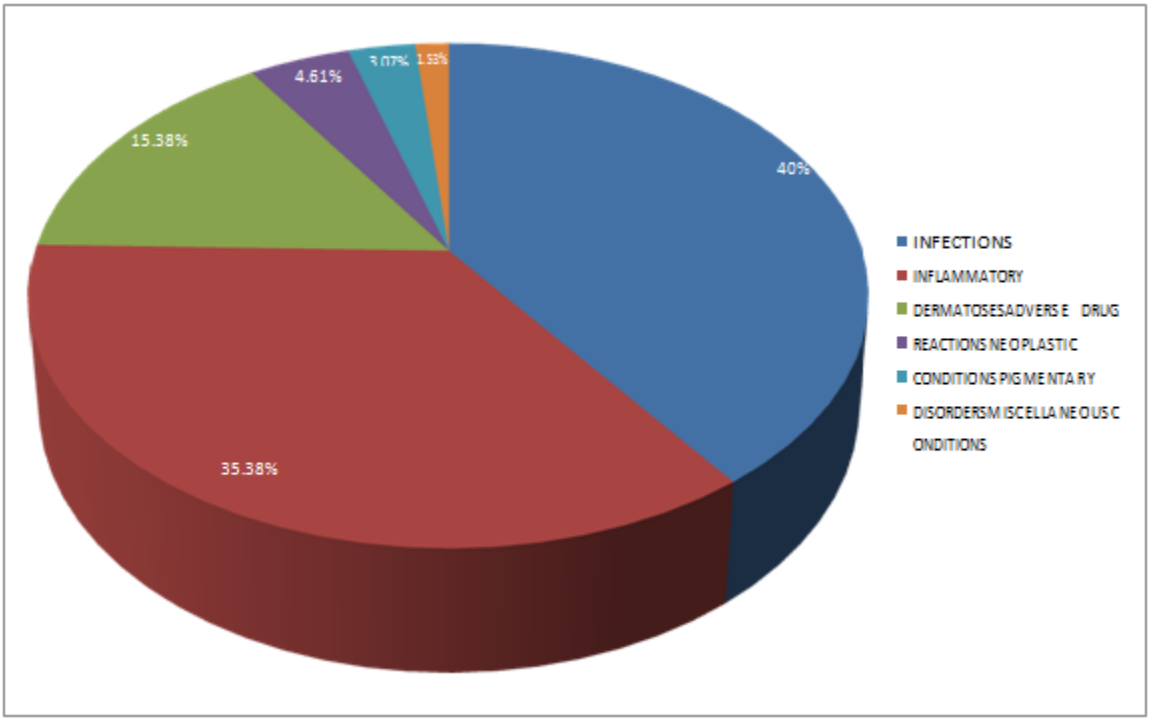


Table1: Lesions Found in the Present Study

Sl.No.	Cutaneous pathology	No.ofcases	Percentage
	Viral Infectious dermatoses	**10**	**15.38**
1.	Verruca	3	4.61
2	Condylomaaccuminata	1	1.53
3.	Herpessimplex	1	1.53
4.	Herpeszoster	3	4.61
5.	Molluscumcontagiosum	2	3.07
	BacterialInfectiousdermatoses	**6**	**9.23**
6.	Folliculitis	4	6.15
7.	Lichenscrofulosorum	1	1.53
8.	Scrofuloderma	1	1.53
	Fungal Infectiuos dermatoses	**7**	**10.76**
9.	Dermatophytosis	4	6.15
10	Cutaneouscandidiasis	2	3.07
11.	Cutaneouscryptococcosis	1	1.53
	ParasiticInfestations	3	4.61
12.	Scabies	3	4.61
	Non infectious Inflammatory dermatoses	**23**	**35.58**
13.	PPE	8	12.30
14.	Psoriasis	3	4.61
15.	PMLE	2	3.07
16.	Lichenplanus	2	3.07
17.	Spongioticdermatitis	2	3.07
18.	Nummular dermatitis	1	1.53
19.	Intra-epidermal pustular dermatitis	1	1.53
20.	Non specific dermatitis	1	1.53
21.	Prurigosimplex	1	1.53
22.	Prurigonodularis	1	1.53
23.	Icthyosis	1	1.53
	Adverse drug reactions	**10**	**15.38**
24.	EMF	3	4.61
25.	FDE	3	4.61
26.	Lichenoid drug eruption	2	3.07
27.	Exanthemic drug eruption	2	3.07
	Pigmentary disorder	**2**	**3.07**

28.	Melanosis	2	3.07
	Neoplastic conditions	**3**	**4.60**
29.	Keratinouscyst	2	3.07
30.	Lentigosimplex	1	1.53
	Miscellaneous	**1**	**1.53**
31.	Lymphangiomacircumsripta	1	1.53



Pie-chart showing spectrum of skin lesions in HIV patients

Table 2: List of Lesions Found in the Present Study

Sl. No.	Clinical Diagnosis	HistopathologicFindings	Correlation Yes/No
	Viral Infectious dermatoses		
1.	Verruca	Marked hyperkeratosis, hyperplasia,papillomatosisoftheepidermis withfibrovascularcore	Yes
2	Condylomaaccuminata	Hyperkeratosis, hyperplasia, papillomatosis ofthe epidermis with fibrovascular core andkoilocytosisoftheepidermis	Yes
3.	Herpessimplex	Herpes Zoster and Herpes Simplex arehistologically indistinguishable. In all the conditions intra epidermal unilocular vescicle with acantholytic cells and keratinocytesshowingballooning degenerationwithmarginationofchromatin	Yes
4.	Herpeszoster		Yes
5.	Molluscumcontagiosum	Handerson-Patterson bodies (Molluscumbodies)werenoticedwithinthecytoplasmofsuprabasalkeratinocytes.	Yes
	:terial Infectiousdermatoses		
6.	Folliculitis	purulentexudatesonthesurfacewiththelossofthe epidermis and partial destruction of hairfollicle with perifollicular infiltration ofpolymorphsinthe dermis.	Yes
7.	PPE	In **Lichen scrofulosorum** the superficial dermis showed ill defined granuloma consisting of lymphocytes and few epitheloid cells. No giantcellswerenoticed.	NO
8.	Scrofuloderma	Ulceration with ill defined granuloma formation and necrosis were noticed with in the mid dermis.	
	Fungal Infectiuos dermatoses		
9.	Dermatophytosis	Two cases of tinea showed refractile hyphaeelements in the stratum corneum and in theothertwobiopsies,refractilehyphaeelementsare observed within the hair follicle in thedermis.Special stain like the PAS useddemonstrated the magenta pink colour of thehyphae.	
10	Cutaneouscandidiasis	Sub-cornealpustulewithpseudohyphaeinthestratum corneum was noticed in both the casesofcandidiasis.	
11.	Cutaneouscryptococcosis	Aggregationofround toovoid sporesinthedermis with sub-epidermal	

		granulomaformationwas observed	
	ParasiticInfestations		
12.	Scabies	Histopathology:Thebiopsyshowedhyperplasiaand hyperkeratosisof epidermis.The dermisshowed prominent Perivascular and interstitialinfiltrate of lymphocytes with numerouseosinophils	
	NoninfectiousInflammatorydermatoses		
13.	PPE	Histopathology: Mild spongiosis, parakeratosisoftheepidermisand moderateperivascularandperi adnexal mononuclear inflammatory cellinfiltration was noticed in all the 8 cases ofPPE.	YES
14.	Psoriasis	The epidermis showedhyperkeratosis,parakeratosisand mildacanthosis.Twocasesshowed microabscess formation within theepidermis. The dermis showedperivascularlymphocyticinfiltration.	YES
15.	PMLE	Histopathology:Mildspongiosis, focalinterfacedermatitiswithhydropic degenerationof thebasalcells	YES
16.	Lichenplanus	Two skin biopsies showed mild acanthosis,papillomatosis, hyperkeratosis with prominentcapillariessurroundedbychronicinflammatorycell infiltration inthedermiswasnoticed.	YES
17.	PPE	**Spongioticdermatitis**:Boththecases,showed spongiosis,hyperplasiaandparakeratosisoftheepidermiswithlymphocyticinfiltrationofthepapillarydermis	NO
18	Erythroderma	**Spongioticdermatitis**:Boththecases,showed spongiosis,hyperplasiaandparakeratosisoftheepidermiswithlymphocytic	NO
		infiltrationofthe papillarydermis	
18.	Nummular dermatitis	irregular acanthosis with elongated, wide reteridgesand mildspongiosis.Intheparakeratoticstratum corneum, aggregates of coagulatedplasma was observed.	YES
19.	Intra-epidermal pustular dermatitis	intra-epidermal pustules filled with moderateneutrophils, few lymphocytes andminimalacantholysis	YES
20.	Non specific dermatitis		YES
21.	Prurigosimplex	Acanthosis, parakeratosis, mild spongiosis oftheepidermisandmildperivascularlymphocytic infiltrationin the superficialdermiswerenoticed.	YES
22.	Prurigonodularis	keratosis, parakeratosis, irregular acanthosiswith elongated rete ridgesof the epidermis,features of interface dermatitisanddermalfibrosis.	YES
23.	Icthyosis	Hyperkeratosis of the epidermis withsuperficial,minimaldermalinflammationwasvisualized.	YES
	Adverse drug reactions		
24.	EMF	Theskin biopsyfromtwopatientsdemonstratedintra-epidermal vesicle associated withextravasated erythrocytesand exocytosis oflymphocytes within the blister cavity andfeaturesofinterfacedermatitis.	YES
25.	FDE	Hydropic degeneration of the basal cell layerandnecrosisofthekeratinocyteswerenoticedinthe epidermis.Upperdermisshowedpigmentary incontinence withfocallymphocyticinfiltration.	YES
26.	Lichenoiddrugeruption	parakeratosis,mildspongiosis andvacuolardegeneration of basal cells in the epidermis.Thedermisshowed mixedinflammatorycell	YES
		infiltrationattheepidermo-dermaljunction.	
27.	Exanthemicdrugeruption	Increasednumberofmelanocytes,spongiosisoftheepidermisandperivascularlymphocyticcuffinginthesuperficialdermiswerenoticed.	YES
	Pigmentarydisorder		
28.	Hyperpigmentation(Melasma, periorbitalhyperpigmentation)	**Melanosis** Increaseinthe numberofmelanocytes in the basal layer and presence ofmelaningranulesthroughout theentirethicknessofepidermiswithnomelaninpigmentinthe dermiswasnoticedinboththe cases. ThesecaseswerehistologicallydiagnosedasMelanosis	YES
	Neoplasticconditions		
29.	Keratinouscyst	Histopathology showeda cystic structurewithin the dermisandlined by cornifiedepitheliumwithdistinctgranularlayerandfilledwithlaminatedkeratin.	YES
30.	Lentigosimplex	elongationofreteridgeswithincreasednumberof melanocytes in the basal layer of theepidermis and increased melanophages in thesuperficialdermis	YES
	Miscellaneous		**YES**
31.	Lymphangiomacircumsripta	a focalarea of atrophied epidermis, belowwhich the dermis showeda large, dilated lymphaticvesselfilledwithclear,eosinophiliclymphatic fluid and few lymphocytes. Manysmall dilated lymphatic vessels were also seeninthemiddermis andsurroundedbyaninflammatoryreaction.	YES

Discussion

Dermatological manifestations are common in HIV/AIDS patients but are usually atypical, moresevere and less responsive to the treatment than the corresponding diseases encountered in HIV-negative patients[10,11]. Recently with the emergence of HIV epidemic, patients have presentedwith a host of new skin disorders, some of which are hallmarks of HIV infection[10]. These skinlesions can be used as clinical markers of disease progression as they are more common inadvancedstages.

The pattern of skin lesions in Indian patients with HIV infection may be different from that in the West[12]. Hence, making an accurate diagnosis is important as it may help patients awaitingmedical care, enable effective HIV treatment, ameliorate symptoms and improve prognosis[13]. For accurate diagnosis of the skin lesions, histopathological examination is must[12,13,14].

Age

In the present study 50.8% of the patients with cutaneous manifestation belongs to the age group of 31-40yrs. This is similar to other worldwide studies.

Sex

Thirty six males and twenty nine females leading to a Male: Female ratio of 1.24:1 was seen.The male preponderance in the study is explained by the fact thatgreater number of malepatients attendsSkin and STD OPD, and by greater involvement of male patients in "high-risk"activities predisposing to HIV infection. Decrease in male to female ratio may be due to less number of patients in the present study as compare to other studies.

Infections and infestations

Viral infections constituted a large group of infectious dermatoses comprising 15.38% of the study population. Herpes Zoster and Herpes Simples are histologically in distinguishable.

Bacterial infections

Three cases presented with acnei form pustules on the face, upper limb and trunk and were diagnosed as Acute Folliculitis.

Folliculitis

One patient presented with exaggerated acneiform pustules over scalp, face, axilla,inguinal perineal and perianal region and was dignosed as follicular occlusion triod. The skin biopsy taken from axillary region was diagnosed as Chronic Deep Folliculitis.

Cutaneous tuberculosis

Mycobacterial infections, in the form of Scroful oderma& Lichen Scroful osorum, were found in two cases (3.07%). In Lichen scrofula osorum the superficial dermis showed ill defined granuloma consisting of lymphocytes and few epitheloid cells. No giant cells were noticed. TrentJT etal[15] in his study found similar findings.

Fungal infections

Dermatophytosis

Dermatophytosis was the predominant fungal infection and was found. Various studies fromIndia and abroad have not found any increase in the overall incidence, but have found an increased severity of dermatophytosis.

Two cases of tinea showed refractile hyphae elements in the stratum corneum and in the othertwo biopsies, refractile hyphae elements are observed within the hair follicle in the dermis.Specialstainlike the PAS used demonstrated the magenta pink colour of the hyphae.

Cutaneous candidiasis

This is shown to be the commonest manifestation in many western studies but was seen in onlytwo cases (3.07%) in the presentstudy. Both the cases presented with erythematous patches inthe inter-digital areas of the foot. Many studies have documented the mucocutaneous lesions of candidiasis in HIV positive patients but involvement of only skin tissue is very rare.

Histopathology

Sub-corneal pustule with pseudo hyphae in the stratum corneum was noticed inboth the cases of candidiasis. The usage of PAS stain demonstrated the pseudo-hyphae within the stratumcorneum. TrentJTetal[15] observed similar findings in his study.

Cryptococcosis

Acutaneous cryptococcos is was documented in our study(1.53%). Who presented with umbilicated papules and pustules, distributed over face, trunk, upper limb and lower limb. Thispatient did not have any associated systemic manifestation except for involvement of skin. In review of literature cutaneous manifestation of cryptococcosis is usually seen as a part of systemic infection. Murakawa GJ et al[16] accounted for 5.9% and After gut K et al[17] accounted for10%of cutaneous lesions oftotal cryptococcal infectionin HIV/AIDS patients. Howeve rprimary cutaneous disease is very rare and that has been documented in our study.

Scabies

Histopathology: The biopsy showed hyperplasia and hyperkeratosis of epidermis.Thedermis showed prominent Perivascular and interstitial infiltrate of lymphocytes with numerous eosinophils. Except for the cellular reaction within the epidermis and dermisit was not possible to demonstrate the structure or any product of mites within the epidermis. Similar difficulty inidentifying the burrow and demonstration of the mites was also emphasized by Porras B et al[18] and PhilipE[19]et al in their studies.

The histopathological findings in all these cases such as PPE, Dermatitis, Acquired Icthyosis, Prurigo Symplex Lichen Planus and PMLE were in no way different from those seen in non-HIV patients[20].

Prurigo Nodularis

The clinically diagnosed Prurigo Nodularis which usually represents bothclinically and histologically the later stages of prurigo simplex showed microscopic features suchas keratosis, para keratosis, irregular a canthosis with elongated rete ridges of the epidermis, features of interface dermatitis and dermal fibrosis. In the study conducted by Smith KJ et al[21]similarfeatures were observed. In addition, features of granulomaannul are have also been described which was not observed in the presen tstudy.

Adverse drug reactions

The incidence of ADR is high as the utility of drugs such as anti-retroviral drugs and other medications used in the treatment of various associated illness and also due to deterioration of the immune functionl[5]. The histological features in no way were different from non HIV infected ADR

Hyper pigmentation

The importance of hyperpigmentation other than being one of the cutaneous markers of HIV andcosmetic significanceis thatitmay be an indication to investigate for TB, histoplasmosis, cryptococcosis, coccidioidomycosis, and endocrine causes[22] as drugs used for treatment and prophylaxis of these conditions cause hyper pigmentation.

Neoplastic conditions

Three cases of benign neoplastic conditions two being keratinous cysts and one case Lentigo Simplex. They are not associated to HIV infection perse, but are incidental findings.

Lymphangioma Circumscriptum

It was an incidental finding, found in one case as clear, colorless fluid filled vescicle over a diffuse swelling in the right axilla.

Conclusion

Skin is the most commonly affected organ in patients with HIV infection /AIDS. The present prospective study highlights the spectrum of dermatopathological findings in HIV/AIDS patients. While some cutaneous findings are nearly exclusive to HIV seropositive individuals, many are found in the general population. However, HIV-infected individuals often have an increased prevalence or severity, a typical presentation, or difficulty with treatment of the disease.

Majority of cases were found in the age group between 31-40 years with most commonly involved site being upper limb.

Non-infectious inflammatory dermatoses out number all other cutaneous lesions. Viral infectionswere the predominant of all infectious dermatoses. There was no recorded case of any cutaneous malignancy in the present study.

Cutaneous biopsy confirmed the diagnosis in many cases and in few cases it revealed clinically unsuspected diagnosis which reiterates the necessity of histopathologic investigations.

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