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Original Article

Clinical and pathological study of autoimmune vesiculobullous disorders

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Abstract

Objective To study the various clinical presentations - age of onset, sex preponderance, course of disease and histopathological patterns of autoimmune vesiculobullous disorders and correlate clinical and histopathological findings and immunofluorescence with clinical and histopathological findings in few affordable cases.

Methods The present descriptive study was undertaken in a tertiary care hospital over a period of 2 years. It included 50 patients of autoimmune vesicobullous diseases fulfilling inclusion criteria. Diagnosis was established by clinical and histopathological findings. Direct immunofluorescence (DIF) testing was done in few affordable patients.

Results Autoimmune vesiculobullous disorders constituted 0.128% of skin disease. Pemphigus vulgaris (62%) constituted the most common vesiculobullous disorder. Females (58%) outnumbered males (42%). The age group ranged from 11 years to 85 years and the mean age was 46.2 (15.6) years. The duration of the diseases ranged from less than a week to more than a year. Tzanck smear findings revealed acantholytic cells in 90.3% cases of pemphigus vulgaris and all cases of pemphigus foliaceus and pemphigus erythematosus. Correlation between clinical and histopathological findings was seen in 96% of cases and that between histopathological and DIF findings in 89% of cases.

Conclusion After the preliminary clinical and cytological diagnosis, histopathology and DIF are required to confirm the diagnosis. Considering the socioeconomic situations of the patients and unavailability of immunofluorescence technique widely, the study showed that clinical features and histopathology are fairly specific and cost-effective in arriving at the diagnosis.

Key words
Autoimmune vesicobullous disorders, pemphigus vulgaris, direct immunofluorescence, correlation.

Introduction

Vesiculobullous disorders represent a heterogeneous group of dermatoses with protean manifestations. The autoimmune vesicobullous disorders are characterized by pathogenic autoantibodies directed against target antigens which are involved in either cell-to-cell adhesion within the epidermis or adhesion of stratified squamous epithelium to dermis or mesenchyme.[1] They have dramatic impact on the patient and

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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]

Over the last two decades, great advances have been made in understanding the clinical behaviour and molecular nature of autoimmune diseases.[3] The most important techniques for the investigation of patients with immunobullous disease are conventional histopathology, and confirmative tests like direct and indirect immunofluorescence. Research techniques such as immunoblotting and immunoelectron microscopy may refine the diagnosis in the individual patient but do not replace the clinician.[2]

Studies including both Western and Indian literature on these diseases have highlighted a particular entity or some specific aspect of it, but a detailed clinical and histopathological study has been attempted by very few people, especially in this part of India. This study was undertaken to evaluate the clinical features, histopathology and immunofluorescence findings and correlation of various autoimmune vesiculobullous disorder of the skin for their diagnostic potential.

Methods

The present descriptive study was conducted in the Department of Skin & STD, Karnataka Institute of Medical Sciences, Hubli from November 15th 2008 to May 15th 2010. The study was approved by Institutional Ethics Committee. A total of fifty cases presenting with an intact/ruptured vesicle or bullae at the time of presentation were selected on a random basis fulfilling the inclusion criteria. Informed consent was taken. The clinical history like age, sex, demography, duration of the disease, site of lesion, any significant family history, any associated systemic disease, any history of drug intake, history of injury, risk factors and complications was noted. Biopsy was done under aseptic condition. Diagnosis established by clinical and histopathological findings. Direct immunofluorescence testing was done in few affordable patients

All cases of autoimmune vesiculobullous disorder with fresh lesion, not on treatment attending the Dermatology Department irrespective of age, sex and associated diseases were included in the study.

Along with autoimmune bullous disorders which were previously treated with steroids or other immunosuppressive drugs, all bullous diseases of infective, inflammatory, genetic, metabolic, traumatic, environmental or drug etiology were also excluded.

Results

Among 43,670 cases that attended the outpatient department of Skin & STD during the study period, we encountered 56 cases (0.128%) with autoimmune vesiculobullous disorders. Fifty cases fulfilled the inclusion criteria and exclusion. Pemphigus vulgaris (PV) constituted the most common vesiculobullous disorder (62%), **(Table 1)**.

Females (58%) outnumbered males (42%). Male: female ratio was 1:1.38. The age group

Table 1 Frequency of autoimmune vesicobullous disorders diagnosed clinically (n=50).

Disease	*N (%)*
Pemphigus vulgaris	31 (62)
Bullous pemphigoid	8 (16)
Pemphigus foliaceus	4 (8)
Dermatitis herpetiformis	2 (4)
Pemphigus vegetans	2 (4)
Linear IgA disease	1 (2)
Pemphigus erythematosus	1 (2)
Subcorneal pustular dermatosis	1 (2)

Table 2 Appearance of primary lesions, Nikolsky sign and Bulla spread sign.

Primary lesions		*Clinical diagnosis*							
		PV (31/50)	*PF (4 /50)*	*PVe (2/50)*	*PE (1/50)*	*BP (8/50)*	*LAD (1/50)*	*SCPD (1/50)*	*DH (2/50)*
Appearance	Flaccid	28 (90.3%)	4 (100%)	2 (100%)	1 (100%)	1 (12.5%)	0	1 (100%)	0
	Tense	3 (9.7%)	0	0	0	7 (87.5%)	1 (100%)	0	2 (100%)
Base	Erythema	29 (93.5%)	4 (100%)	0	1 (100%)	6 (75%)	1 (100%)	1 (100%)	0
	No erythema	2 (6.4%)	0	2 (100%)	0	2 (25%)	0	0	2 (100%)
Nikolsky sign	Present	29 (93.5%)	2 (50%)	1 (50%)	0	0	0	0	0
	Absent	2 (6.4%)	2 (50%)	0	1 (100%)	8 (100%)	1 (100%)	1 (100%)	2 (100%)
Bulla spread sign	Present	29 (93.5%)	2 (50%)	1 (50%)	0	0	0	0	0
	Absent	2 (6.4%)	2 (50 %)	0	1 (100%)	8 (100%)	1 (100%)	0	2 (100%)

BP: bullous pemphigoid, DH: dermatitis herpetiformis, LAD: linear IgA disease, PE: Pemphigus pustular dermatoses, PF: pemphigus foliaceus, PV: pemphigus vulgaris, PVe: pemphigus vegetans, SCPD: subcorneal pustular dermatosis.

Table 3 Findings of Tzanck smear

Type of cells	*PV (n= 31)*	*PF (n=4)*	*PE (n=1)*	*PVe (n=2)*	*SCPD (n=1)*	*LAD (n=1)*	*BP (n=8)*	*DH (n=2)*
Acantholytic cells	28 (90.3%)	4 (100%)	1 (100%)	1 (50%)	0	0	0	0
Eosinophils	4 (12.9%)	0	0	0	0	0	5 (62.5%)	0
Neutrophils	22 (71.0%)	4 (100%)	1 (100%)	2 (100%)	1 (100%)	1 (100%)	3 (37.5%)	2 (100%)
Lymphocytes	5 (16.1%)	0	0	0	0	0	0	0

BP: bullous pemphigoid, DH: dermatitis herpetiformis, LAD: linear IgA disease, PE: Pemphigus pustular dermatoses, PF: pemphigus foliaceus, PV: pemphigus vulgaris, PVe: pemphigus vegetans, SCPD: subcorneal pustular dermatosis.

Table 4 showing epidermal and dermal changes on histopathology in autoimmune vesicobullous lesions.

Findings	*PV*	*PF*	*PVe*	*PE*	*BP*	*LAD*	*SCPD*	*DH*
Subcorneal cleft	0	4 (100%)	-	1 (100%)	0	0	1 (100%)	0
Suprabasal cleft	29 (93.5%)	-	2 (100%)	-	1 (12.5%)	0	0	0
Row of tombstone appearance	25 (80.6%)	-	2 (100%)	-	0	0	0	0
Acantholytic cells	27 (87.1%)	1 (25%)	1 (50%)	1 (100%)	0	0	0	0
Spongiosis	30 (96.7%)	1 (25%)	2 (100%)	1 (100%)	1 (12.5%)	0	1 (100%)	0
Sub epidermal cleft	1 (3.2%)	0	0	0	7 (87.5%)	1 (100%)	0	2 (100%)
Papillary edema	29 (93.5%)	4 (100%)	2 (100%)	1 (100%)	8 (100%)	1 (100%)	1 (100%)	1 (50%)
Predominantly neutrophilic infiltration	22 (70.9%)	4 (100%)	2 (100%)	1 (100%)	5 (67.5%	1 (100%)	1 (100%)	2 (100%)
Predominantly eosinophilic infiltration	9 (29.0%)	0	0	0	3 (32.5%)	0	0	0
Papillary microabscesses	0	0	0	0	0	0	0	2 (100%)

BP: bullous pemphigoid, DH: dermatitis herpetiformis, LAD: linear IgA disease, PE: Pemphigus pustular dermatoses, PF: pemphigus foliaceus, PV: pemphigus vulgaris, PVe: pemphigus vegetans, SCPD: subcorneal pustular dermatosis.

Table 5 showing findings on direct immunofluorescence (DIF) in autoimmune vesicobullous diseases.

Findings		*PV*	*PF*	*PVe*	*PE*	*BP*	*LAD*	*SCPD*	*DH*
IgG deposition	Intercellular	21	3	2	1	-	-	-	-
	BMZ	-	-	-	-	6	-		-
IgA deposition	Intercellular	-	-	-	-	-	-	-	-
	BMZ	-	-	-	-	1	1	-	
IgM deposition	Epidermis	-	-	-	-	-	-	-	-
	Dermis	-	-	-	-	-	-	-	-
C3 deposition	Intercellular	21	3	2	1	-	-	-	-
	BMZ	-			-	6	-	-	-
Negative		1	-	-	-	1	-	-	2

BMZ: Basement membrane zone, BP: bullous pemphigoid, DH: dermatitis herpetiformis, LAD: linear IgA disease, PE: Pemphigus pustular dermatoses, PF: pemphigus foliaceus, PV: pemphigus vulgaris, PVe: pemphigus vegetans, SCPD: subcorneal pustular dermatosis.

Table 6 Clinical, histopathological and direct immunofluorescence findings (DIF) findings.

Disease entity	*Clinical diagnosis*	*Positive consistent histopath*	*Negative consistent histopath*	*No of patients in whom DIF done*	*Positive DIF*	*Negative DIF*	*Final diagnosis*
Pemphigus vulgaris	31	30	1	22	21	1	PV (N=31)*
Bullous pemphigoid	8	7	1	7	6	1	BP (N=8)**
Pemphigus foliaceous	4	4	0	3	3	0	PF (N=4)
Pemphigus vegetans	2	2	0	2	2	0	PV (N=2)
Dermatitis herpetiformis	2	2	0	2	0	2	DH (N=2)
Pemphigus erythematosus	1	1	0	1	1	0	PE (N=1)
Linear IgA disease	1	1	0	1	1	0	LAD (N=1)
Subcorneal pustular dermatosis	1	1	0	0	0	0	SCPD (N=1)
Total	50	48	2	38	34	4	50

BP: Bullous pemphigoid, DH: dermatitis herpetiformis, LAD: linear IgA disease, PE: Pemphigus pustular dermatoses, PF: pemphigus foliaceus, PV: pemphigus vulgaris, PVe: pemphigus vegetans, SCPD: subcorneal pustular dermatosis.
*One case of PV showed subepidermal cleft on histopathology, but DIF showed features of PV.
**One case of BP showed suprabasal cleft on histopathology, but DIF was negative for BP.

ranged from 11 years to 85 years and the mean age was 46.2 (15.6) years. While majority of patients, 29.0% of PV, 75% of pemphigus foliaceus (PF), 50% of pemphigus vegetans (PVe) and each patient of pemphigus erythematosus (PE), subcorneal pustular dermatosis (SCPD), presented in 5th decade, whereas 50% of bullous pemphigoid (BP) presented in 7th decade. Both the youngest (11years) and oldest (85 years) patients had PV.

Among 31 patients with PV, 22 (71%) patients and 7 (22.5%) patients had oral cavity and trunk as the first site of involvement, respectively. While all cases (100%) of BP, PF, DH, and SCPD had trunk as the first site of involvement while, axilla and groin were the first to be involved in all PVe patients.

The duration of the disease ranged from less than a week to more than a year. Majority of the patients (34%) presented with skin lesions no later than 1 month. Eleven (22%) cases had skin lesions for more than 1 year with exacerbations and remissions. Burning sensation was the chief complaint (25/50, 50%) in this study followed by itching (15/50, 30%) and pain (10/50, 20%). Vesicle/bulla was the most common primary lesion in PV and BP. While 28/31 (90.3%) cases of PV and 1/8 (12.5%) cases of BP had flaccid bullae, 3/31 (9.7%) cases of PV and 7/8 (87.5%) cases of BP had tense vesicle/bullae (**Table 2**). Both positive Nikolsky's sign and bulla spread sign were seen in 29/31 (93.5%) cases of PV and 50% cases of PF. All patients (100%) of PV, PF, PE, LAD, DH, 50% cases of PVe, 6 out of 8 (75%) cases of BP had crusting. Excoriations were seen in 3 out of 8 (37.5%) cases of BP, both cases of DH and also in LAD. Vegetative lesions were seen only in PVe. Pigmentary changes seen were hyperpigmentation (54%) and hypopigmentation (40%). There was no pigmentary change in 3 (6%) cases, 2 cases of PV and 1 case of SCPD.

While there was no mucosal involvement in DH, PF, PE, LAD, PVe, SCPD and 4 cases each of PV and BP, buccal mucosa and lips were involved in 14/31 (45.2%) cases of V. The sole involvement of buccal mucosa and palate was seen in 11 (35.5%) and 2 (6.5%) cases, respectively. Among BP cases, 4 (50%) had oral lesions with predominant palatal involvement. There was no involvement of ocular, genital or nasal mucosa in this study. Nails were involved in 9 cases (7 cases of PV and 2 of BP). Nail involvement was in the form of pigmentation, transverse ridges, Beau's lines, onychomadesis and onycholysis and corresponded to the extent of severity of the disease.

Oral candidiasis (32.3%) was the most common associated disease seen in patients with PV followed by hypertension (12.9 %) and diabetes mellitus (9.6%). One case each had oral candidiasis, diabetes, hypertension, acrofacial vitiligo in BP.

Tzanck smear findings revealed acantholytic cells in 28/31 (90.3%) cases of PV and all cases of PF and PE; the predominant inflammatory infiltrate being neutrophils in 22 cases (71%). **(Table 3**). The presence of acantholytic cells in PV and PF was highly significant with $P<0.001$. The predominant infiltrate in BP was eosinophils (62.5%)

Histopathological examination showed suprabasal cleft in 29/31 (93.5%) cases and classical row of tombstone appearance in 25/31 (80.6%) cases of PV **(Table 4)**. One case of clinically diagnosed and DIF positive PV and clinically diagnosed and DIF negative BP had sub epidermal cleft and suprabasal split, respectively. Acantholytic cells were seen in 30/38 (78.9%) cases of pemphigus group of diseases. Subepidermal cleft was seen in7 out of 8 (87.5%) cases of BP, both the cases of DH and one case of LAD. Papillary edema was seen in majority of the cases. Neutrophilic infiltration was the predominant infiltrate in all the conditions and was seen with 67.5% of BP and 70.9% of PV. Papillary microabscesses were seen in both the cases of DH.

DIF was done in 38 cases due to economic constraints, and was positive in 34 cases. Four cases (1 case each of PV and BP and 2 cases of DH) were negative (**Table 5**). Both the patients of DH were put on oral dapsone, and both responded to it within 48 hours. DIF findings revealed intercellular deposition of IgG and C3 in 27/38 (71.1%) cases of pemphigus group of diseases. Six out of 7 (85.7%) cases of BP showed linear deposition of IgG and C3 in the basement membrane zone which also included IgA in one case. Both cases (100%) of DH showed negative DIF.

Correlation of histopathological and direct immunofluorescence findings was seen in PV, BP, PF, LAD, PE and PV (**Table 6**). While 31 clinically diagnosed cases, PV in 30 cases and BP in one case, 8 clinically diagnosed cases of BP were proved to be BP in 7 cases and PV in one case. Correlation between clinical and histopathological findings was seen in 96% of cases and that between histopathological and DIF findings in 89% of cases.

Discussion

The incidence of autoimmune vesiculobullous disorders among the OPD cases in the study period (one and half year) was 0.128%. This was comparable with the study done by Kanwar *et al.*[4] which showed an incidence of 0.3%. However, it should be noted that ours is a hospital-based study and so the above number does not reflect the true incidence of autoimmune vesiculobullous disorders in the community.

In the present study, pemphigus group of diseases constituted 76% (38/50) followed by BP 16% (8/50), DH 4% (2/50), LAD and SCPD 2% each. Among pemphigus group of diseases, PV constituted majority. This finding is similar to the studies done by Kanwar *et al.*[4], Arya *et al.*[5], Nanda *et al.*[6], Chams-Davatchi *et al.*[7] and Ljubojevic *et al.*[8]

Pemphigus vulgaris

In the present study, PV constituted 81.6% cases among the cases of pemphigus group. This was comparable to the study done by Tsankov *et al.*[9], Micali *et al.*[10] and Ljubojevic *et al.*[8] While Arya *et al.*[5] showed 61.4% and Handa *et al.*[11] showed

PV as high as 97.6%. This suggests geographic variation of the disease.

The age of the patients ranged from 11 to 85 years. Majority (29%) presented in 5th decade in our study when compared to 4th decade (25.4%) in the study done by Ahmed *et al.*[12] Our study showed female predominance. Male: female ratio was 0.63:1. This was in contrast to the studies done by Handa *et al.*[11] and Arya *et al.*[5] which showed male predominance. The site of onset of lesion was mucosal in 71% cases which was higher than that seen in the study done by Arya *et al.*[5] (37.2% cases).

28 (90.3%) had classical features of PV, i.e. flaccid vesiculobullous lesions. Mucosal involvement was present at one time or the other during the disease course in 87.1% of the cases. Nikolsky's sign was positive in 93.5% of cases. Similar findings have been reported by Handa *et al.*[11] and Arya *et al.*[5] Oral candidiasis (32.3%) was the most common associated condition followed by hypertension (12.9%) and diabetes mellitus (9.6%). These findings were comparable to the study done by Chams-Davatchi *et al.*[7] One case was associated with underlying chronic lymphocytic leukemia which is uncommon.

In the present study, Tzanck smear revealed acantholytic cells in 28 cases (90.3%) of PV. Huda *et al.*[13] and Singh *et al.*[14] studies showed acantholytic cells in Tzanck smear in 100% of cases. Tzanck cell may not be present in all the cases of pemphigus group due to various reasons like secondary infection and ruptured bullae. Out of 31 clinically diagnosed cases of PV, consistent histopathological features were seen in 30 cases. The remaining one case diagnosed as BP histopathologically, was proved to be PV on DIF. Acantholysis was seen in 27 cases (87.1%) and this was comparable to the study done by Arya *et al.*[5] Row of tombstone appearance was seen in 25 (80.6%) cases and this was higher to that seen in Arya *et al.*[5] study.

DIF was done in 22 out of 31 cases of PV patients due to economic constraints. 21 (95.4%) cases showed positive DIF. While Kumar *et al.*[15] showed 100% positive DIF, Chams-Davatchi *et al.*[7] study had 417 cases of PV out of 1111 among which 389 (93.28%) were positive. This shows that even the most definitive investigation may be negative and histopathology plays a vital role in such conditions.

Pemphigus foliaceus

PF (4/38) constituted 21.1% in our study. This was in accordance with the study done by Fernandez *et al.*[15] The age group commonly affected was between 40-49 years (75%). The initial site of involvement was skin. All the patients had flaccid vesicles and erosions covered with crusts, which are similar to that observed by Arya *et al.*[5] and Fernandez *et al.*[16] One patient presented as exfoliative dermatitis. This shows that the disease is protean in its manifestation. Involvement of mucous membrane was not present in patients with PF. This finding was similar to the study done by Fernandez *et al.*[16] study but differed from that of Arya *et al.*[5] study where mucous membrane was involved in 20% of the cases. This variation could possibly be due to decreased involvement of mucous membrane in PF as compared to PV. Nikolsky's sign was positive in 2 (50%) cases, while Arya *et al.*[5] and Fernandez *et al.*[16] showed a higher percentage.

Tzanck smear revealed acantholytic cells in all the cases (100%). The salient histopathological features of PF observed in our study were acantholysis (100%) and subcorneal bulla (100%). Subcorneal bulla was seen in 60% of cases in Arya *et al.*[5] study and 80% of cases in Fernandez *et al.*[15] study. Direct

immunofluorescence was positive in all the (100%) cases. Chams-Davatchi *et al.*[7] study showed 88% and Inchara *et al.*[17] showed 100% DIF positivity. The DIF finding may be similar to PV. Histopathology helps to differentiate between PV and PF in such cases.

Pemphigus vegetans

PVe constituted 5% (2/38) cases in the present study. This was higher compared to studies done by Arya *et al.*[5] and Micali *et al.*[10] Both the cases presented in 4th decade with flaccid blisters and vegetating skin lesions (papules) similar to Arya *et al.*[5] study. Base was non-erythematous in both the cases. Nikolsky's sign was positive in one case in contrast to both cases seen in study done by Arya *et al.*[5] This might be because of difficulty in eliciting Nikolsky's sign in axilla and groin.

Histopathological features included suprabasal cleft, hyperkeratosis and papillomatosis in both (100%) cases and this was in concordance with the findings seen in Arya *et al*.[5] DIF was positive in both cases (100%). Inchara *et al* [17] study had one case of PVe where DIF was negative. It implies that clinical and histopathological diagnosis will help in such cases. DIF also helps in differentiating PV from other conditions like Darier disease, Hailey-Hailey disease where it will be negative.

Pemphigus erythematosus

There was one case (2%) of PE in our study. The 47-year-old male patient had flaccid fluid filled lesion over face, upper back and upper chest. Nikolsky's sign could not be elicited. Tzanck smear showed acantholytic cells. Histopathology showed subcorneal cleft with neutrophilic infiltration. DIF showed granular deposits of IgG and C3 in the epidermis. DIF was helpful in this case, as both PE and PF show similar histopathology findings.

Subcorneal pustular dermatosis

There was one case (2%) of SCPD in our study. A 42-year-old female presented with 3-year history of intensely pruritic tiny pustules arranged in annular pattern, distributed mainly over trunk, sparing palms, soles, face and scalp. Tzanck smear was negative. Histopathology showed subcorneal cleft with neutrophils. DIF was not done for this patient.

Subepidermal bullous disorders

Patients with BP constituted 16% (8/50) of the total cases of autoimmune vesiculobullous disorders. This was in contrast with the study done by Chan *et al.*[18] which was 63.7%. This difference could be because of small sample size.

The mean age of onset of BP was 59.13 years which was less compared to studies by Bernard *et al.*[19], Wong *et al.*[20] and Nanda *et al.*[16] This suggests changing pattern of the disease. Females were more in number and the male: female ratio was 1:1.66 which is comparable to the study done by Bernard *et al*.[19] and Wong *et al*.[20] Patients presented mainly with severe itching which was statistically significant (p<0.001). Burning sensation and fever were seen in few patients.

Only one patient had oral lesions. This was in contrast to the study done by Kanwar *et al.*[4] (70%) and Bernard *et al.*[19] (24.63%). Majority (7/8) had generalized skin lesions while one patient had lesion confined to anterior chest (over mammary area). These observations were comparable to the study done by Kanwar *AJ et al*.[4] The lesions were over erythematous base in 6 out of 8 (75%) cases. Underlying diabetes

mellitus and hypertension was seen in one case each.

Subepidermal blister was seen in 7 of 8 (87.5%) cases. Suprabasal cleft was seen in 1 case and was histopathologically reported as PV. This might be due to biopsy of the older lesion. Predominant neutrophilic infiltration was seen in 5 (62.5%) cases and predominant eosinophilic infiltration seen in 2 (25%) cases. The latter is comparable to Nishioka *et al*.[21] study which showed 32% of eosinophilic infiltration. One unique feature observed in this study was DIF which was done in 7 out of 8 cases of BP of which 6 were positive and 1 case was negative. The negative DIF case was a localized BP. Other studies done by Kippes *et al.*[22] and Cozzani *et al.*[23] showed 100% positivity in DIF.

Dermatitis herpetiformis

DH constituted 2 (4%) cases among the autoimmune vesiculobullous disorders. Kanwar *et al.*[4] showed 12.12% which is quite high when compared to this present study. Both patients were females, one aged 11-year and other 24-year, and showed intensely pruritic papules and vesicles distributed predominantly over extremities and trunk with no history of gluten sensitivity. On histopathology, papillary microabscesses and neutrophilic infiltration were seen in both cases. Direct immunofluorescence was negative in both the case. The diagnosis was established by the presence of papillary microabscesses in the papillary dermis and spontaneous resolution of the symptoms and lesions within 2-3 days of starting dapsone. Inchara *et al*.[16] also showed similar findings with only 20% DIF positivity.

Linear IgA disease

We observed one case of LAD, which constituted 2% of total autoimmune vesiculobullous diseases. The patient was 18-year male presented with intensely pruritic tense vesicles and bullae all over the body. He had oral involvement also. Nikolsky's sign and bulla spread sign were negative. Tzanck smear showed good numbers of neutrophils. Histopathology showed subepidermal bullae with neutrophilic infiltration. DIF showed linear deposition of IgA along the basement membrane along with C3. The patient responded to oral dapsone within 10 days.

Conclusion

Clinical examination and cytology are the initial steps in making a diagnosis of autoimmune vesiculobullous disorders. Histopathological examination and direct immunofluorescence are required for making a definitive diagnosis in autoimmune vesiculobullous disorders. DIF is helpful in confirming the diagnosis. As DIF features are same in almost all types of pemphigus group of disorders, histopathology remains the cornerstone in diagnosis. Considering the socioeconomic situations of the patients and unavailability of immunofluorescence technique widely, the study showed that clinical features and histopathology are fairly specific and cost-effective in arriving at the diagnosis. DIF is only a supplement not a substitute. However, a large sample sized study is required to further confirm these observations.

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