ORIGINAL ARTICLE

A Systematic Histopathological Analysis of Dermatopathology in Western Uttar Pradesh, India: A Four Year Study

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Abstract

Diagnosing Dermatological disorders can be challenging at times. Dermatopathology is the most important diagnostic modality in field of dermatology. Since Dermatopathology is yet to develop as a subspeciality, histopathological analysis of dermatological disorders is usually less discussed. To analyze dermatopathological diagnosis made over four years in Subharti Medical College, Meerut, Uttar Pradesh, India. Prospective and retrospective evaluation of all dermatopathological conditions made over 4 year duration in Subharti Medical College, Meerut, Uttar Pradesh, India. There were total of 1140 skin biopsy specimens. In 73.47%cases,there were inflammatory diseases, most frequently Bullous lesions and Psoriasis followed by Lichenoid dermatitis. Infectious diseases were observed in 22.99% cases. Tumours included 3.27% of cases and Alopecias 0.26% cases. Frequency of dermatopathological diagnosis reflected an overview of clinical spectrum of dermatological disorders in this area. In this study in Western Uttar Pradesh state of India, inflammatory diseases form major component of entire dermatopathological spectrum. Our findings further emphasize that leprosy is most common infectious disease reflecting high endemicity of Leprosy in this state of Uttar Pradesh. Different dermatopathological diagnoses observed in this study using routine histopathology with few special stains shows that still lot can be achieved if further specialized services are developed, hence establishing the need of Dermatopathology as subspeciality division in Pathology laboratory diagnostic services.

Key Words

Dermatopathology, India, leprosy

Introduction

Dermatological disorders are widely prevalent across the world with varied spectrum of clinical presentations. They vary widely as a result of geographic location, climate, socioeconomic status, personal habits and internal factors such as age, gender, and heredity. (1) Despite the high frequency of certain skin diseases in developing countries, they have so far not been regarded as a significant health problem in the development of public health strategies. WHO review of epidemiological studies reported high prevalence figures for skin diseases (21-87%) in children (2) Studies in African countries show prevalence of skin diseases between 11.5%-60%.(3-6) Dermatological disorders are among five most frequent causes of morbidity and account for 30% of all the medical ailments at primary health care level in sub-Saharan African countries(SSAC) (7) There is need for such prevalence studies in different parts of world to know the exact scenario of dermatological burden.

In India prevalence of skin disease in rural central India have been reported to be 60% (8) whereas studies from Telangana district in school children reveal 41% prevalence of dermatological diseases with female preponderance. (9)

Although studies have been reported about specific

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dermatopathological conditions but there is more need of analytical prevalence studies to enlighten and emphasize dermatological spectrum in wide variety of diseases.

In this study we systematically analyzed all the histopathological diagnoses of skin biopsy specimens processed in four year period in Department of Pathology, Subharti Medical College, Meerut. Subharti Medical College is private medical college in western Uttar Pradesh state of India and caters to many nearby rural and urban population. To the best of our knowledge, the obtained findings provide a first systematic analysis of the spectrum and type of dermatopathological diagnosis in this region.

Material and Methods

Following Institutional Research Ethics Board Approval, we have assessed and included in this retrospective and prospective study all histological diagnosis between 2013 and 2016 in Department of Pathology, Subharti Medical College, Meerut. The specimens were all routine dermatological analyses obtained by punch biopsy or surgical excision. Clinical information, wherever available, was used to strenghthen dermatopathological diagnoses.

We collected all histology slides and anonymously recorded all the diagnoses. Evaluation of all the histopathological sections was done by two pathologists. In case of discordance, final diagnoses has been done with discussion of cases between the pathologists and also interdepartmental clinicopathological discussion with clinical dermatologists.

Light microscopy studies were performed on tissue fixed in 10% neutral buffered formalin, routinely processed and subsequently embedded in paraffin.Sections were stained with autostainer/ Haematoxylin and eosin stain. Staining with Periodic acid schiff (PAS) or Ziehl-Neelsen, Fite-Faracco stain, Alcian blue,Reticulin stain,Verhoeff,Van giesen stain were used in required cases.

Histopathological diagnoses were made according to internationally recognized criteria and then classified in the following groups and subgroups. Inflammatory(Inflammatory not otherwise specified ,n.o.s), Lichenoid dermatitis, lichen planus, Psoriasis, Cutaneous lupus erythematosus, Scleroderma/Morphea, Bullous disorders, Granulomatous dermatitis,Vasculitis,Panniculitis and Mastocytosis. Infections(Leprosy, Tuberculosis, Fungal, Leishmaniasis and Molluscum contagiosum.) Tumours(Benign and Malignant); Alopecias.

Category Inflammatory not otherwise specified,n.o.s, included abscesses, suppurative inflammation ,prurigo lesions, drug reactions, insect bite reactions, allergic and contact dermatitis etc. Cases included in entity Granulomatous dermatitis include Necrobiotic granuloma, Foreign body granuloma, Xanthogranulomatous reaction and Sarcoidosis.

Specific granulomatous pathology of Cutaneous tuberculosis(CTB) and Hansen's disease were classified accordingly with clinicopathological correlation.

All data were anonymously registered into an Microsoft office excel document, for simple statistical analyses

Results

We have included total of 1140 histopathological diagnosis of skin biopsy specimens obtained over four year period. Nine skin biopsies which were not representative were considered as inadequate(n=9;0.79% of the total skin biopsies) and were excluded from analyses.

A specific dermatopathological diagnosis and classification was possible in most of the cases. The histopathological diagnoses were broadly classified in Inflammatory, Infectious, Tumours (benign and malignant), Alopecias. Majority of cases were of Inflammatory diseases during the whole study period corresponding to 73.47% cases followed by Infectious diseases, Tumours and Alopecias (*Table 1*)

Discussion

Dermatological diseases are gaining importance as they are known to have significant impact on quality of life.(10) Although the known causes that lead to the incidence and spread of skin diseases are genetic, racial, geographical conditions, occupation and diet. However, exact cause of occurrence of skin diseases is yet to be established well in many countries.(9) Factors determining pattern of skin diseases in India are influenced by the developing economy, level of literacy, social backwardness, varied climate industrialization, access to primary health care and different religious ritual and cultural factors(8)

To the best of our knowledge this study provides the first comprehensive and systematic data about the histopathological diagnoses of skin biopsy specimens made in Western Uttar Pradesh. This new knowledge gives insight into the spectrum of dermatopathological problems. Specifically we found inflammatory diseases to be more common(73.47%) with the second most common frequent disease were Infections(22.99%) followed by Tumours(3.27%). The observed histopathological findings correlated well with the spectrum of clinical diagnosis which were analysed systematically during study.

Study by Grover *et al* (11) and Jain *et al* (8)revealed

Table 1. Dermatopathological diagnosis

Dermatopathological diagnosis	2013	2014	2015	2016	Total(n)
Total skin biopsies	**303**	**396**	**233**	**208**	**1131(9 inadequate biopsies)**
All inflammatory	**217**	**301**	**176**	**137**	**831(73.47%)**
Inflammatory n.o.s.	132	178	129	92	531
Lichenoid dermatitis	08	17	08	04	37
Lichen planus	05	10	02	02	19
Psoriasis	21	24	03	12	60
Cutaneous LE	05	08	04	05	22
Scleroderma/Morphea	06	10	06	02	24
Bullous disorders	13	30	12	10	65
Granulomatous dermatitis	04	06	05	05	20
Vasculitis	12	05	02	03	22
Panniculitis	11	11	03	02	27
Mastocytosis		02			02
Infectious diseases	**72**	**83**	**47**	**58**	**260(22.99%)**
Leprosy	56	63	34	38	191
Tuberculosis	05	17	11	14	47
Fungal	11	02	01	04	18
Leishmaniasis	00	01	01	00	02
Molluscum contagiosum				02	02
Tumours	**07**	**09**	**11**	**10**	**37(3.27%)**
Benign	***04***	***05***	***06***	***07***	***22***
Adnexal lesions	02	05	04	06	17
Intradermal Melanocytic Nevus	02	0	01	01	04
Cellular blue nevus	0	0	01	00	01
Malignant	***03***	***04***	***05***	***03***	***15***
Squamous cell carcinomas	02	01	02	02	07
Basal cell carcinoma	01	02	02	01	06
Adnexal tumours	0	01	01	0	02
Alopecias	**00**	**01**	**01**	**01**	**03(0.26%)**

prevalence of skin disorders with female preponderance and major group of population in their study was in there second and third decades and third and fourth decades respectively. In our study the major group of study population was in second and third decade. Male preponderance was noted with male female ratio being 1.66:1(*Table 2*).

Inflammatory diseases: The high prevalence of inflammatory diseases in our study representing 73.47% of all histopathological diagnoses is most likely to be related to difficulty in distinguishing some dermatoses on the basis of overlapping similar clinical features. Clinicopathological correlation is also required for the accurate diagnoses of dermatoses on skin colour. Because inflammatory dermatoses are easily treated themselves by patients by using combination creams available over the counter and other alternative medicine causing variation in clinical pictures, hence skin biopsies are highly valuable to make proper and accurate diagnoses. In the literature there are few studies with spectrum of histological analyses of inflammatory skin conditions in Indian patients although clinical analysis of dermatological conditions show eczema as the most common dermatosis in rural central India(8) whereas in other parts of world dermatitis was on the top of the list among studied group of skin diseases being reported to be 45.73% in Switzerland (12)and 57.7% in Kuwait(13).Similar dermatopathological studies in Subsaharan African region reported high frequency of Inflammatory dermatoses(7,14,15).

In our study Bullous lesions(n=65) and Psoriasis(n=60) were the most frequent specific inflammatory entities followed by Lichenoid lesions(n=37) corresponding to 7.8%,7.6% and 4.4% of the total inflammatory diseases.

Bullous disorders are a complex group of disorders which provide diagnostic challenge and dilemmas to clinical dermatologists and pediatricians. Study from Cuttack, India showed maximum incidence of the vesiculobullous diseases in age group of 1-6 years with Impetigo being the most common vesiculobullous disease with the highest incidence of 42%.(16) Similar study by Goyal etal in UP revealed Staphylococcal and Impetigo to be commonest entities in neonates.(17) Our study included wide spectrum of bullous lesions in various age groups and diagnosis was based on routine histopathology only. All the case were clinicopathologically correlated.

Clinical studies from India show prevalence of psoriasis varies from 0.44 to 2.8% (18) whereas Beltraminelli etal reported Psoriasis vulgaris as most frequent inflammatory

Table 2. Age and Gender Wise distribution of the study population

Age group	Total number	Male	Female	Ratio
0-10	40	25	15	
11-20	170	100	70	
21-30	295	180	115	
31-40	280	190	90	
41-50	188	110	78	
51-60	88	48	40	
61-70	48	36	12	
71-80	20	15	05	
81-90	02	01	01	
Total	1131	705	426	1.66:1

skin condition in dermatopathological study.(7)

Pinkus has defined Lichenoid reaction as a histologic pattern which is characterized by an epidermal basal cell damage that is intimately associated with a massive infiltration of mononuclear cells in the papillary dermis. They represent a heterogeneous group of conditions that resemble idiopathic Lichen Planus (LP) in terms of their clinical appearance and demonstrate a lichenoid tissue reaction.(19)

By analyzing distinctive histopathological features of the various lichenoid eruptions, differential diagnosis can be narrowed and final diagnosis can be made with appropriate clinicopathological correlation. Mahesh Kumar U etal have demonstrated that histopathology is a dependable tool for identifying the underlying cause in lichenoid eruptions, for an early diagnosis and the appropriate treatment.(20)

We also observed substantial cases of Lichenoid dermatitis(4.4%)which may be due to varied reasons including drug reactions, oral lichenoid lesions can be due to betel quid and arecanut chewing habit which is widely prevalent in this population. Solanki etal reported high degree of correlation between oral lichenoid reactions and quid chewing habit(21)

The estimated prevalence of LP is in the range of 0.22% to 5% worldwide (22-26).We observed 19 cases of lichen planus on histopathology reflecting 2.2% of total cases under Inflammatory diseases.

Mastocytosis involves increase in clonal tissue mast cells often affecting children. It is rare disease occurring sporadically with varied presentations.(27)We found two cases of mastocytosis in pediatric age group. Toulidine blue stain was used as special stain to highlight mast cells .Vasculitis encompasses heterogeneous group of disorders characterized by destruction of blood vessels by inflammatory process. Clinical presentations may vary in severity from a self-limited skin rash to multisystem disease which can prove fatal at times. To establish the diagnosis laboratory tests done include usually a biopsy of an involved tissue and angiogram if clinically indicated. Study from northeast of Iran showed Behcet's disease, cutaneous leukocytoclastic vasculitis, and granulomatosis with polyangiitis (Wegener's) to be the most common forms of vasculitis(28) whereas in our study leucocytoclastic vasculitis was most common form in cases(n=22) of vasculitis in our study.

Panniculitis is inflammation of the fat which may have a sudden onset or may occur as a feature of systemic illnesses such as pancreatitis, bacterial septicaemia, systemic lupus erythematosus, polyarteritis and malignancy(29) In our study 27 cases of panniculitis were recorded with septal panniculitis being the commonest pattern.

Infectious diseases: Interestingly Infectious diseases represented 22.99% of all histopathological diagnoses. Specifically Hansen's disease constituted majority of this category,73.4% (n=191) of these cases followed by CTB in(n=47; 18%) and Fungal infection in(n=18;6.9%) of cases. Special stains such as Fite-Farraco, Ziehl Neelsen stains and PAS stain were done to aid the diagnoses.

The global registered prevalence of Leprosy at the end of first quarter of 2014 was estimated as 0.32 per 10000 population(30)whereas in Indian scenario 86000 cases were on record as on April 1, 2014, giving a prevalence rate (PR) of 0.68 per 10,000 population(31) Leprosy is a great mimic and may confuse even the experienced personnels. In our study two cases which were clinically diagnosed as Xanthogranulomatous reaction were found to be cases of Hansen's diasease-Lepromatous type on histopathology with positive Fite Farraco stain. Referral networks need to be integrated and organized in order to achieve Leprosy control services. Although, elimination target for leprosy has been achieved, but it seems new leprosy cases will keep

appearing for at least some years as some level of disease transmission is still continuing or subclinical cases will manifest disease (32).Development of modalities to screen and detect sub-clinical infection are required to expedite early diagnosis and treatment. Timely detection and adequate managementb of leprosy reactions may help in preventing morbidity and reducing its potential to produce deformities. Hence routine skin biopsy should be encouraged to aid and strenghthen both clinically diagnosed and suspicious cases. (33)

The prevalence of Cutaneous tuberculosis in India was found to be 0.26% (34).Cutaneous tuberculosis(CTB) continues to be a significant medical problem even with the advent of highly effective antituberculous drugs. It constitutes about 1.5% of all extra pulmonary tuberculosis. The diagnosis of Cutaneous TB is based on the characteristic clinical morphology of the lesions as well as laboratory tests.(35) Although histologically granulomas can be seen in other conditions including cutaneous leishmaniasis, leprosy, atypical mycobacterial infections, fungal infections like chromomycosis and sporotrichosis thereby emphasizing the role of combination of laboratory diagnostic tests for cutaneous tuberculosis including histopathology testing and isolation of M. tuberculosis in culture of skin specimens or by PCR .Results from histopathology and bacteriology correlate and are complementary to each other, indicating that performing these two tests will increase the establishment of the diagnosis of CTB. Our study included spectrum of Cutaneous tuberculosis lesions on routine histopathology. ZN stain was done in all the cases. However, Acid fast bacilli could be demonstrated in only few cases.

Fungal infections are extremely common in the tropical region and some of them are serious and even fatal. Humans are the normal hosts for this group and transmission may occur by direct contact or indirectly by fomites(36) however, host factors such as immunologic status and local factors such as trauma, excessive moisture or occlusive clothing may constitute risk factors when combined with exposure to the etiologic fungi. Fungal infections can be well prevented by a meticulous personal hygiene.(37) India is a tropical country and it's climate is conducive for dermatophytosis(38) hence prompt diagnosis and treatment is required

Usually the diagnosis of cutaneous fungal infection is easily made on clinical examination of the lesion and direct microscopic examination of skin scrapings with potassium hydroxide. Histopathological examination is rarely required to confirm dermatophytic infections. There is often a discord between the clinical and histopathological findings and many times clinical appearance can have a poor histopathological correlation. Use of routine stains like PAS and Silver Methanamine can help to reach a correct diagnosis and initiate appropriate treatment. Fungal staining should be done in skin biopsies with non-specific clinical details and microscopic findings for best patient management(39)

Our study shows relatively less number of fungal infections which may reflect less biopsies performed for clinically evident fungal infection. Due to self treatment by most patients by using commonly available topical ointments typical clinical picture may be altered henceforth emphasizing routine practice of doing simply skin biopsy procedure with subsequent histopathological examination.

Finally approximately 0.7% cases of each entity ex. Cutaneous leishmaniasis(n=2) and Molluscum contagiosum(n=2) were observed during our study period. This may not be the reflection of the actual toll due to habit of self medication.

Clinically diagnosed cases of Leishmaniasis were confirmed histopathologically by demonstration of parasites in parasitized macrophages in skin biopsy by use of Giemsa-stain. About 1.5 million new cases of cutaneous leishmaniasis are reported every year worldwide. Poverty, malnutrition, environmental changes, collection of domestic garbage in suburbs and migration of susceptible populations could also be play important roles in etiology of the disease(40).Few number of cutaneous leishmaniasis lesions may be due to non-endemic region of population studied.

Molluscum contagiosum (MC) is an infection of the skin and mucous membrane caused by a DNA virus from the poxvirus family. Clinically dome shaped lesion with central umbilication is diagnostic. However, histopathological examination can aid the clinical diagnosis especially when lesion has undergone secondary changes. Demonstration of Molluscum bodies or Henderson-Paterson bodies is characteristic feature on histopathology. Usually these lesions spontaneously resolve when left untreated within 6-18 months in children and immunocompetent adults However, in immunocompromised and HIV infected adults the lesions can get protracted if left untreated. (41)Due to typical clinical lesions in presenting patients and abruptly healing nature of these lesions less number of cases may have been biopsied in our study.

Skin Tumours: Skin tumours represented 3.27% of all the histopathological diagnosis constitute a small but significant proportion of patients with benign and malignant tumours. In our institutional study, there was predominance of benign lesions encompassing

Intradermal Melanocytic Naevi, one case of Cellular blue naevus, benign adnexal lesions including cylindroma,syringoma, pilomatricoma, eccrine poroma, trichoepithelioma etc.Of the 15cases of malignant tumours,07 cases were of squamous cell carcinoma 6 cases were of basal cell carcinoma(including one case of Nevoid basal cell carcinoma syndrome and one case of Xeroderma pigmentosum) and two cases of Meibomian carcinoma.

Clinically diagnosed case of Xeroderma pigmentosum (XP) was 14 year old child who presented with multiple nodular lesions all over the body, two lesions showed basal cell carcinoma on histopathological examination. One of the lesions on face presenting with severe sunburn had ulcerated with necrotic debris and live maggots.

Epidemiologic data and experimental evidence indicate that Ultraviolet B (UVB) radiation (wavelength 290-320 nm) includes the most important wavelengths for the induction of skin cancers. Due to assumed protective effects of eumelanin in the brown skin of the Indian population, clinical dermatologists encounter less skin cancer patients in India. Detrimental effects of pollution may lead to depletion of ozone in the atmosphere, henceforth, increasing the levels of UVB radiation at the surface of the earth and subsequently the risk of skin cancer(42).Sharma etal in their study on adnexal tumours reported preponderance of benign adnexal tumours with commonest tumour to be clear cell hidradenoma with sweat gland differentiation, while pilomatricoma is the most common type of hair follicle tumor.(43)

Alopecias: Only 0.26%(n=3) of Alopecias are noted,which is not the exact reflection of clinical scenario.

Alopecia is a common cause of psychological stress which can occur at any age & sex.(44) Histopathological examination of scalp biopsies is necessary to distinguish Scarring alopecia from the Non-scarring type. Also, based on histopathological patterns, Primary Cicatricial Alopecia(PCA) is categorised into lymphocytic, neutrophilic, mixed, and nonspecific types. This classification is important because different treatment modalities may be used depending on the histological type of PCA. Although there is no hope for regrowth of destructed hair, prevention of disease progression is possible through early and correct diagnosis.(45)Alopecia areata (AA) is a nonscarring, autoimmune hair loss on the scalp, and/or body.

Among the three cases of alopecias in our study two cases were histopathologically diagnosed as Alopecia areata and one case was of Scarring Alopecia .Scalp biopsies are rarely performed in our setting probably of non cooperation by patients of Alopecias who are unwilling to undergo procedure. Moreover patients of alopecias and other scalp disorders come to the out patient skin department after using alternative medicines and variable modalities of treatment including various hair oils and creams etc, hereby altering the clinical presentations.

Dermatological disorders can provide diagnostic challenge at times. However, this challenge can be overcome if clinicians are fully versed with different types of biopsy techniques and provide the pathologist with an adequate clinical history. We found 0.79% of inadequate biopsies in our study which were not representative and are excluded from the analyses.

Dermatopathology has been somewhat slow to develop as a separate subspecialty in India.

Specialized services such as Immunofluorescence studies and Immunohistochemistry are not available in most places due to high cost involved(46).

Spectrum of dermatological conditions in our study is reflection of histological diagnosis in Western Uttar Pradesh, India. Our vision is to provide accurate and proper diagnosis with appropriate clinicodermatopathological correlation inorder to aid in providing targeted treatment approach to the patient .

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