Clinical and Histopathological Spectrum of Vesiculobullous Lesions of skin- A Study of 40 cases

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Abstract

Background: Vesiculobullous lesions of skin areheterogenous group of dermatological disorders and are not uncommon. These lesions may present with common clinical presentation as blister clinically, but histopathological features differ.

Aims & Objective: This study is under taken to study the clinical and histopathological features of vesiculobullous disorders.

Materials and Methods: A total 40 cases of clinically diagnosed blistering disorder were included, the punch biopsy of the lesion was taken. The biopsy was studied for histopathological fetures like level of blister formation, acantholysis, spongiosis, basement membrane zone distruction, presence or absence of inflammation.

Results: In the present study amongst 40 cases, Pemphigus vulgaris was diagnosed in 12 (30%) cases and detected as most common type, followed by Bullous Pemphigoid in 11 (27.5%) cases. Herpes gestationis (Bullous Pemphigoid) was diagnosed in only one case. Commonly the blisters were seen on trunk, extremeties, axilla and groin. The lesions were slightly male preponderance in the present study. Most of the cases found between 41-70 years of age.

Conclusion: The distribution of vesiculobullous lesions in relation to gender, age group, presenting site and histopathological features differ in each type. Histopathological examination gives valuable clue in the diagnosis of particular type of blistering disorder.

Key words: Vesiculobullous, Blister, Histopathological, Clinical, Disorder.

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Introduction

Skin is the largest organ of the body and various diseases along with its manifestations can commonly involve the skin out of which vesiculobullous lesions form one of predominant group.

Vesicles (blister less than 0.5 cm in diameter) and bullae (blister greater than 0.5 cm in diameter) occur in many skin disease, occur in all the layers of epidermis from stratum corneum to basal layers and sub-epidermally. Each entity in this group has distinct clinical features and lesions share number of histologic features but only some extent have common pathogenic mechanism E.g.; Bullous pemphigoid and Pemphigus vulgaris are autoimmune in nature, whereas epidermolysisbullosa is inherited disease caused by non-immunologic mechanism[1,2,3].

These diseases produce visually dramatic clinical lesions and in some instances (e.g.: Pemphigus vulgaris) are uniformly fatal if untreated.[1]

Though the vesiculobullous lesions of skin are not uncommon in dermatological practice, only few studies are available to determine the distribution in each sex, age group, site and to determine common subtype among entire spectrum of noninfectious vesiculobullous lesions of skin.

The greatest diagnostic accuracy is obtained by correlating the clinical and histopathological findings. In the present study, the histopathological features and distribution of lesions in relation to age, sex and site were studied.

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.

Materials and Methods

In this study we have included 40 punch biopsies obtained from the patients who were diagnosed clinically as having blistering disorder. The clinical history of the patient like Age, Sex, duration of the lesions, site of the lesion, significant family and personal history, history of associated diseases and other relevant history like drug intake were noted. After detailed clinical examination the site for the biopsy was selected, patient consent was taken after explaining the details of biopsy procedure. The biopsy is done on young/ early small lesion after paintingthe bullous area along with surrounding area with antiseptic and anesthetizing with 2% xylocaine.

The punch biopsy of intact blister is obtained by 'easy punch' and was included epidermis, dermis and

surrounding area along with subcutaneous tissue. The obtained biopsy gently fixed in a 10% formalin solution, the biopsy site is then sutured and dressed. Analgesics were prescribed and suture removed on 7th day after the procedure. Gross examination of the skin biopsy included measurement of size, shape of the biopsy, blister or surface ulceration were noted, then the entire blister cavity submitted for routine processing and embedded in paraffin wax, the sections were cut at 5mm thickness and stained with Hematoxylin and eosin. Histpathological examination of sections included plane of separation, whether subcorneal, intraepidermal, suprabasilar or subepidermal was noted. Mechanism of blister formation whether by acantholysis, spongiosis, basement membrane zone destruction, cytolysis, presence or absence of inflammation and type of inflammatory cell infiltrate were noted. In the present study, only noninfectious vesiculobullous lesions were included and infectious vesiculobullous lesions were excluded.

Results

In the present study 0f 40 skin biopsies obtained from the patients, who were clinically diagnosed as non-infectious Vesciculo-bullous disorders, Pemphigus vulgaris was detected in 30% cases and it was the most common type among 40 cases. Bullous pemphigoid was the second most common type and was detected in 27.5% cases, this was followed by pemphigus foliaceus which was encountered in 12.5% cases and was the second commonest type in pemphigus group. No other entities of Pemphigus group were detected. Pemphigoidgestationis (HG) was detected in only one case (2.5%), and was the least common type among all entities detected in the present study (Table 1 shows distribution of various vesciculobullous disorders).

In the present study, the common age group of presentation was between 41 to 50 years, (25% cases). Most of the cases occurred between 41 to 70 years and only 2 cases were found between 0 to 10years. Pemphigus vulgaris was detected most commonly between 41 to 50 years with mean age of 37.08 years. Bullous pemphigoid was detected commonly between 61 to 70 years with mean age of 60.5 years. Patients with Pemphigus Foliaceus presented with mean age of 42.2 years. Patients with Dermatitis herpetiformis were presented with mean age of 34.5 years, one case was presented at the age of 3 years. Patients with Erythema multiforme presented between 20 to 65 years. Patients with Darier's disease presented with mean age of 22 years, Subcorneal pustular dermatosis was found in 2 cases, and both were below 20 years of age. (Table 2 shows mean age of presentation in various blistering disorders).

In the present study, males were affected predominantly than females with overall male to female ratio of 1.35:1. Pemphigus vulgaris, Bullous pemphigoid, Dermatitis herpitiformis, Erythema multiforme were found most commonly in males whereas pemphigus foliaceus occurred predominantly in females. Subcornealpustulardermatosis and pemphigoidgestationis were encountered only in females. Darier's disease was detected in 2 cases with equal sex distribution. Table 3 Shows distribution of various Blistering disorders in each gender).

In the present study, trunk, extremities, axilla and groin were the commonest sites involved in Pemphigus vulgaris, Bullous pemphigoid, Pemphigus foliaceus, Darier's disease and Sub Corneal Pustular Dermatitis. Extremities were the site of presentation in all the cases with dermatitis herpetiformis. In case of pemphigoidgestationis the predominant site of involvement was periumbilical region but also lesions occurred on extremities.

Oral mucosa was involved in 25% cases of pemphigus vulgaris, and 2 cases of Erythema multiforme (66.66%) no other disease presented with mucosal involvement.

In the present study, 52.5% lesions were presented with intraepidermal blisters, where assubepidermal blisters were encountered in 47.5% cases (Table 4 Shows Histopathological features with level of split). Acantholysis was seen in 42.5% cases and basement membrane zone destruction in 35% cases (Table 5 shows type of mechanism in blister formation). Most of the lesions presented with mixed inflammatory cell infiltrate (27.5% cases), followed by eosinophils (25%), Neutrophils (22.5% cases) and lymphocytes (20% cases) (Table 6 Shows type of inflammatory infiltrate predominant in the lesion). Inflammation was absent in 2 cases (5%) and both were Darier's disease. Intraepidermal blister, acantholysis and mixed inflammatory cell infiltrate were the common histopathological features in the present study group.

Discussion

The Vesciculobullous diseases are alarming skin conditions where blister formation occurs in various levels and clinically present as blisters. Histopathological examination is an important tool in the diagnosis of blistering diseases.

Though immunoflurecence helps in the confirmation, histopathological examination with clinical correlation is sufficient for the diagnosis of most cases[4]. Similar to our study Khan W A et. al, Khannan C K et. al, Arundhati S et.al showed Pemphigus Vulgaris is the commonest type ollowed by Bullous Pemphigoid with the frequency of 60% and 16.6%, 38% & 26%, 38.2% and 16.2% respectively. However Thejasvi Krishnamurthy et.al and Noorul Kabir et.al, Bullous Pemphigoid is the commonest followed by Pemphigus Vulgaris with the frequency of 21.6% & 18.9%, 32.3 and 23.5% respectively.

Thejasvi Krishnamurthy et.al studied 74 blistering disorders, Bullous Pemphigoid (21.6%) was the

commonest type followed by Pemphigus Vulgaris(18.9%).

Common age incidence between 21 to 50 years (71%), Male preponderance 61%, all the lesions of this study group was male preponderance[5]. In the study group of Khan W A and Valand A G, amongst 60 cases, Pemphigus Vulgaris (60%) was the commonest type followed by Bullous Pemphigoid (16.67%)[6], Similarly Khannan C K and Mahesh Bhat M studiedseries of 50 cases in which Pemphigus Vulgaris (38%) followed by Bullous Pemphigoid (26%)[7], Arundhati S et.al studied 68 biopsy specimens of Vesciculobullous disorders revealed 38.2% cases of Pemphigus Vulgaris, which was the commonest type amongst their study group followed by 16.2% cases of Bullous Pemphigoid[8] and these studies are comparable with our study group.Jindal A et.al evaluated 53 cases of clinically diagnosed autoimmune blistering diseases, with female preponderance (30 females and 23 males)[9], A K M Nurul Kabir et.al studied 34 cases in which though Pemphigus group of lesions predominated, Bullous Pemphigoid (11cases) was the commonest followed by Pemphigus vulgaris (08cases), maximum number cases were seen in fourth and fifth decade, both the sexes were affected equally. In the present study, Pemphigus Vulgaris was the commonest type followed by Bullous Pemphigoid, males were affected slightly more and maximum cases were seen between 41 to 70 years of age.

In the present study, 25% cases of pemphigus vulgaris had mucosal lesions and cutaneous lesions over trunk, upper extremities and axilla. Handa F et al[10], Chattopadhyay SP et al[11], Shafi et al[12], Arya et al[13] and Seo PG et al[14] have reported Pemphigus Vulgaris between 13 to 68 years of age, 31 to 50 years of age, mean 40 years of age (Range between 20 to 85 years), 21 to 60 years of age, and mean age of 43.3 years respectively. Childhood pemphigus is a rare disease, almost all variants of pemphigus can occur but Pemphigus Vulgaris is the most common type after endemic Pemphigus Foliaseus and the mean age of onset is 12 years as stated by Dipankar et al[15]. Handa F et al[10] observed Pemphigus Vulgaris in younger age group in Indian compared to other parts of the World. Shafi M et al[12] reported two Indian patients with Pemphigus Vulgaris and the age of onset was 26 years and 29 years, similar findings were seen in the present study.

Handa F et al[10] reported a case of pemphigus foliaceus (PF) in 4th decade. Shafi M et al[12] reported, PF between 21 to 30 years of age, Average age of presentation was 51 years in the study of Seo PG et al[14]. Arya et al[13] observed pemphigus foliaceus, lesions to involve trunk, extremities, and face, whic was similar to our present study.

Arya et al[13] and L. Jubojevics et al[16] reported acantholysis and suprabasal blister to be the feature of pemphigus vulgaris and subcorneal blister in the pemphigus foliaceus. These observations were similar to our present study.

In the present study bullous pemphigoid was the second most common type with male predilection and was seen commonly between 60 to 70 years of age. There were only 3 cases below 60 years of age (mean age of 58.18 years). The common sites affected were trunks and extremities, similar observations were made by Laskharis et al[17]. In the study by Samuel F Bean[18] et al, all the 7 patients with Bullous Pemphigoid showed subepidermal blister with eosinophilic infiltration. In the present study similar features were noted but Occasional neutrophilic and lymphocytic infiltration was seen in 3 cases.

Aronson AJ et al[19] reported dermatitis herpitiformis in a 15 years old female with lesions on face, neck and trunk Similar histopathological features were noted in our patients with dermatitis herpitiformis. lbricht et al observed dermatitis herpetiformis between 2nd and 4th decade[20]. On Histopathology subepidermal blister, neutrophilic and few eosinophilic leukocytes in the papillary dermis forming microabcesses at the tips of the dermal papillae were noted[21,19].

Ackerman AB et al stated Erythema multiforme to have male predominance and described histopathologically lymphocytic infiltration along the dermo-epidermal junction[22]. The present study also showed similar results.

In the present study, delayed presentation was noticed and only two cases of Dariers Disease were reported, one was 19 years old female and other was 25 years old male, both presented with lesions on extremities and chest, histopathologically both showed suprabasal clefting, acantholysis and dyskeratotic cells. Similar observations were made by Bedi BMS et al and Garg BR et al[23].

Kanwar A J et al[24] reported 2 cases in younger patients which tallies with reports from India where appears to occur usually in males and relatively younger age group. Ise S and Ofuji S reported a middle aged women with the lesions on face trunk and upper arms[25]. Madavmurty P et al reported a 22 years old male patient with lesions on the arm[26]. Mittal RR reported 15 cases, in which histopathological examination revealed subcorneal pustules filled with neutrophils[27]. Present study shows similar results.

Herty KC et al[28] reported 3 cases, 28 years old female was presented with blisters on abdomen and extremities in the 5th month of pregnancy, 33 years female presented with blisters on abdomen and extremities in her 4th month of pregnancy and the 37 years old female presented with lesions on her trunk and extremities which were developed 2 days after delivery, Histopathological examination showed subepidermal blister with eosinophilic inflammatory cell infiltration in all the three cases. Hisae N et al[29] reported a case of 38years old women with blister and erythema on trunk, limbs and abdomen which

developed 10 days after the delivery which was diagnosed as Pemphigoid Gestationis. In the present study only one case was diagnosed as pemphigoid gestationis, in 25 years old female with similar histopathological features.

Conclusion

The non-infectious vesiculobullous lesions of skin are a group of disorders having blister as a common clinical presentation, but the distribution of lesions in each sex, age group and presenting site varies in different vesiculobullous disorders. Among entire spectrum of vesiculobullous lesions, Pemphigus Vulgaris and Bullous Pemphigoid occur more commonly. Histopathologically, the features differ in various vesiculobullous lesions, the blister may be intraepidermal or subepidermal, with or without inflammation, presence of acantholysis, spongiosis and basement membrane destruction all these are important in the diagnosis of particular type of lesion.

Table 1: Showing distribution of various vesiculobullous disorders

Lesion	No. of Cases	Percentage
Pemphigus Vulgaris	12	30
Bullous Pemphigoid	11	27.5
Pemphigus foliaceus	5	12.5
Dermatitis herpetiformis	4	10
Erythema Multiforme	3	7.5
Darier's disease	2	5
Subcornealpustular dermatitis	2	5
Herpes gestationis (pemphigoidgestationis)	1	2.5
Total	40	100

Table 2: Showing the Range and Mean Age of Presentation

Lesion	Range of age	Mean Age
Pemphigus Vulgaris	10-60 years	37.08 yrs
Bullous Pemphigoid	45-70 yrs	60.5 yrs
Pemphigus foliaceus	28-60 yrs	42.2 yrs
Dermatitis herpitiformis	03-50 yrs	34.5 yrs
Erythema multiforme	20-65 yrs	46.6 yrs
Darier's disease	19-25 yrs	22 yrs
Subcornealpustulardermatosis	13-18 yrs	15.5 yrs
Herpes gestationis (pemphigoidgestationis)	25 yrs	25 yrs

Table 3: Showing sex distribution of Lesions

Lesion	No. of Cases	Male		Female		Male to Female Ratio
		No. of Cases	Percentage	No. of Cases	Percentage	
Pemphigus Vulgaris	12	7	58.33	5	41.66	1.4:1
Bullous Pemphigoid	11	8	72.72	3	27.27	2.67:1
Pemphigus foliaceus	5	2	40	3	60	1:1.5
Dermatitis herpetiformis	4	3	75	1	25	3:1
Erythema multiform	3	2	75	1	25	2:1
Dariers disease	2	1	50	1	50	1:1
Subcorneal Pustulardermatosis	2	0	0	2	100	0:2
Herpes gestationis (pemphigoidgestationis)	1	0	0	1	100	0:1
Total	40	23	57.5	17	42.5	1.35:1

Histopathological features

Table 4: Types and frequency of diseases depending on level of split

Intra epidermal	No. of cases	Percentage
Subcorneal (included 5 cases of PF and 2 cases SCPD)	07	17.5
Suprabasal (included 12 cases of PV and 2 cases of DD)	14	35.0
Total	**21**	**52.5**
Subepidermal	**No. of cases**	**Percentage**
Bullous pemphigoid	11	27.5
Dermatitis herpitiformis	4	10

Erythema multiforme	3	7.5
Pemphigoidgestationis (herpes gestationis)	1	2.5
Total	**19**	**47.5**

Table 5: Mechanism of blister formation

Mechanism	Type of Lesions	No. of Cases	Percentage
Acantholysis	PV-11, PF-5, DD-2	18	45
Epidermal basement membrane zone destruction/ disruption	BP – 11, DH-4	15	37.5
Keratinocyte degeneration and cytolysis	EM-3 PG-1, SCPD-2	6	15
Spongiosis	PV-4	4	10

Table 6: Type of inflammatory cells in lesions

Inflammatory cell type	No. of Cases	Percentage
Mixed	11	27.5
Eosinophils	10	25
Neutrophils	9	22.5
Lymphocytes	8	20
Absent	2	5

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