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Histomorphological spectrum of noninfectious vesiculobullous lesions of skin: A rural area based study

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Abstract
Background: Vesiculobullous lesions are the major contribution of various skin disorders. They are primary morphological representation of various pathological stimuli. Histopathology plays major role in the initial phase of diagnosis helps in further evaluation to identify the underlying etiology.
Aim and Objective: To study the prevalence of various morphological types of vesiculobullous skin lesions in different age groups in a rural area.
Methodology: A Retrospective study conducted from May 2018 to May 2021, at Katuri Medical College & Hospital, Guntur. A study of vesiculobullous lesions of the skin biopsies of 90 cases was received to the department of pathology, at Katuri Medical College & Hospital, for 3 years. Complete clinical and relevant history was recorded. The specimens were routinely processed and H&E-stained slides were studied.
Results: Out of 454 skin biopsies, of which 90 cases (19.8%) were diagnosed as vesiculobullous lesions by histopathologically. Pemphigous vulgaris comprised 38 cases (42.23%) followed by Bullous pemphigoid 24 cases (26.67%), in clinically suspected Autoimmune Bullous Disorders.
Conclusion: Clinical examination has greater significance in diagnosis still histopathological examination plays vital role, helps to arrive at a definitive diagnosis in the majority of vesiculobullous disorders. Skin biopsy is inexpensive, carried out as OPD procedure with minimal discomfort to the patient.

Keywords: vesiculobullous disorders, skin biopsies, histopathological examination, pemphigus, pemphigoid

Introduction
Skin forms not only a protective covering but is a part of the immune apparatus of body [1]. Many internal diseases may manifest themselves in the skin [2]. Vesiculobullous disorders represent a heterogeneous group of dermatoses. They have a dramatic impact on the patient and their family and have severe economic consequences for the family and health services. The diseases have been the subject of intensive investigation in recent years [2]. There is a wide variety of bullous disease, some of which can be extremely debilitating and even fatal, some bullous lesion may have serious sequelae, necessitating early treatment and intervention to prevent further morbidity and mortality [3]. However, HPE is needed for a definite diagnosis [4]. Bullous lesions are frequently a source of dismay to the pathologist. Skin biopsy is easily intended with precision, direct immunofluorescent microscopy in conjugation with histopathology gives the best diagnostic yield in bullous lesions to make a clear reporting [1]. There is a wide variety of bullous lesion. So it is presented based on the site, shape and size of the bulla and also changes in the bulla, epidermis and dermis[5]. Blisters in the various disorders occur at different levels within the skin; histological assessment is essential for accurate diagnosis and provides insight into the pathogenic mechanisms. Knowledge of the molecular structure of the intercellular and cell-to-matrix attachments that provide the skin with mechanical stability helps understand these diseases. Diagnosis of the disease requires a thorough histopathological examination. The initial basis of identification starts with the site of the lesion followed by classification according to location as suprabasal, intraepidermal, subcorneal and subepidermal group, then change within the bullous lesion is seen that is the presence of acantholytic cells and inflammatory cells. Adjacent epidermal changes are also noted like villi, accentuation of normal dermal papillae,

hyperkeratosis, parakeratosis, spongiosis and acanthosis and also the site of disease and age of the patient is important in diagnosis [5]. Over the last two decades, great advances have been made in understanding the clinical behaviour and molecular nature of autoimmune diseases [6].

Aim and Objective: To study the occurrence of various types of vesiculobullous skin lesions in Katuri medical college and Hospital, Guntur.

Materials and Methods: A Retrospective study conducted from May 2018 to May 2021, at Katuri Medical College & Hospital, Guntur. A study of vesiculobullous lesions of the skin biopsies of 90 cases was received to the department of pathology, at Katuri Medical College & Hospital, for 3 years. Complete clinical and relevant history was recorded.
The punch biopsy was done on early lesions included the epidermis, dermis and subcutaneous tissue below the lesion as well as the uninvolved perilesional the area 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 an automated tissue processor.
Serial sections of 3-5 μm thickness were taken. The tissue received was processed by routine paraffin processing and stained using H&E stains. 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 a pathologist and histopathological types of vesiculobullous lesions were reported and categorized.
Immunofluorescence was done wherever necessary. Records of clinical and Histopathological data wherever available, were correlated and the results were compared.

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

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

Results
During this period total of 454 skin biopsy specimens were received out of which Vesiculobullous lesion biopsies were 90 in number which constituted 19.8% of skin biopsy specimens.

Table 1: Distribution of cases according to their presentation

Type of lesions	No. of cases	Percentage
Pemphigus Vulgaris	38	42.23%
Bullous pemphigoid	24	26.67%
Pemphigus foliaceus	12	13.34%
Spongiotic dermatitis	05	5.56%
Erythema multiforme	03	3.34%
Bullous drug eruption	03	3.34%
Dermatitis Herpetiformis	02	2.23%
Epidermolysis Bullosa	02	2.23%
Bullous SLE	01	1.12%
Total	90	100%

Among 90 skin biopsies, 38 (42.23%) cases were of Pemphigus Vulgaris followed by 24(26.67%) cases of Bullous pemphigoid and 12 (13.34%) cases of Pemphigus foliaceus which include formed the majority of the cases. Less common lesions included Spongiotic dermatosis, Erythema multiforme, Dermatitis Herpetiformis, Bullous drug eruption, Bullous SLE, Epidermolysis Bullosa.
Majority of patients presented between 40-49 yrs of age (40 %). Females (57.78%) outnumbered males (42.23%).

Table 2: Distribution of patients according to Age and vesiculobullous disorder

Lesions	10-19	20-29	30-39	40-49	50-59	60-69	70-79	>80	Total
Pemphigus Vulgaris	-	7	13	18	-	-	-	-	38
Bullous pemphigoid	-	-	02	10	12	-	-	-	24
Pemphigus foliaceus	03	1	4	4	-	-	-	-	12
Spongiotic dermatitis	-	-	-	1	1	02	1	-	05
Erythema multiforme	-	1	-	-	02	-	-	-	03
Bullous drug eruption	-	-		02			01		03
Dermatitis Herpetiformi s	-	-	1	1					02
Epidermolysi s Bullosa	-	1					1		02
Bullous SLE	01	-							01
Total	04	10	20	36	15	02	03		90

Pemphigus vulgaris presented most commonly in the age group of 40-49 years in 18 cases followed by 30-39 years 13 cases and 20-29 years 7 cases. Bullous pemphigoid presented commonly in the age group of 50-59 years 12 cases. Pemphigus foliaceus commonly in 30-39 and 40-49 years 4 cases each.

Table 3: Distribution of patients according to the epidermal changes

Lesion	Tombstone Appearance	Hyperkeratosis	Spongiosis	Acanthosis	Acantholysis	Apoptotic Cells
Pemphigus	30(78.94%)	15(39.47%)	15(39.47%	7(18.42%)	26(68.42%)	2(5.2%)
Vulgaris			)			
Bullous pemphigoid		18(75%)	12(50%)	3(12.5%)		
Pemphigus foliaceus			5(41.6%)	1(8.34%)	2(16.67%)	
Spongiotic dermatitis			5(100%)	1(20%)		
Erythema multiforme				2(66.7%)		
Bullous drug eruption		2(66.7%)				
Dermatitis Herpetiformi s			1(50%)			

Epidermolysi s Bullosa		2(100%)				
Bullous SLE			1(100%)	1(100%)		

Tombstone appearance was seen in 30(78.94%), acantholysis 26(68.42%), 15(39.47%) hyperkeratosis and spongiosis 15(39.47%) were common in the biopsy of Pemphigus Vulgaris. Spongiosis is commonly seen with Spongiotic dermatitis.

Hyperkeratosis is a common finding with Epidermolysis Bullosa 2(100%). Acanthosis was common with Erythema multiforme,

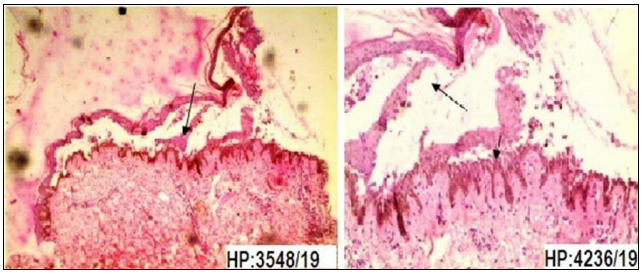

Fig 1: Pemphigus Vulgaris showing suprabasal blister containing acantholytic cells and a row of tombstones appearance(x40 H&E)

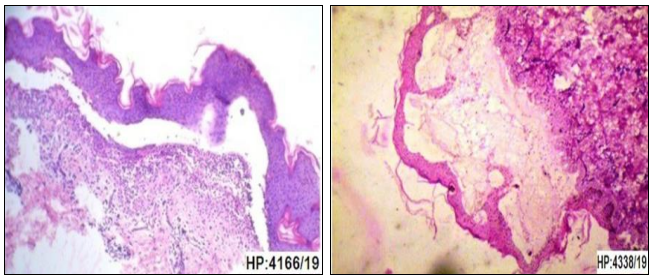

Fig 2: Bullous pemphigoid showing subepidermal blister containing few eosinophils, lymphocytes and fibrin(x40 H&E)

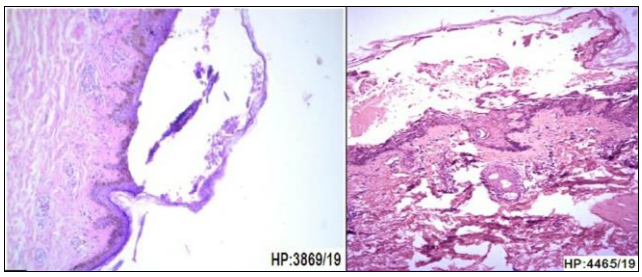

Fig 3: Subcorneal bulla in Pemphigus foliaceus (x40 H&E)

Pemphigus Vulgaris, 38 cases of PV were encountered which constituted 42.23%, the largest group in the present study. Most of the cases were in the age group of 30-49 years. In most of the cases, bulla was seen in the suprabasal region (30 cases –78.94%). Acantholysis was seen in 26 cases (68.42%). Eosinophilic spongiosis was seen in 15 cases (39.37%) and a row of tombstones in 30 cases (78.94%).

Bullous pemphigoid is the second largest group in the present study. There were 24 cases, which constituted 26.67% of the total number of cases.

Most of the cases were seen in the age group of 40-59 years. The subepidermal bulla was seen in all the cases. Inflammatory cell infiltrate was rich in 4 cases and poor in 4 cases. Hyperkeratosis was observed in 18 cases (75%). Inflammatory cell infiltrate mainly composed of eosinophils with few lymphocytes.

Pemphigus foliaceous was observed in 12 cases and constituted about 13.34% of the total number of cases. Most of the cases were in the age group of 30-49 years. The youngest patient was 14 years and the oldest one was 49 years. In the present study, subcorneal bulla was seen in 11 out of 12 cases and in one case, there was a detachment of the stratum corneum without bulla being seen.

Eosinophilic spongiosis was seen in one case.

Two cases of Dermatitis herpetiformis was reported which accounts for 2.23% of cases.

Sections studied showed epidermis and dermis. Dermal papillae showed neutrophilic infiltrate. The Upper and mid dermis showed perivascular infiltrate of lymphocytes, neutrophils and few eosinophils.

Discussion

Vesiculobullous skin lesions comprise a group of eruptions of different aetiology and prognosis but sharing a common characteristic, the formation of a blister cavities within different layers of the epidermis or beneath the epidermis. Most of the basic types can be diagnosed by light microscopy. It is still one of the simplest and a most consistent method for diagnosis and classification of vesiculobullous skin lesions.

The study conducted over 36 months at the Department of Pathology, katuri medical college and Hospital, Guntur. 452 skin biopsy specimens were received out of which 90 cases were of vesiculobullous skin lesions constituting 19.8 % of skin biopsy specimens.

The age range in Bullous pemphigoid (40-59 years) is slightly higher than in Pemphigus Vulgaris (30-49 years), in another study by Basheer A Adam also, it was found that the age range in Bullous pemphigoid was 40-80 years (a little higher than in Pemphigus Vulgaris) and in Pemphigus Vulgaris was 30-60 years.

In the present study, there was a Female preponderance was seen (male: female 1:1.3). Pemphigus Vulgaris was the most common clinically diagnosed disease accounting for 38 cases (42.23%), which constituted the largest group in the present study. Bullous pemphigoid was the second most common disorder in this study.

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