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Original Research Article

Histomorphological study of vesiculobullous lesions of skin: a study of 66 cases at tertiary care center

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ABSTRACT

Background: 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 outcome. However, these disorders are still associated with substantial morbidity, considerable mortality and impaired quality of life. Histopathological examination is helpful in definitive diagnosis of vesiculobullous disorder which is very essential for specific treatment and an appropriate desirable outcome. Aim was to study and classify various vesiculobullous lesions of the skin.
Methods: It was a hospital based prospective and retrospective study conducted for a period from January 2016 to July 2019 in the department of pathology at Government medical college, Surat, Gujarat. Total of 66 patients, aged 3-70 years with vesiculobullous lesions of both sexes attending the department of dermatology were selected and analysed clinically. The specimens were routinely processed and hematoxylin and eosin stained slides were studied.
Results: In the present study, majority of patients presented between 41-50 years of age (32%) with male to female ratio of 1.08:1. Pemphigus vulgaris constituted the most common vesiculobullous disorder (30.30%) followed by pemphigus foliaceous (24.24%) followed by bullous pemphigoid (15.05%). Bullae were located intra epidermally in (36%+24.78%) and sub epidermally in 24% of the patients.
Conclusions: Thorough histopathological workup and clinical correlation is essential to confirm diagnosis of vesiculobullous lesions of skin.

Keywords: Pemphigus, Vesiculobullous

INTRODUCTION

Skin is a double layered membrane covering the exterior of skin.[1] It represents a window to the internal well-being of disease. Many internal diseases may manifest themselves in the skin.[2]

Vesiculobullous diseases are heterogeneous group of disorders in which primary lesion is a vesicle or a bulla on the skin or mucous membrane or both. Among the various dermatological conditions, vesiculobullous lesions form one of the most frequent clinical problems. It is one of the archetypal reaction patterns of skin damages caused by both external and internal factors and conditions.[2] Various types of pathologic processes can lead to development of vesiculobullous eruptions over body such as inflammatory, infective, autoimmune, drug induced as well as genetic conditions.[2-4]

Vesicles and bullae are fluid filled cavities formed within or beneath the epidermis. Vesicles are less than 0.5 cm in diameter and bullae are blisters greater than 0.5 cm in diameter.[4,5]

There are wide variety of vesiculobullous disorders, some of which can be extremely debilitating and even fatal.[6] Some vesiculobullous lesions may have serious sequel which requires early treatment and intervention to

prevent further morbidity and mortality.[7] These lesions show formation of vesicle or bulla within different layers of the epidermis or beneath the epidermis.[8,9]

Bullous lesions are also classified based on site, shape and size of the bulla and also changes in the bulla in epidermis and dermis.[7] Blisters In various disorders blisters occur at different levels within the skin. Based on site they are classified as suprabasal, intraepidermal, subcorneal and subepidermal. Thus, for accurate diagnosis and better understanding of underlying the pathogenic mechanisms, histological assessment is essential.[10]

Though histopathological study is sufficient in most of the cases, it is often accompanied by immunofluorescence antibody tests. Direct immunofluorescence (DIF) antibody testing is a gold standard for confirmation of the diagnosis as many lesions have overlapping microscopic features. These rapid and reliable immunofluroscent techniques permit early diagnosis and treatment of potentially life-threatening disorders.[11]

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.

Most commonly employed technique for diagnosis of vesiculobullous lesions is punch biopsy as it is safe, simple, inexpensive and minimally invasive OPD procedure without any major complications, causing minimal discomfort to the patient and no scarring. The greatest diagnostic accuracy is obtained by correlating the clinical and histopathological findings. Thus, present study was carried out to study histopathological changes in vesiculobullous disorder of the skin by light microscopy and to correlate clinical and histopathological aspects of vesiculobullous lesions of skin.

Aims and objectives

To study the clinical features of various vesiculobullous lesions in relation to age, sex and site. To evaluate the common types of vesiculobullous lesions. To study the histopathological features of vesiculobullous lesions.

METHODS

This was a prospective and retrospective study conducted at the department of pathology at, Government Medical College affiliated to civil Hospital Surat, for a period from January 2016 to July 2019 after obtaining approval of ethical committee of our institute. A punch biopsy was obtained in each case and was received at the department of pathology for histopathological examination. The punch biopsy was given thin sections wherever appropriate and processed as per standard protocol. Formalin fixed and paraffin embedded sections were stained routinely with H and E technique. Special stains were applied wherever necessary. Final histopathological diagnosis was given in each case correlating with the clinical findings.

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 other skin lesions, Inadequate, poorly preserved skin biopsies an, inconclusive reports were excluded from study.

RESULTS

The present study was a retrospective and prospective study carried out at the department of pathology at tertiary care hospital affiliated with medical college Surat for a period of year January 2016 to July 2019. During this period total 587 skin biopsy specimens were received out of which vesiculobullous lesion biopsies were 66 in number which constituted 11.24% of skin biopsy specimen and they were reviewed with aspect to age, sex, site, clinical details and histological patterns.

Among 66 skin biopsies 20 (30.30%) cases were of pemphigus vulgaris followed by 16 (24.24%) cases of pemphigus foliaceous, 9 (13.63%) cases of bullous pemphigoid and 6 (15.05%) cases of dermatitis herpentiformis. Less common lesions included, Darier's disease, Hailey disease, Grovers disease, subcorneal pustular dematosis, subepidermal bullous disease and erythema multiforme (Table 1).

Present study showed maximum lesions were in the age group of 41-50 year with 18 cases, followed by 21-30 years age group and 31-40 years of age group with 15 cases (22.72%) each. Males were predominantly affected in age group of 21-30 years, 31-40 years and 41-50 years with 11 cases each followed 51-60 years with 7 cases. Female were mainly affected in age group of 41-50 years with 7 cases, followed by age group of 21-30 years and 31-40 years with 4 cases each.

Pemphigus vulgaris presented most commonly in age group of 21-30 years in 7 cases, followed by 31-40 years in 6 cases and 41-50 years 5 cases. Pemphigus foliaceous presented commonly in age group of 31-50 years in 5 cases, followed by 21-30 years in 4 cases. Bullous pemphigoid presented commonly in the age group of 41-50 years in 4 cases, followed by 51-60 years in 3 cases (Table 2).

Table 1: Distribution of vesiculobullous (blistering) skin lesions.

Lesion	Male	Female	Total
	N (%)	N (%)	N (%)
Pemphigus vulgaris	14 (21.21)	6 (9.09)	20 (30.30)
Pemphigus foliaceous	8 (12.12)	8 (12.12)	16 (24.24)
Bullous pemphigoid	7 (10.60)	2 (3.03)	9 (13.63)
Darier' s disease	2 (3.03)	2 (3.03)	4 (6.06)
Dermatitis herpetiformis	3 (4.54)	3 (4.54)	6 (9.09)
Subcorneal pustular dermatosis	3 (4.54)	0	3 (4.54)
Hailey Hailey disease	4 (6.06)	0	4 (6.06)
Grover's disease	2 (3.03)	0	2 (3.03)
Erythema multiforme	1 (1.51)	0	1 (1.51)
Subepidermal bullous disease (clinically suspicious IgA bullous disease	1 (1.51)	0	1 (1.51)
Total	45 (68.18)	21 (31.81)	66 (100)

Table 2: Age wise distribution of vesiculobullous lesions.

Nature of lesion	11-20 years	21-30 years	31-40 years	41-50 years	51-60 years	61-70 years	71-80 years	Total
Pemphigus vulgaris	0	7	6	5	1	1	0	20
Pemphigus foliaceous	2	4	5	3	0	2	0	16
Bullous pemphigoid	0	0	1	4	3	0	1	9
Darier's disease	0	3	0	0	1	0	0	4
Dermatitis herpentiformis	3	0	0	2	0	1	0	6
Subcorneal pustular dermatosis	0	1	1	1	0	0	0	3
Hailey Hailey disease	0	0	0	2	2	0	0	4
Grover's disease	0	0	1	1	0	0	0	2
Erythema multiforme	0	0	0	0	1	0	0	1
Subepidermal bullous disease	0	0	1	0	0	0	0	1
Total	5	15	15	18	8	4	1	66

Most common lesion in males and female was pemphigus vulgaris with 14 cases and 6 cases respectively. Most common site for pemphigus vulgaris was back and extremities and with 9 cases and 5 cases respectively.

Table 3: Plane of separation of lesions.

Intra epidermal	No. of cases (%)
Intra epidermal-subcorneal	19 (28.78)
Intra epidermal-supra basal (PV+DD)	24 (36.36)
Subepidermal	16 (total) (24.24)
Bullous pemphigus	9 (13.63)
Dematitis herpentiformis	6 (9.0)
Erythema multiformis	1 (1.51)

On the basis of the plane of separation, the vesiculobullous lesions have been broadly divided into two categories, intraepidermal and sub epidermal. The intraepidermal lesions are further subdivided into suprabasal and subcorneal. In the present study majority of the cases showed plane of separation at the intraepidermal- suprabasal (36.36%) region followed by subcorneal (28.78%) and subepidermal (24.24%). The most common inflammatory infiltrate in the bullous cavity was neutrophilic infiltrate followed by mixed inflammatory infiltrate, eosinophilic, and lymphocytic infiltrate.

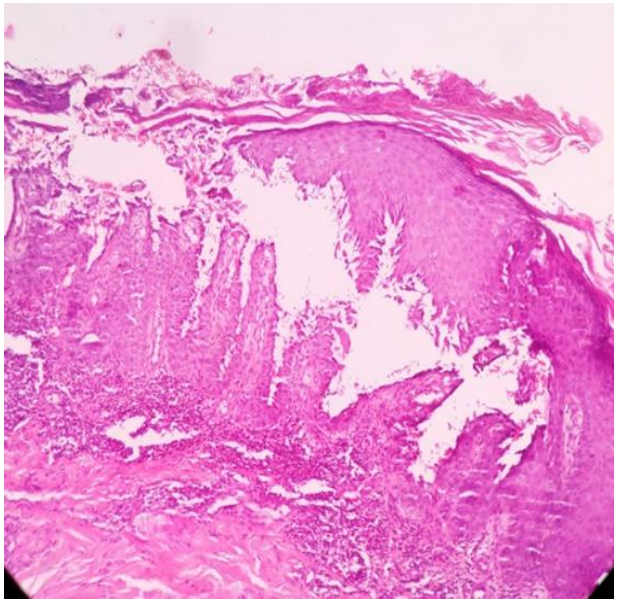

Figure 1: Microscopic appearance of intraepidermal bulla with tombstone appearance of dermis in pemphigus vulgaris in H&E stain (10X view).

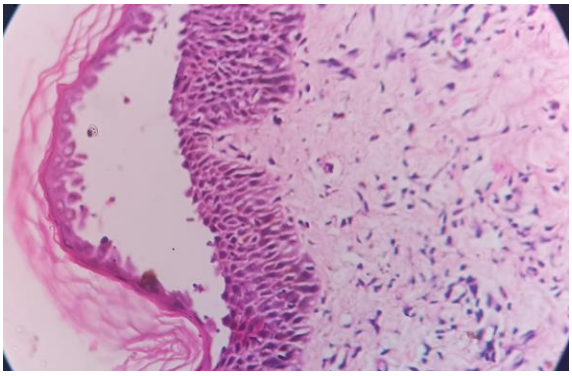

Figure 2: Intra epidermal bulla (H&E stain,10x view).

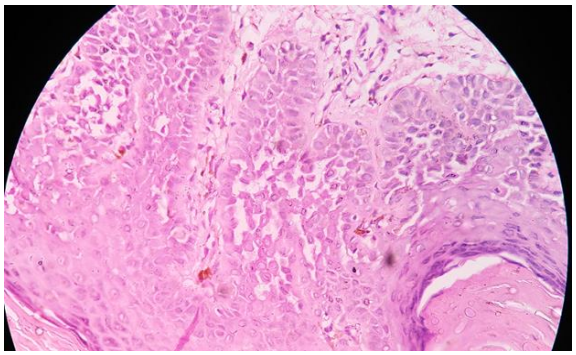

Figure 3: Microscopic appearance of hailey disease in H& E stain (40X view).

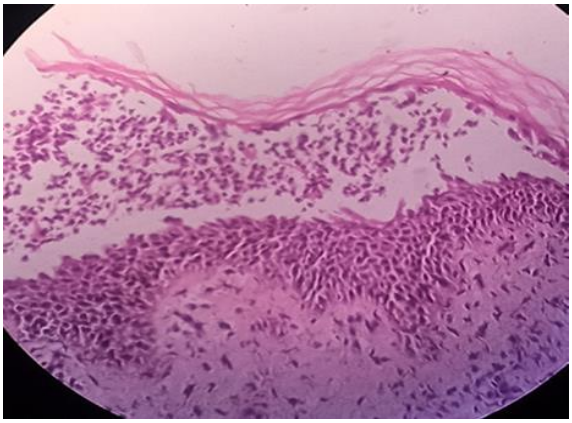

Figure 4: Neutrophilc infiltrate in bullous cavity.

DISCUSSION

The vesiculobullous lesions are the alarming skin condition where blister formation occur at various levels. Histopathological examination is an important tool in the diagnosis of these lesions. Though, various primary cutaneous diseases present clinically with vesiculobullous lesions, their etiology, pathogenesis, severity and course differs. Therefore, accurate diagnosis of these diseases is essential for appropriate management to avoid or minimize associated morbidity and mortality. Clinically, all the patients with vesiculobullous diseases may not present with classical morphology and distribution of the lesions. The number of patients presenting with clinical features like vesicles and bullae, involvement of mucous membranes, Nikolsky's sign and Bulla spread sign is different in various studies conducted in India. The difference may be due to prevalence of the diseases, severity and stage of the disease at presentation and status of the treatment. Most of these lesions have characteristic light microscopic and immunofluorescence patterns which are of great help in reaching an accurate diagnosis. The blister separation plane, type of inflammatory infiltrate and mechanism of blistering are specific for each disease.

In the present study males were predominantly affected than females. In present study of the 66 patients, 41 were males (62.12%) and 21 were females (31.81%). Our study was in concordance with the studies by Kumar et al, Kumar et al, Khan et al, Murthy et al.[3,12-14] While Pavani et al, Deepthi et al, Anupama et al, Arundhathi et al, showed female preponderance.[6,10,11,15]

The maximum number of patients were in the age group of 41-50 year with 18 cases (27.27%), followed by 21-30 years age group and 31-40 years of age group with 15 (22.72%) cases. The mean age of presentation was in concordance with studied done by Kumar et al, Anupama et al, Makrand et al, Deepti et al, Kumar et al, Pavani M et al, Kushtagi et al.[3,6,7,10-12,16] Extremities and back were commonly involved.

Pemphigus vulgaris is observed to be the commonest and largest group of vesiculobullous lesion in present study comprising of 20 cases which accounts for 30.3% of the cases followed by pemphigus foliaceous comprising of 16 cases which accounts for 24.24% followed by bullous pemphigoid comprising of 10 cases which accounts for 13.6% of the cases which was comparable with the studies of Patel et al, Khan et al, with the frequency of 54.4%, 6.06%, 3.03% and 55.55%, 44.45%, and 16.67% cases respectively.[4,13]

Another studies done by Murthy et al and Anupama et al showed pemphigus vulgaris as most common vesiculobullous lesion with 18.9% and 36% cases, followed by 21.6% and 20% cases of bullous pemphigoid, followed by 8.1% and 4% cases of Pemphigus foliaceous.[6,14]

Similar to our study, Khannan et al, Arundhati et al, Kumar et al, Kushtagi et al, Selveraj et al showed pemphigus vulgaris was the commonest type followed by bullous pemphigoid with the frequency of 38% and 26%, 38.2% and 16.2%, 43.1% and 13.9%, 30% and 27.5% and 62.2% and 2.22% respectively.[3,15-18] However Krishnamurthy et al, Kabir et al, Pavani et al showed bullous pemphigoid was the commonest followed by pemphigus vulgaris with the frequency 21.6% and 18.9%, 32.35% and 26.4% and 38.09% and 23.8% respectively.[11,14,19] Study done by Jindal et al showed pemphigus vulgaris was the commonest vesiculobullous disorder with 31.6% cases followed by dermatitis herpentiformis with 18.3% cases.[20] In the present study the plane of separation was intraepidermal- in majority of

the cases (30.30%) followed by subcorneal (28.78%) and sub epidermal planes (24.24%). Our study was similar to the study by Dipti et al, Kumar et al, Anupama et al and Arundhanti et al.[6,10,12,15]

CONCLUSION

Skin is largest organ of the body presenting with diversity of diseases. However clinical presentation of several skin lesions show overlapping appearance and pose difficulty in diagnosis on clinical ground alone, hence, histopathological examination remains gold standard for diagnosis of such lesions.

Clinical examination is the initial step in making a diagnosis of vesiculobullous disorders. Histopathological examination and DIF are required for making a definitive diagnosis. DIF is helpful in scenarios where clinical and/or histopathological features are inconclusive. In comparison to DIF, histopathology remains the cornerstone in differentiating PV from PF. Hence, clinical, histopathological and DIF features are considered together to arrive at final diagnosis as these methods may not be diagnostic individually in each and every case. Histopathological examination with clinical correlation helps in to gives the best diagnostics yields in bullous lesions to make a clear diagnosis.

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