ORIGINAL RESEARCH PAPER

Dermatology

A RETROSPECTIVE STUDY OF CLINICAL AND HISTOPATHOLOGICAL SPECTRUM OF IMMUNOBULLOUS DISORDERS AT A TERTIARY CARE CENTRE IN WESTERN INDIA.

KEY WORDS: Immunobullous disorders, histopathology, pemphigus.

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ABSTRACT

Background: Immunobullous disorders are characterized by antibody-mediated bullous lesions affecting the skin and mucosa.
Aims: To study clinical presentation and histopathological pattern of different immunobullous disorders.
Methods: A retrospective study of 150 cases of immunobullous disorders were studied over a span of two years. Detailed clinical examination and investigations were carried out.
Results: Among the cases studied, 102 cases (68%) belonged to pemphigus vulgaris. Clinical diagnosis & histopathological findings were consistent in 97.33% (146/150) cases.
Among cases presented with itching, 66.95% cases had either eosinophil or neutrophil infiltrate in dermis as a finding in histopathological section and 53.04% had similar infiltrate in blister cavity.
Conclusion: It is imperative that the clinical differential diagnosis can be correlated with the gross and microscopic observations in order to render a clinically meaningful diagnosis and further management of the patients.

Introduction:
Blistering diseases are alarming skin conditions where blister formation occurs in various ways and cannot be differentiated clinically. Vesicles are well circumscribed, fluid filled elevations,one to ten mm in size ,while bullae are larger blisters measure over one cm[1].

Immunobullous disorders are a heterogenous group of disorders in which autoantibodies target structures essential for integrity of skin and mucous membrane leading to blister formation[2]. This autoimmune response directed to structural proteins mediating cell-cell and cell-matrix adhesion in the skin[3].

Autoimmune blistering diseases are classified based on the location of the bulla as intraepidermal and subepidermal as well as depending on the the ultrastructural site of deposition of immunoreactants and on the molecular target of autoantibodies [2,3].

The pioneering work of Ernst H. Beutner, Ph.D. and Robert E. Jordon, M.D. confirmed the autoimmune nature of these diseases[4].

To arrive at a diagnosis, clinical examination should be aided by histopathological examination and immunofluorescence features of immunobullous disorders[5].

Methods:
A retrospective study of total of 150 cases of immunobullous disorders from the inpatient and outpatient department of our institute was done over a period of two years, from October 2014 to September 2016 irrespective of age and sex. Patients, who were not willing to be the part of the study or undergo the required investigations, were excluded. From all patients relevant data such as age, sex, age at the onset of disease, primary sites affected, course of disease, itching, treatment history was collected.

All patients were thoroughly examined and the extent and severity of disease, mucous membrane involvement, types, morphology, nature of blister and discharge were noted Tzanck smear and gram stain were prepared from the blister by scraping the base of the deroofed bulla and studied under light microscope to find out acantholytic cells as well as inflammatory cells.

Biopsy samples were taken from lesion along with surrounding normal areas and the specimen were preserved in 10% formalin and sent for further processing and histopathological examination. The sections stained with Haematoxylin and Eosin stain were histopathologically evaluated under light microscope for the confirmation of the diagnosis. These sections were scrutinized under scanner, 10x, 40x and 100x.

Other investigations like hemogram with ESR, liver function tests, renal function test, urine routine microscopy, ultrasonography and chest x ray were carried out to rule out systemic involvement.

Results:
The maximum number of patients at the time of presentation belonged to the age group of 40-60 years (44%). So, it is considered as immunologically most active group.

Among all immunobullous disorders, most cases had pemphigus vulgaris (68%) followed by bullous pemphigoid (15.2%) and pemphigus foliaceous (8.7%). 2% cases were of chronic bullous disorder of childhood, dermatitis herpetiformis and lichen planus pemphigoids each and 1 case each (0.67%) of IgA pemphigus, bullous systemic lupus erythematosus and epidermolysis bullosa acquisita. Pemphigus vulgaris was the most common type of autoimmune vesiculobullous disorder.

Age of onset was varying according to type of disorder, as most common age group affected in pemphigus vulgaris was 40-60 yrs (49%) and that of in bullous pemphigoid was 60-80 yrs (65.22%). Male: Female ratio was found to be 1.17:1.

Acantholysis is a sign of loss of cell to cell adhesions, it is most characteristic feature of pemphigus group of disorders[(6)]. Tzanck smear was positive (presence of acantholytic cells in smear) in 66% of all patients of autoimmune vesiculobullous disorders. Out of them 88.89% patients were belonging to the diagnosis of pemphigus vulgaris followed by pemphigus foliaceous (10.10%) and IgA pemphigus (around 1%). Out of rest 51 (34%) patients where there were no acantholytic cells, 45.1% were belonging to bullous pemphigoid group followed by lichen planus pemphigoid, dermatitis herpetiformis and chronic bullous disorder of childhood (5.88% each). Epidermolysis bullosa acquisita and bullous systemic lupus erythematosus were comprising total 3.92% of patients (1.96%) patients in each group.

In bedside tests like Nikolsky sign, suggestive of disease activity, was positive in 11.33% cases and bulla spread sign was positive in 6% cases.

On histopathological study, level of cleft **(Table 1)** was maximum at suprabasal location (66%) followed by subepidermal (22.67%) and (10%) subcorneal location. Minimum cases had intraepidermal cleft (1.33%).

According to clinical diagnosis of the patients, histopathological findings were consistent in 97.33% (146/150) cases. 97.05 % cases of pemphigus vulgaris were clinically and histopathologically consistent followed by pemphigus foliaceous patients (92.3%). In other conditions like IgA pemphigus, bullous pemphigoid, lichen planus pemphigoid, chronic bullous disorder of childhood, dermatitis herpetiformis, bullous systemic lupus erythematosus and epidermolysis bullosa acquisita, clinical diagnosis and histopathological findings were 100% consistent.

Among the cases presented with flaccid bullae clinically (77.33%), 81.03% cases had suprabasal cleft followed by subcorneal cleft (11.21%) and least patients had subepidermal cleft (6.9%). Out of 32 (21.33%) patients (who had tense bulla clinically) there was subepidermal cleft in 81.25% cases and suprabasal cleft in rest 15.63% cases **(Figure 1)**.

Itching was correlated with type of infiltrate in blister cavity and dermis **(Table 2)**. Among the cases presented with itching (76.7%), 66.96% cases had either eosinophil or neutrophil infiltrate in dermis as a finding in histopathological section and 53.04% had similar infiltrate in blister cavity.

Discussion:

Clinically, all immunobullous disorders may not present with classical morphology and distribution of the lesions. Presentation may vary depending on the severity of the lesions and prior treatment received for the disease.

In our study highest prevalence was seen in the age group of 40-60 years (44%) which is comparable to Sharma et al.[4] Male : female ratio (1.17:1) was comparable to other studies with male preponderance.[2,8]

In the current study, Pemphigus group of disorders was the most common immunobullous disorder and Pemphigus vulgaris (68%) was the most common subtype followed by Pemphigus foliaceous (8.7%) and this was in accordance with several other studies[3,5,9-11]. Disparity in percentage may be due to geographical variation of these diseases.

In present study most of patients (66%) had suprabasal cleft followed by subepidermal cleft (22.67%), which was followed by subcorneal cleft (10%) and intraepidermal cleft (1.33%) comparable to Sharma et al[7].

97.05% patients of pemphigus vulgaris were clinically and histopathologically consistent which was comparable with Jindal et al. But it was not consistent in cases of chronic bullous disease of childhood and pemphigus foliaceous[3].

In pemphigus vulgaris suprabsal cleft was present in 99 (97.05%) patients comparable to other studies[11,12]. On histopathological examination infiltrate in bulla and acantholysis was present only in 35.29% and 46.08% patients respectively in our study which was lower as compared to other studies[11,12] . This may be because of loss of blister roof in histopathological examination of many patients in present study.

Among the cases of pemphigus foliaceous 92.30% cases had subcorneal cleft and 38.46% cases had acantholytic cells in the blister cavity.

Among the cases of bullous pemphigoid 100% cases had subepidermal cleft. 86.95% cases had infiltrate in blister cavity and 100% cases had dermal infiltrate comparable to Leena et al[12].

Conclusion:

Ordinary light microscopy is one of the simplest and most consistent method for diagnosis and classification of vesiculobullous disorders. It also reveals some of the basic types of immunobullous disorders. It is imperative to correlate the clinical differential diagnosis with the gross and microscopic observations in order to render a clinically meaningful diagnosis. Individually, none of these methods are conclusive of the immunobullous disorder.

Tables:

Table 1: Clinical diagnosis and level of cleft

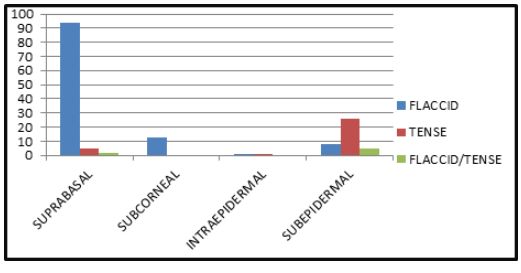
CLINICAL DIGNOSIS	LEVEL OF CLEFT			
	SUPRA BASAL	SUB CORNEAL	INTRA EPIDERMAL	SUB EPIDERMAL
PEMPHIGUS VULGARIS	99(97.05%)	2(1.96%)	1(0.98%)	0(0%)
PEMPHIGUS FOLIACEOUS	0(0%)	12(92.3%)	1(7.69%)	0(0%)
IgA PEMPHIGUS	0(0%)	1(100%)	0(0%)	0(0%)
BULLOUS PEMPHIGOID	0(0%)	0(0%)	0(0%)	23(100
LECHEN PLANUS PEMPHIGOIDES	0(0%)	0(0%)	0(0%)	3(100%)
CHRONIC BULLOUS DISEASE OF CHILDHOOD	0(0%)	0(0%)	0(0%)	3(100%)
DERMATITIS HERPETIFORMIS	0(0%)	0(0%)	0(0%)	3(100%)
BULLOUS SYSTEMIC LUPUS ERYTHEMATOSUS	0(0%)	0(0%)	0(0%)	1(100%)
EPIDERMOLYSIS BULLOSA ACQUISITA	0(0%)	0(0%)	0(0%)	1(100%)
TOTAL	99	15	2	34

Table 2: Comparison of clinically presence of itching and infiltrate in dermis on histopathology:

ITCHING	BIOPSY FINDINGS INFILTRATE IN DERMIS								TOTAL
	NO INFILTRATE	N*	E+	L‡	E,L	E,N	N,L	N,E,L	
YES	0	3	0	38	16	4	36	18	115 (76.7%)
NO	0	0	0	23	1	0	9	2	35 (23.3%)
TOTAL (%)	0 (0.0%)	3 (2.0%)	0 (0.0%)	61 (40.7%)	17 (11.3%)	4 (2.7%)	45 (30.0%)	20 (13.3%)	150 (100.0%)

(N*- Neutrophils, E+ - Eosinophils, L - Lymphocytes

Figure 1: Comparison of clinically nature of blister fluid and infiltrate in blister on histopathology:



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