

Original Research Article**Histopathological Pattern Analysis in Non Neoplastic Skin Biopsies: A Prospective Study of 142 Cases****Bhargavi Mohan^a, Manjunatha H.K.^b, Geethamani V.^c, Sushma T.A.^d, Thejaswini M.U.^e, Thej M.J.^f**^aAssistant Professor ^bProfessor ^cProfessor and Head ^{d,e,f}Associate Professor, Department of Pathology, BGS, Global Institute of Medical Sciences – Bengaluru - 560060, Karnataka.**Abstract**

Background: Non neoplastic skin lesions form the majority of morbidity from skin diseases, however majority of them are often diagnosed as non specific dermatitis. The objective of this study was to analyse and classify non neoplastic skin lesions based on histopathological pattern and to study the relative frequency of various lesions along with age and sex distribution.

Materials and methods: This was a prospective study comprising of 142 cases; from March 2016 to February 2017, done at BGS Global Institute of Medical Sciences. Routine staining with H&E and special stains and Immunofluorescence, wherever needed, were performed. Microscopic findings were studied by two pathologists independently.

Results: A total of 142 cases were studied of which papulosquamous disorders (38%) were the most common lesions followed by dermatitis (27%) and pigment disorders (14%).

Conclusion: The high frequency of non specific dermatitis as a final diagnosis may reflect the common reaction pattern of many skin lesions; however detailed evaluation of skin lesions and a pattern based classification, can reduce the frequency of nonspecific diagnosis.

Keywords: Skin Lesions; Non Neoplastic; Histopathology.

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**(Received on 13.01.2018,
Accepted on 09.02.2018)**

Introduction

There are about 2000 known skin diseases; seen across various age groups [1]. Of which non-neoplastic skin lesions form the majority of the morbidity from skin diseases [2]. Although some of these lesions are easy to diagnose clinically, a substantial number fall under the “non specific dermatitis” group. Often, a good clinical history along with an adequate skin biopsy is helpful in making a correct histopathological diagnosis [3]. The present study is an attempt to classify non neoplastic skin lesions based on histopathological pattern; and to study the relative frequency of various lesions along with age and sex distribution.

Materials and Methods

The material for the present study comprised skin biopsies from patients received in the Department of Pathology, BGS Global Institute of Medical Sciences, Bengaluru; from March 2016 to Feb 2017. This was a prospective study comprising of 142 cases. All non neoplastic skin lesions were included; and all neoplastic skin lesions and oral mucosal biopsies were excluded from our study. Specimens were fixed in 10% formalin, processed and 3-5 μ thick sections were cut. Routine staining with H&E and special stains (PAS, AFB, Verhoeff-van gieson, Alcian blue and Fite faraco stain) and Immunofluorescence,

wherever needed, were performed. Serial sectioning and step deeper were taken where ever necessary. Microscopic findings were studied by two pathologists independently. Relative frequency of various lesions along with age and sex distribution of the lesions were analysed.

Results

A total of 142 cases were studied of which papulosquamous disorders were the most common lesions (38 %) followed by Dermatitis (27%) and pigment disorders (14%), (Chart 1) with 30 % of the patients presenting in the age group of 31-40 years (Table 1). Of the 142 cases, 87 cases (61%) were females and 55 cases (39%) were males. (Chart 2). In both males and females, the most common lesion was papulosquamous disorders (Chart 2).

Papulosquamous lesions were more common in the older age group with a slight female predilection. The most frequently encountered tissue reaction pattern was the psoriasiform pattern, with psoriasis constituting the highest percentage of cases (34% of the number of papulosquamous lesions).

There were 6 cases (4%) of granulomatous lesions. The most common etiology of granuloma in our study was Leprosy accounting for 5 cases. Fite faraco stain was done to demonstrate Lepra bacilli. There were 6 cases of viral infection and 2 cases of fungal infection.

There were 7 cases of bullous diseases; of which 3 cases were diagnosed to be bullous pemphigoid, one case of Dermatitis Herpetiformis and one case of Linear Ig A disease, one case of Pemphigus foliaceus and one case of Pemphigus vulgaris. Immunofluorescence was done on all cases for confirmation.

Distribution of Non neoplastic skin lesions (n=142)

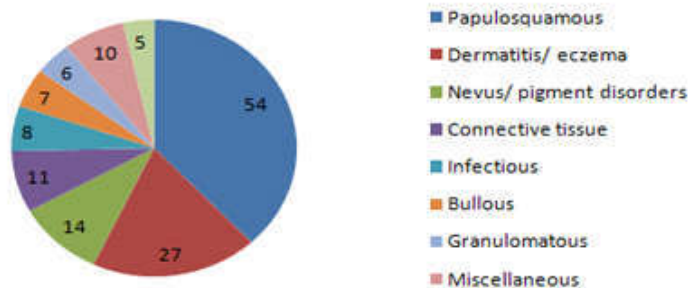


Chart 1: Distribution of number of cases (n=142)

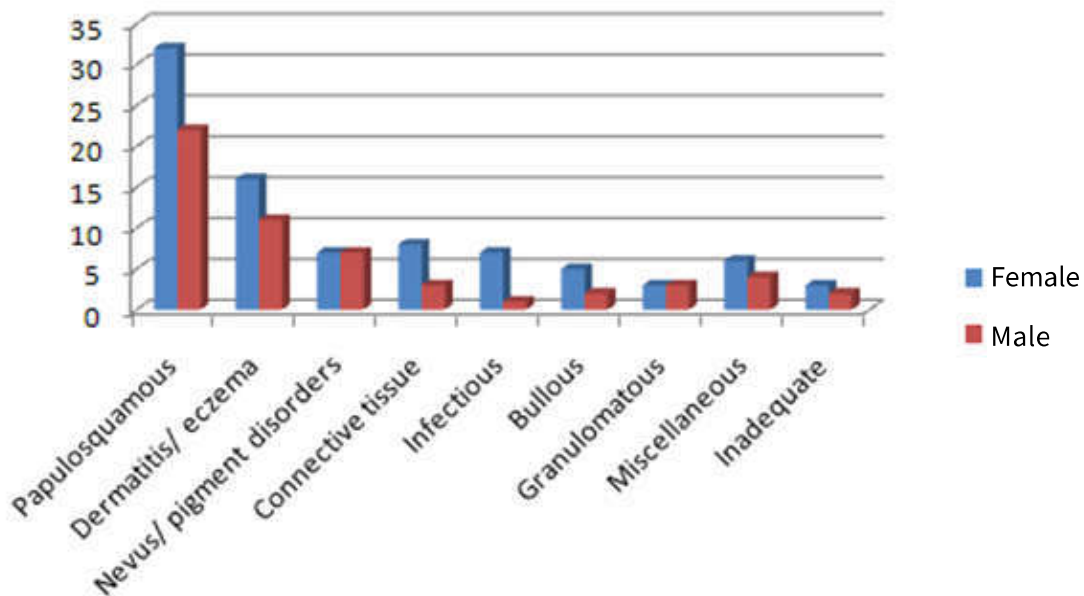


Chart 2: Sex distribution of the cases

Table 1: Age group distribution of various lesions

Skin lesion	<21	21-30	31-40	41-50	51-60	61-70	71-80	>81	Grand Total
Papulosquamous	8	8	9	15	8	6			54
Dermatitis/eczema	5	3	3	5	7	3		1	27
Nevus/pigment disorders	2	1	5	3	3				14
Connective tissue	1	4	5	1					11
Infectious	2	3	2	1					8
Bullous		1	2	1		1	2		7
Granulomatous	1		1	1	1	2			6
Miscellaneous	4	1	2		1	2			10
Inadequate	1	2	1	1					5
Grand Total	24	23	30	28	20	14	2	1	142

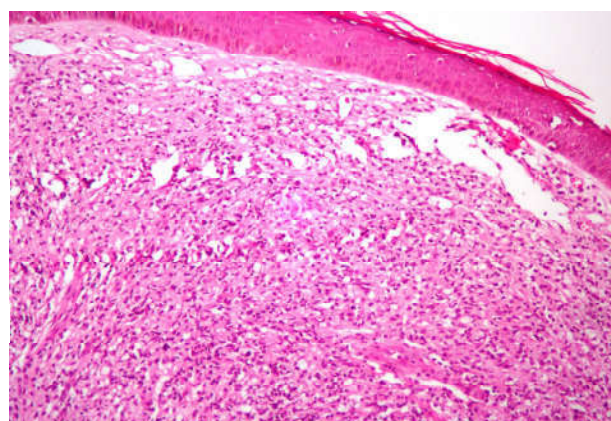


Fig. 1: Histoid leprosy

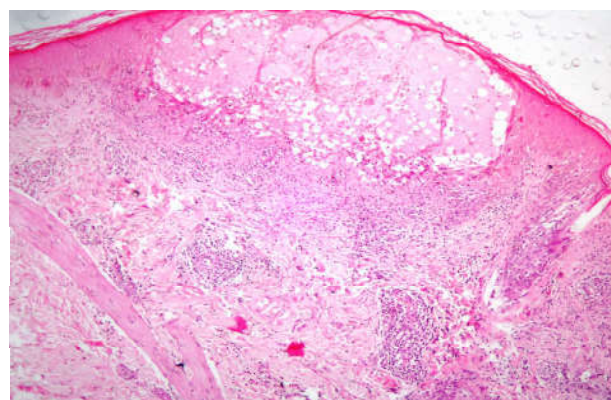


Fig. 2: Viral (Herpes simplex) Dermatitis

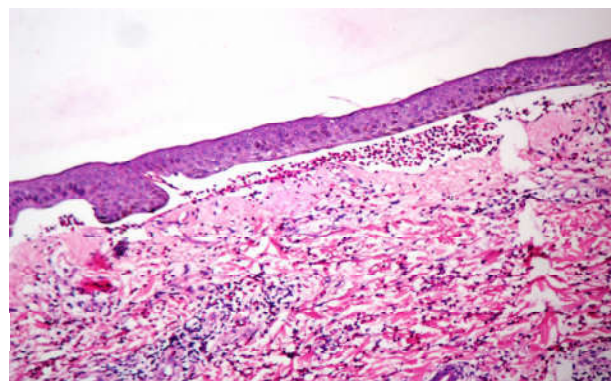


Fig. 3: Bullous pemphigoid

Discussion

Histopathological diagnosis helps dermatologists, in grouping patients into various disease groups that share similar outcome, and a common set of responses to therapy. It helps to prognosticate and manage the outcome of patients. Although histopathology remains the gold standard, not all lesions are amenable to definitive specific histologic diagnosis [3]. The limitation of histopathology in arriving at a specific diagnosis may be due to (1) inadequate sample size, (2) inappropriate biopsy site, (3) overlapping clinical and histological features, (4) inadequate or often absent clinical history, (5) treatment effect [4]. However, a histologic image represents a true synthesis of all molecular events acting in a given microscopic scene and thus, the best approximation to the goal of improving diagnostic accuracy can be achieved by correlation of findings at the molecular, histologic, and gross anatomic levels with patient's physical findings and clinical history [3].

Skin has the same components at different anatomical sites, but in varying proportions; so that the skin has different morphology at different sites. Understanding of the normal histology of skin is central to recognising cutaneous pathology. The epidermal layer is composed primarily of keratinocytes along with a small population of langerhans cells, melanocytes, merkel cells, and unmyelinated axons. Langerhans cells originate in the bone marrow and are functionally and immunologically related to the monocyte-macrophage series. They have antigen processing and presenting capacity. Merkel cells thought to arise from stem cells and have neurosecretory function, are specialized epithelial cells that express cytokeratin, desmosomal proteins and neuroendocrine markers. Separated from the epidermis by a structurally and chemically complex basement membrane zone, the dermis consists of endothelial and neural cells, fibroblasts, monocyte/macrophages and mast cells enveloped within a matrix of collagen and glycosaminoglycan. Adnexae extend from the epidermis into the dermis and consist of specialized cells for hair growth, epithelial renewal (stem cells), and temperature regulation. Adnexal epithelium

also appears to provide a safe haven for certain precursor cells (e.g., for melanocytes and dendritic cells) in an environment sequestered from deleterious environmental influences at the skin surface. The dermal microvascular represents an ensemble of cells responsible for cutaneous nutrition, immune cell trafficking, regulation of vessel tone, and local hemostasis [3].

Modern pathology emphasizes on pattern recognition. Pattern recognition helps to identify a small list of possible differential diagnosis. Further, observation of the sections aided by ancillary techniques will help in making a more definitive diagnosis [3]. Classification of skin lesions are either pattern based or pathogenesis based. We have used pattern based classification to make a diagnosis and integrated them in the pathogenesis based classification according to the ICD-10 of the disorders of skin and subcutaneous tissue.

Papulosquamous disorders constituting 38% of the cases was the largest disease group in our study followed by dermatitis/ eczema (19%). The persistent irritating and poor cosmetic effects of these lesions explains the willingness of these patients to undergo biopsy, and thus may be the reason for their high frequency [2]. Papulosquamous lesions were more common in the older age group with a slight female predilection. The most frequently encountered tissue reaction pattern was the psoriasiform pattern, with psoriasis constituting the highest percentage of cases (34% of the number of papulosquamous lesions).

Often in the differential diagnosis of Psoriasis; Chronic eczematous dermatitis, superficial fungal infections, Lichen Simplex chronicus and Pityriasis rubra pilaris should be considered. Chronic eczematous dermatitis shows more prominent spongiosis, with more irregular psoriasiform hyperplasia. It doesn't tend to have parakeratotic mounds. It is often associated with dermal eosinophilia. Superficial fungal infections can be confirmed by the presence of fungus using special stains such as PAS or GMS stain. Lichen simplex chronicus is characterised by irregular acanthosis, wedge shaped hypergranulosis and superficial dermal fibrosis. Munro microabscesses are less frequent. Pityriasis rubra pilaris is characterised by alternating parakeratosis and orthokeratosis in checkerboard pattern. Parakeratosis is seen shouldering the hair follicle and follicular keratin plugs are common [3].

The high frequency of dermatitis/ eczema group is attributable to the common reaction pattern of many non neoplastic lesions [2]. Since the pathogenesis of most dermatitis is unknown, they are best classified morphologically rather than based on etiology [5]. Leprosy (figure 1) was the most common lesion followed by fungal dermatitis and viral dermatitis (figure 2). Leprosy presents as macules or nodules affecting both skin and peripheral

nerves. Histologically in lepromatous leprosy there is extensive inflammatory infiltrate in dermis separated by a narrow grenz zone. Five cases showed positive fite faraco stain with globi of lepra bacilli within foamy macrophages. Tuberculoid leprosy on the other hand showed epithelioid cell granulomas in the dermis with evidence of neural invasion [5]. Cutaneous tuberculosis is an infection caused by mycobacterium tuberculosis and occurs by three routes; direct extension from underlying tuberculosis focus, inoculation and through blood. Lupus vulgaris was the most common form of cutaneous tuberculosis in our study. Lupus vulgaris is generally seen in patients with good immunity and isolation of acid fast bacilli is often uncommon in these cases [6,7,8].

Among the pigment disorders, the most common lesion was intradermal nevus followed by compound nevus and junctional nevus. Nevus had equal sex predilection in our study and was observed more commonly in 31-40 years age group.

Vesiculobullous lesions constituted 4.93% of our cases. Autoimmune bullous diseases of skin and mucous membrane are uncommon, disabling and potentially lethal diseases. For a quick and reliable diagnosis, histology along with immunofluorescence is needed. It is important to subclassify them because prognosis and therapy vary among variants of autoimmune bullous diseases [9]. All our cases were confirmed with immunofluorescence findings and substantiated (figure 3). In the differential diagnosis of Pemphigus vulgaris; Grave's disease, Bullous impetigo, Hailey-Hailey Disease, Darier disease, Acantholytic acanthoma and Warty Dyskeratoses have to be considered.

Bullous pemphigoid should be differentiated from Epidermolysis Bullosa Acquisita, which on indirect immunofluorescence with salt split skin shows linear deposition of antibodies on the floor of the blister. Linear IgA Bullous Dermatitis shows abundant neutrophils, and Direct Immunofluorescence shows linear deposition of IgA at the dermoepidermal junction. Cicatricial pemphigoid is characterised by subepidermal bulla associated with dermal fibrosis. Porphyria cutanea tarda should be differentiated from other causes of pseudoporphyria such as chronic renal failure (in dialysis), medication (tetracycline, NSAIDs, Cephalosporins) where in urinary porphyrin levels are normal. Porphyria cutanea tarda should also be differentiated from Bullous pemphigoid, Toxic epidermal necrolysis, Bullous amyloidosis and bullous lupus erythematosus [3].

Granulomatous diseases comprised about 4.23%. Connective tissue disorders comprise about 7.7%. Granulomatous diseases and connective tissue disorders will usually have a biopsy performed no matter how confident the clinical diagnosis is. This is based on the fact

that the patient might have to use therapy for prolonged period of time or with the attended possible complication of therapy, and to rule out an infectious etiology before administering steroids [2].

Sarcoidosis characterised by naked granulomas, asteroid body and schaumann bodies have to be differentiated from foreign body granulomas, cutaneous tuberculosis (tuberculin skin test, AFB culture and Quantitative TB gold, ZN stain on biopsy), Tuberculoid leprosy, lupus vulgaris and Granuloma rosacea. Granuloma annulare histologically presents in two patterns: Interstitial pattern and the Palisaded pattern. Interstitial pattern should be differentiated from Interstitial Granulomatous Dermatitis, and interstitial Mycosis fungoides.

Palisaded pattern of Granuloma annulare should be differentiated from Necrobiosis lipoidica, Rheumatoid nodule and Granulomatous dermatitis. Interstitial Granulomatous dermatitis is a subtype of Reactive Granulomatous Dermatitis presenting as linear cords or annular erythematous plaques usually on lateral upper trunk and proximal limbs. It has to be differentiated from Palisaded Neutrophilic Granulomatous Dermatitis where there is more prominent neutrophilia with basophilic degenerated collagen, palisading histiocytes, neutrophils with nuclear debris and focal leukocytoclastic vasculitis. Cutaneous Crohn also known as metastatic Crohn disease is a granulomatous lesion and is lymphocyte rich with ulceration and typically presents with abundant eosinophils [3].

Conclusion

Histopathologic examination serves as the Gold standard for arriving at a diagnosis, in majority of skin disorders, provided a good clinical history is available. Step deeper sectioning often provides valuable information towards making a diagnosis. The high frequency of non specific dermatitis as a final diagnosis may reflect the

common reaction pattern of many skin lesions; however detailed evaluation of skin lesions and a pattern based classification, can reduce the frequency of nonspecific diagnosis.

Acknowledgement

We thank the Department of Dermatology for providing us the biopsies that were used in the study.

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