Original Article

DOI: 10.21276/APALM2200

Histomorphological Studyof Vesiculobullous Lesions of Skin

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ABSTRACT

Background: Vesiculobullous disorders are a complex group of disorders which continue to be an enigma. Wide variety of pathological processes can lead to development of Vesiculobullous eruptions over the body. They may occur in many dermatoses which include various inflammatory, infective, autoimmune, drug induced as well as genetic conditions.

Each entity of vesiculobullous lesion has similar or confusing clinical features but different histopathological morphology. Histopathological examination is helpful in definitive diagnosis of vesiculobullous disorder which is very essential for specific treatment and an appropriate desirable outcome.

Aim: To study and classify various vesiculobullous lesions of the skin in various categories.

Material and Method: A prospective observational study of vesiculobullous lesions of the skin biopsies of 93 cases were received to the department of pathology over a period of 3 years. Complete clinical and relevant history was recorded. The specimens were routinely processed and haematoxylin and eosin stained slides were studied.

Result: A total of 93 cases of vesiculobullous lesions of the skin were diagnosed. Among these lesions, Pemphigus vulgaris were seen in 34 (36.55%) cases, Bullous pemphigoid in 22(22.65%) cases of and spongiotic dermatosis in 14 (15.05%) cases. The maximum numbers of cases (32.25%) were in 4th to 5th decades.

Conclusion: Thorough histopathological workup and clinical correlation is essential to confirm diagnosis of vesiculobullous lesions of skin.

Keywords: *Vesiculobullous Disorders, Skin Biopsies, Histopathological Examination*

Introduction

The vesiculobullous skin lesions comprise a group of eruptions of different etiology and prognosis. These lesions share a common characteristic, the formation of blister cavities within different layers of the epidermis or beneath the epidermis.[1] There are wide variety of vesiculobullous disorders, some of which can be extremely debilitating and even fatal. Some vesiculobullous lesions may have serious sequele which requires early treatment and intervention to prevent further morbidity and mortality.[2]

Bullous lesions can be classified based on site as suprabasal, intraepidermal, subcorneal and subepidermal. These lesions also classified on the basis of shape and size of the bulla and also changes in the bulla, epidermis and dermis.[3]

Clinical examination of these lesions is not sufficient for definite diagnosis however histopathological examination is simplest, one of the most valuable and most consistent method for diagnosis and classification of vesiculobullous skin lesions.

This study is undertaken to evaluate the histopathological features of vesiculobullous lesions of skin.

Material and Methods

The present descriptive histopathological study of 93 cases of vesiculo-bullous lesions of the skin was conducted in the Department of Pathology, ACPM Medical College, Dhule, Maharashtra, India over a period of 3 years. The data was collected in predesigned proforma from the patients who were clinically diagnosed as having vesiculobullous lesions from the Department of Dermatology. Skin biopsies were taken and clinical details were collected.

Inclusion Criteria:

All skin biopsies from the cases with vesiculobullous disorders and suspected cases of vesiculobullous disorders irrespective of age, sex and associated diseases was taken.

Exclusion criteria:

Vesiculobullous skin lesions associated with papulosquamous lesions. Inadequate and poorly preserved skin biopsies were excluded.

The punch biopsy was done on early lesions which included the epidermis, dermis and subcutaneous tissue below the lesion as well as the uninvolved perilesional area in order to prevent the detachment of the roof of the blister from its base. The specimens were received in 10% neutral buffered formalin. The specimens were processed in automated tissue processor. Serial sections of 3-5 µm thickness were taken. A minimum of three sections were taken and stained with haematoxylin and eosin. Detailed light microscopic examination was done. The separation plane of the blister, the mechanism of blister formation and the character of the inflammatory infiltrate were observed. Each slide was carefully examined by two pathologist and histopathological types of vesiculo-bullous lesions were reported and categarized.

Results

During this period total 684 skin biopsy specimens were received out of which Vesiculobullous lesion biopsies were 93 in number which constituted 13.59% of skin biopsy specimens. Among 93 skin biopsies 34 (36.55%) cases were of Pemphigus vulgaris followed by 22(22.65%) cases of Bullous pemphigoid and 14 (15.05%) cases of Spongiotic dermatosis which include formed the majority of the cases. Less common lesions included Pemphigus foliaceus, Erythema multiforme, Dermatitis Herpetiformis, Subcorneal pustular dematosis, Bullous drug eruption, Bullous SLE, Milker's nodule, Dyshidrotic Dermatitis, Epidermolysis Bullosa. [Table1] Pemphigus vulgaris presented most commonly in age group of 40-49 years in 17 cases, followed by 30-39 years 9 cases and 20-29 years 4 cases. Bullous pemphigoid presented commonly in the age group of 50-59 years 8 cases. Spongiotic dermatitis commonly in 30-39 and 40-49 years 4 cases each. [Table 2]

In 25 cases (73.5%) out of 34 cases of Pemphigus vulgaris burning sensation was the chief complaint followed by pain and itching. Itching was the most common symptoms in Bullous pemphigoid and was seen in 18(81.8%) out of 22 cases. 12 out of 14 cases of Spongiotic dermatitis cases present with itching. In present study 80 cases (86.02%) presented with blisters. Pemphigus vulgaris showed blisters in 32 (94.11%) of cases, Bullous pemphigoid showed blisters in 22(100%) of cases. Spongiotic dermatitis 8 (57.14%) and erythema multiforme 1(33.33%) cases presented with blisters. [Fig 1a-1d].

In our study vesicle/bulla were the common primary lesion accounting for 66 cases (70.97%) and pustules seen in 20 cases (21.50%). Pemphigus vulgaris, Bullous pemphigoid, Pemphigus foliaceus, Dermatitis Herpetiformis and Bullous drug eruption were mainly presented as bulla. Subcorneal pustular dematosis, Bullous SLE and Dyshidropic dermatosis [Fig 2a,2b 2c] were mainly presented as pustule. Crusting, papule and ruptured lesion were found in 7 cases which include Spongiotic dermatitis and milker's nodule.

Tomb stone appearance was seen in 25(73.52%), acantholysis 5(14.7 %), hyperkertosis and spongiosis 12(35.3%) were commonly in biopsy of Pemphigus vulgaris [Fig.1a, 1b]. Spongiosis is commonly seen with Spongiotic dermatitis [Fig.1d] and Bullous drug eruption. Hyperkeratosis is common finding with Dyshidropic dermatosis [Fig, 2b] 3(100%) and Milker's nodule 2(100%). Acanthosis was common with Spongiotic dermatitis, Erythema multiforme, Milker's nodule. [Table 3]

The dermal infiltrate was found in 33(97.05%) lesion of Pemphigus vulgaris, 20(90.90%) lesion of Bullous pemphigoid and all lesion of Spongiotic dermatitis, Dermatitis Herpetiformis, Pemphigus foliaceus, Bullous drug eruption, Bullous SLE, Milker's nodule, Epidermolysis Bullosa. Perivascular infiltration noted in 30 (88.23%) of Pemphigus vulgaris, 17 (77.27%) of Bullous Pemphigoid, 12 (85.23%) of Spongiotic dermatitis and all lesion of Pemphigus foliaceus [Fig 2d] and Dermatitis Herpetiformis, Bullous drug eruption, Milker's nodule and Epidermolysis Bullosa. Papillary micro abscesses noted in Dermatitis Herpetiformis.

Out of the 93 cases, 81(87.1%) cases were clinically diagnosed as one of the varieties of vesiculobullous lesions, which were confirmed on histopathology. The cases which were diagnosed mainly on histopathologically included the early lesions of Pemphigus vulgaris, bullous pemphigoid, Subcorneal Pustular dermatosis, Dermatitis Herpetiformis and Milker's nodule. Histologically ambiguous cases included the 2 cases in which diagnosis was inconclusive. Biopsy sent was inadequate as it included only the epidermis portion. This was probably because the biopsy taken from the bulla did not include the adjacent perilesional skin due to which the roof of the bulla was detached from the base. This emphasizes the importance of inadequate biopsy, which should include the epidermis, dermis and subcutaneous tissue below the lesion, as well as the perilesional area, to prevent detachment of the roof of the blister from the base. Repeat biopsies were taken in those cases.

Discussion

Skin is the single largest organ of the body. It represents a window to the internal well-being. Various diseases along with its manifestations can commonly involve the skin and mucous membranes out of which vesiculobullous lesions form a predominant group.[4] Factors that affect the delicate homeostasis existing among skin cells may result

Table No.1: Distribution of cases according to their presentation:

Type of lesions	No. of cases	Percentage
Pemphigus Vulgaris	34	36.55%
Bullous pemphigoid	22	23.65%
Spongiotic dermatitis	14	15.05%
Subcorneal pustulardermatosis	4	4.30%
Bullous SLE	4	4.30%
Erythema multiforme	3	3.22%
Dyshidrotic Dermatitis	3	3.22%
Pemphigus foliaceus	2	2.15%
Bullous drug eruption	2	2.15%
Milker's nodule	2	2.15%
Epidermolysis Bullosa	2	2.15%
Dermatitis Herpetiformis	1	1.07%
Total	**93**	**100%**

Table No. 2: Distribution of patients according to Age and vesiculobullous disorder:

Lesions	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80& above	Total
Pemphigus Vulgaris	-	1	4	9	17	1	1	1	-	**34**
Bullous pemphigoid	-	1	2	4	2	8	4	-	1	**22**
Spongiotic dermatitis	-	1	1	4	4	-	3	1	-	**14**
Subcorneal pustulardermatosis	-	-	-	-	1	1	-	-	-	**2**
Bullous SLE	-	-	1	-	1	-	1	1	-	**4**
Erythema multiforme	-	-	-	1	2	1	-	-	-	**4**
Dyshidrotic Dermatitis	-	1	1	-	1	-	-	-	-	**3**
Pemphigus foliaceus	-	-	-	2	1	0	-	-	-	**3**
Bullous drug eruption	-	-	1	1	-	-	-	-	-	**2**
Milker's nodule	-	-	-	1	-	1	-	-	-	**2**
Epidermolysis Bullosa	1	1	-	0	0	0	-	-	-	**2**
Dermatitis Herpetiformis	-	-	-	-	1	-	-	-	-	**1**
Total	**1**	**5**	**10**	**22**	**30**	**12**	**9**	**3**	**1**	**93**

Table No. 3: Distribution of patients according to the Epidermal changes:

Lesion	Tomb tone Appearance (%)	Hyperkeratosis (%)	Spongiosis (%)	Acanthosis (%)	Acantholysis (%)	Apoptotic Cells (%)
Pemphigus Vulgaris	25(73.53)	12(35.29)	12(35.29)	5(14.7)	23(67.64)	2(5.88)
Bullous pemphigoid	-	2(22.72)	9(40.9)	1(4.54)	-	-
Spongiotic dermatitis	-	6(42.85)	10(71.42)	9(64.28)	6(42.85)	4(28.51)
Subcorneal pustulardermatosis	-	-	1(50)	1(50)	1(50)	-
Bullous SLE	-	-	1(33.33)	2(66.66)	-	-
Erythema multiforme	-	-	-	1(100)	-	-
Dyshidrotic Dermatitis	-	1 (25)	-	3(75)	-	-
Pemphigus foliaceus	-	-	2(100)	-	1(50)	-
Bullous drug eruption	-	2 (50)	-	-	-	-
Milker's nodule		2 (100)	1 (50)	2 (100)	-	1
Epidermolysis Bullosa	-	3(100)	-	-	-	-
Dermatitis Herpetiformis	-	-	1 (50)	-	-	-

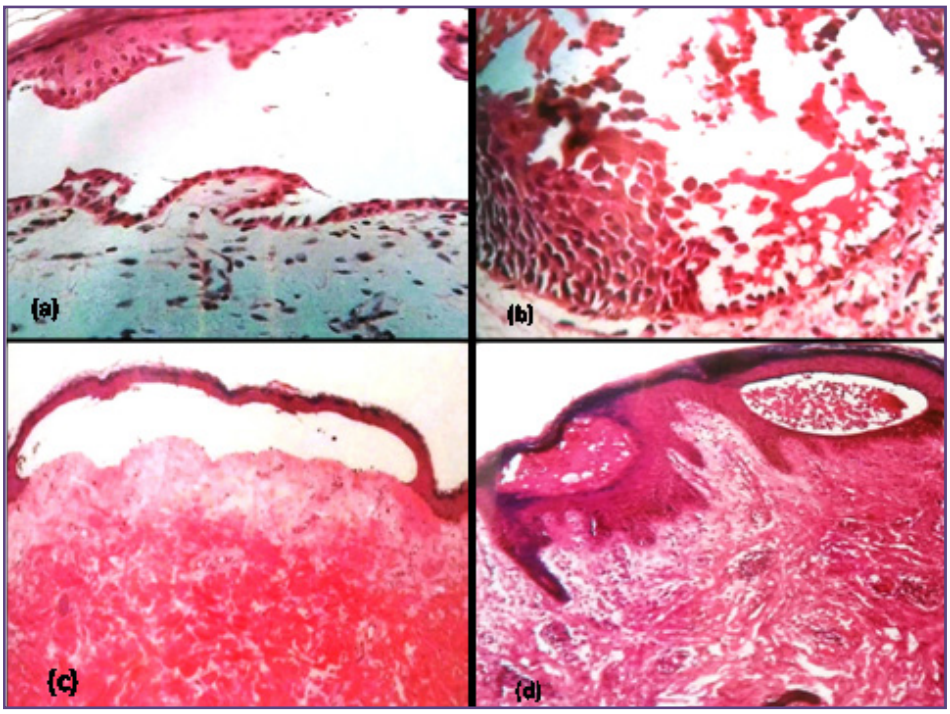

Fig 1: (a) HPE-pemphigus vulgaris showing suprabasal cleft and tombstone appearance(H&E;x400) (b) pemphigus vulgaris showing basal cells attached to the basement membrane and acantholytic cells and acute inflammatory cells in blisters(H&E;x400) (c) Bullous Pemphigoid showing subepidermal cleft(H&E;x400) (d) Spongiotic dermatitis showing intraepidermal vesicles filled with inflammatory cells.

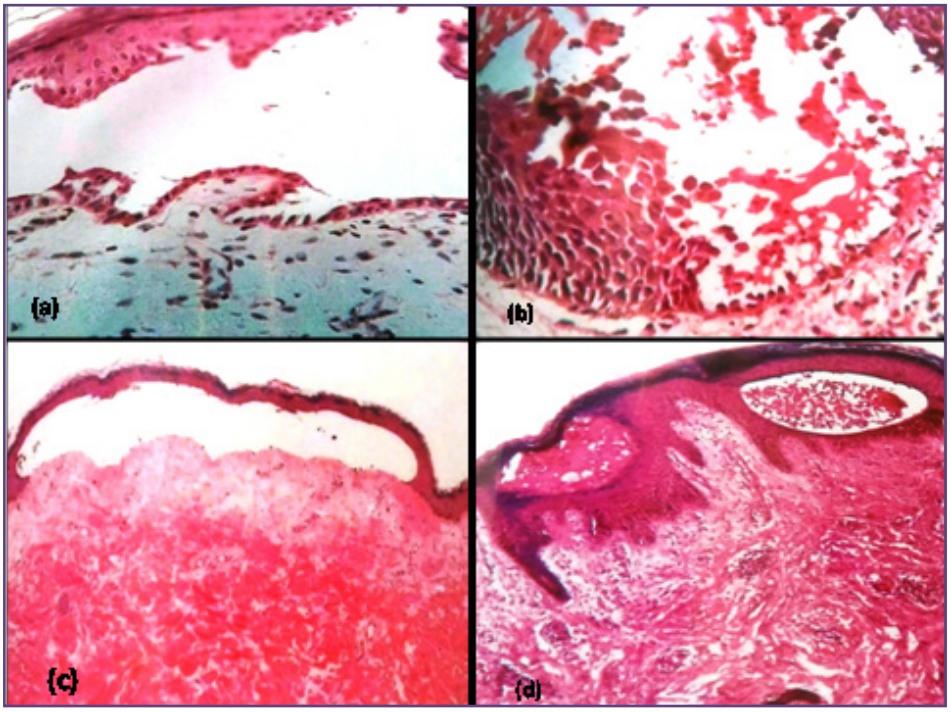

Fig 2 : (a) HPE- Subcorneal pustular dermatosis showing subcorneal pustules filled with acute inflammatory cells (H&Ex400)(b) Dyshidrotic dermatosis showing large intraepidermal vesicle with intact and compact hyperkeratosis (H&Ex400)(c) Bullous SLE showing subepidermal cleft and neutrophils in papillary dermis (d) Pemphigus foliaceus showing subcorneal bulla.

in diverse conditions. These processes can be studied in a biopsy specimen which is easily and safely obtained. However, clinical dermatology and histopathology of skin are separate facets of the same subject.

Skin biopsies are easily intended with precision, so histopathology gives the best diagnostics yields in bullous lesions to make a clear diagnosis.

In the present study Pemphigus vulgaris was the most common vesiculobullous disorder constituting 34(36.55%) out of 93 cases followed by Bullous pemphigoid 23.65% (22cases) Spongiotic dermatitis include 15.05% (14) cases. Our findings are most consistent with Deepti S.P. et al[5] study and Arundhati S.et al [6] study. Similar results also noted by Nanda A et al [7] and Nurul Kabir AKM et al.[8] The present study showed various vesiculobullous disorder like Subcorneal pustular dermatosis, Dermatitis Herpetiformis, Bullous SLE, Milker;s nodule, Dyshidrotic dermatitis which are observed in Murthy T.K et al [9] study. In present study majority of patients of pemphigus vulgaris were between 18-70 years age group which is similar to UzunS et al [10] study. Bullous pemphigoid ranged from35-70 years similar to UzunS et al.[10]

In the present study there was a female preponderance 1:1.83 and coincide with UzunS et al [10] and Patel PR et al [11] study. The most common symptoms of pemphigus vulgaris were burning sensation (73.52%) followed by pain (64.7%) and itching (58.82%). Similar findings also noted by Deepti S.P. et al [5] and Vora D et al.[12] Suprabasal bulla was seen in 91.17% same as that of Arya SR et al.[13] Row of tombstone appearance seen in 25 (73.53%) of cases which is higher than the Arya SR et al [13] and Vora D et al [12] study. Deepti S.P. et al [5] reported 88.2% of suprabasal bulla and 70.5% of row of tombstone appearance which is consistent with our study. Inflammatory cells were noted in 61.76% which is higher than that of all three above mentioned study. It was due to taking biopsy before starting medication like steroid and NSAIDs.

In present study bullous pemphigoid constituted 23.65% with male to female ratio (M: F) ratio being 1:1.44 which is similar to Uzun S et al [10] , Langan S et al [14] and Budimir J et al [15] study. Deepti S.P. et al [5] observed 26% cases of bullous pemphigoid which is slightly higher than our study. 21cases out of 22 (95.45%) showed sub epidermal blister. One case had suprabasal cleft. This might be due to an older lesion being biopsied and regeneration of epidermis. Inflammatory cells were noted in bulla 18 out of 22 (81.8%) and dermal infiltrate 20 out of 22 (90.9%) similar to Leena JB et al [16] study. Predominant inflammatory cells were neutrophils and eosinophils similar to Nishioka K et al [17] study.

14 cases of vesiculobullous lesion presented with spongiotic dermatitis in present study with age group 10-69 years. M/F ratio is 1:1.33. Patient presented with bulla pruritic pustule similar to case study by Abreu VAN et al [18] study in which a 15 year old female presented with intense pruritic rash. Murthy T.K et al [9] reported 8.1% cases of pemphigus foliaceus which is higher than our study. Our findings of pemphigus foliaceus, subcorneal pustular dermatoses and erythema multiforme were comparable with other studies. [9,11] Banu L et al [19] and Dipti SP et al [5] show 3 cases and 2 cases with subepidermal bulla and papillary microabscess in all cases of dermatitis herpitiformis. Similar histological finding was observed in our case with neutrophilic infiltrate and perivascular infiltrate.

Conclusion

Clinical and histomorphological study of vesiculobullous diseases can be used in confirming the diagnosis of diseases. Clinical data is essential for histopathological interpretation. Biopsy from early unruptured vesicles is more informative. Repeat biopsies are necessary in view of altered histopathological features due to age of lesions, drug treatments and secondary infections

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Financial or other Competing Interests: None.