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Original Research Article

Clinicopathological and immunofluorescence study of vesiculobullous disorders

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ABSTRACT

Background: Vesiculobullous diseases are mostly immune mediated and diagnosed based on the clinical features, histology and Immunofluorescence. The aim of the study was to identify the immunofluorescence pattern in auto immune vesiculobullous diseases and correlate it with the clinical profile and histology.
Methods: Patients attending the dermatology outpatient department in a tertiary hospital with vesiculobullous diseases, suggestive of auto immune aetiology were evaluated clinically. Histopathology and direct immuno-fluorescence were done in all patients.
Results: During the one year period from June 2008 to July 2009, 40 patients with vesiculobullous disorders clinically suggestive of auto immune aetiology attended the outpatient department. Out of the 40 patients, 22 (55%) patients were diagnosed to have intraepidermal with female preponderance and 18 patients (45%) sub epidermal blistering diseases. Bullous pemphigoid was the commonest sub epidermal disease, seen in 8 patients.
Conclusions: In all cases diagnosed clinically as pemphigus a histological diagnosis of pemphigus was made (100%). The clinical variants of pemphigus could also be diagnosed in all cases histologically (100%). The positive and negative predictive value was 100% in pemphigus group cases. Histology of all patients showed subepidermal bulla (100%). A specific diagnosis could be made in 18 patients with sub epidermal disease (100%). DIF was found to be an invaluable tool in diagnosing different diseases belonging to the sub epidermal group, but it was not of much help in sub classifying variants of pemphigus.

Keywords: Vesiculobullous diseases, Histology, DIF

INTRODUCTION

Patients with vesiculobullous diseases form a significant percentage of both outpatient and inpatient cases attending the Department of Dermatology and Venereology. The diagnois of vesiculobullous diseases is based on clinical correlation and histopathological findings. Majority of vesiculobullous disease sareimmune mediated, hence immunofluorescence as a diagnostic aid in dermatology has revolutionized the diagnostic capability as well as understanding of the pathogenic mechanisms of vesiculobullous diseases. Although both direct and indirect immunofluorescence can be used, it is the former which helps in identifying the pattern and exact site of immunoglobulin deposition.[1]

Aim

The aim was to identify the immunofluorescence pattern in vesiculobullous diseases and study the correlation between clinical histopathological and immuno-fluorescence patterns.

METHODS

Patients with vesiculobullous diseases attending the outpatient clinic of the Department of Dermatology and Venereology in a tertiary care hospital in North Kerala during a one year period from June 2008 to June 2009 were included in the study. Ethical clearance was obtained from the Institutional Research Committee. Children below two years, patients with viral infections (Herpes simplex, herpes zoster and varicella) and other vesiculobullous disorders not clinically suggestive of an auto immune aetiolgy were excluded from the study. After a detailed history and thorough clinical examination, base line investigations and a Tzanck smear was done to arrive at a clinical diagnosis. Histopathological and direct immunofluorescence (DIF) study was done in all patients. The immunofluorescence findings were correlated with the clinic-histological diagnosis.

Simple statistical methods were used to analyse the data. Frequencies and percentage were calculated and 95% confidential intervals were given for percentages.

RESULTS

During the one year period from June 2008 to July 2009, 40 patients with vesiculobullous disorders clinically suggestive of auto immune aetiology attended the outpatient department. The age of the patients ranged from 10 years to 80 years with maximum number of patients being in the 61-70 age group (25%). The study group comprised of 16 (40%) males and 24 (60%) females (Table 1). The male female ratio was 0.66:1. Out of the 40 patients, 22 (55%) patients were diagnosed to have intraepidermal and 18 patients (45%) sub epidermal blistering diseases.

Pemphigus group

The age of patients varied from 10 years to 80 years. There were 9 males (40.9%) and 13 females (59.09%). The different variants of pemphigus are shown in Table 2.

Table 1: Age and sex distribution of patients.

Age group (in years)	Male	Female	Total
0-10	1	0	1
11-20	0	2	2
21-30	1	2	3
31-40	2	4	6
41-50	3	5	8
51-60	4	2	6
61-70	4	6	10
71-80	1	3	4
Total	16	24	40

Table 2: Different variants of pemphigus.

Clinical diagnosis	Number of cases
Pemphigus vulgaris	16
Paraneoplastic pemphigus	2
Pemphigus erythematosus	1
Pemphigus foliaceus	3
Total	22

Pemphigus vulgaris

Among the 22 patients belonging to the pemphigus group, the clinical diagnosis of pemphigus vulgaris was made in 16 patients. Pemphigus vulgaris mucosal involvement as the initial presentation was seen in 37.2% of the patients. Blisters arising from non erythematous skin and erosions were seen in majority of the patients (Figure 1A). Histopathological examination in all 16 patients showed subrabasal acantholysis, acantholoytic cells in blister and tomb stoning of basal layer, diagnostic of pemphigus vulgaris (Figure 1B). Direct immuno-fluorescence (DIF) was done for all cases and showed IgG and C3 throughout the epidermis (Figure 1C). The correlation of histopathological examination and DIF is shown in Table 3.

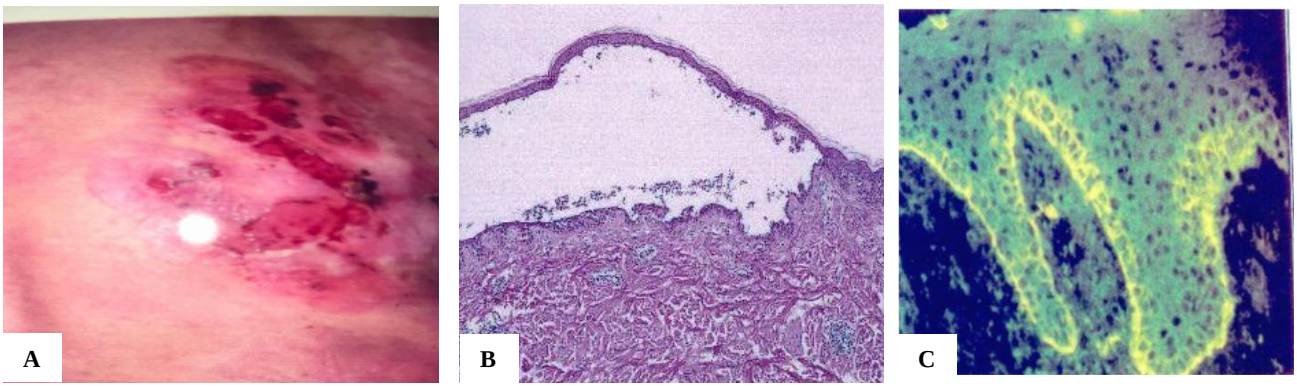

Figure 1 (A) Pemphigus vulgaris; (B) pemphigus vulgaris (H&E X10); (C) DIF: basement membrane and intercellular immunofluorescence (pemphigus vulgaris).

Table 3: Histopathological and DIF diagnosis of pemphigus vulgaris.

No. of patients	HPR	DIF
15	Pemphigus vulgaris: Suprabasal acantholysis, acantholytic cells in the blister cavity, tombstoning of basal layer, few neutrophils: diagnostic of pemphigus vulgaris	IgG & C3 ICS deposits throughout epidermis, suggestive of pempigus vulgaris
1	Pemphigus vulgaris: Suprabasal acantholysis, acantholytic cells in the blister cavity, tombstoning of basal layer, few neutrophils: diagnostic of pemphigus vulgaris	Strong IgG & C3 in upper epidermis only. Diagnosis of pemphigus foliaceus

Table 4: Histopathological and DIF diagnosis of pemphigus variants.

Clinical diagnosis and no. of cases	Histology	DIF
Pemphigus foliaceus- 3	Epidermis with blister in stratum granulosum, few neutrophils and acantholytic cells consistent with pemphigus foliaceus (N=1)	IgG and C3, strong ICS in upper epidermis: pemphigus foliaceus
	Epidermis with focal spongiosis, intraepidermal split with occasional acantholytic cells consistent with pemphigus foliaceus (N=1)	IgG and C3 deposits throughout epidermis
	Mild hyperkeratosis, subcorneal blister, plenty of neutrophils and acantholytic cells consistent with pemphigus foliaceus (N=1)	IgG and C3 deposits throughout epidermis
Pemphigus erythematosus- 1	Epidermis with focal spongiosis, intraepidermal split with occasional acantholytic cells suggestive of pemphigus erythematosus (N=1)	IgG ICS in upper epidermis; IgM, IgA, fibrinogen in BMZ Suggestive of pemphigus erythematosus/ Paraneoplastic pemphigus
Para neoplastic pemphigus- 2	Mild hyperkeratosis, subcorneal blister, plenty of neutrophils and acantholytic cells	IgG &C3 in the intercellular and basement membrane zone

Pemphigus foliaceus

There were 3 cases diagnosed as pemphigus foliaceus clinically. Histology showed sub corneal blister with acantholytic cells. DIF showed Ig G and C3 in the upper epidemis in one case only. Table 4 shows the histopathological features of pemphigus foliaceus along with the DIF findings.

Among the clinically and histopathologically diagnosed cases of pemphigus foliaceus, a definite diagnosis by immunofluorescence could be made only in one case. In the other two cases only a diagnosis of pemphigus could be made.

Pemphigus erythematosus

Clinically one case was diagnosed as pemphigus erythematosus which showed histological evidence (intra epidermal vesicle) of the same. Table 4 shows the histological and DIF features of pemphigus erythematosus.

Even though the DIF studies showed features suggestive of pemphigus erythematosus, the possibility of paraneoplastic pemphigus that also shows similar DIF findings could not be ruled out. Absence of features like dyskeratotic keratinocytes with vacuolar interface dermatitis suggestive of paraneoplastic pemphigus was not evident in this case. So a diagnosis of pemphigus erythematosus was made.

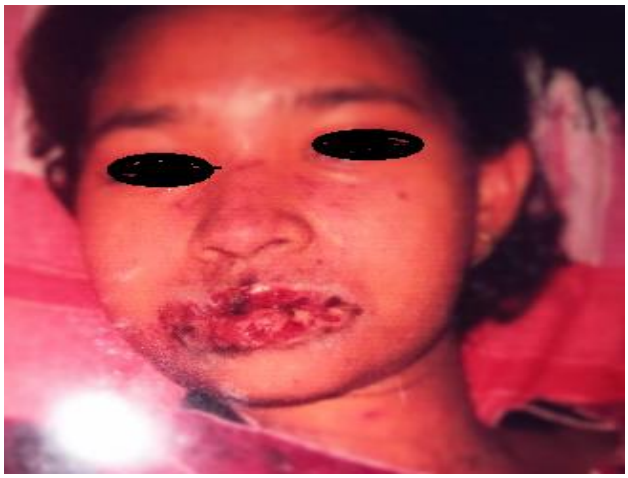

Figure 2: Recalcitrant oral erosions in paraneoplastic pemphigus.

Paraneoplastic pemphigus (PNP)

Two cases clinically diagnosed as paraneoplastic pemphigus presented with highly variable cutaneous lesions and severe mucosal erosions (Figure 2). The histology showed features consistent with PNP; DIF findings are shown in Table 4. DIF showed features suggestive of paraneoplastic pemphigus in one case clinically and histologically diagnosed as pemphigus erythematosus.

For a clinical diagnosis a correlation between clinical, histological and immunofluorescence findings are mandatory. Table 5 shows the clinical and final diagnoses of the pemphigus group of disorders.

Table 5: Final diagnosis of the pemphigus group of disorders.

No of cases	Clinical diagnosis	Histology	DIF	Final diagnosis
16	Pemphigus vulgaris	Pemphigus vulgaris (n=16)	Pemphigus vulgaris (N=15) Pemphigus foliaceus (N=1)	Pemphigus vulgaris (N=15) Pemphigus foliacues (N=1)
3	Pemphigus foliaceus	Pemphigus foliaceus (n=3)	Pemphigus (N=2) Pemphigus foliaceus (N=1)	Pemphigus foliacues (N=3)
1	Pemphigus erythematosus	Pemphigus erythematosus (n=1)	Pemphigus erythematosus/ paraneoplastic pemphigus (N=1)	Pemphigus erythematosus (N=1)
2	Paraneoplastic pemphigus	Paraneoplastic pemphigus (n=2)	Paraneoplastic pemphigus (N=2)	Paraneoplastic pemphigus (N=2)

Sub epidermal group of blistering disorders

Among the 40 patients in the study group, 18 patients (45%) were clinically diagnosed to have sub epidermal blistering disease, their age group varied from 10 to 80 years. The age and sex distribution of the patients is shown in Table 6. The 18 patients in the sub epidermal group were further classified based on history, clinical examination and base line investigations including Tzanck smears (Table 7).

Table 6: Age and sex distribution of sub epidermal group of patients.

Age (in years)	Male	Female	Total
0-10	1	0	1
11-20	0	1	1
21-30	0	0	0
31-40	0	2	2
41-50	1	3	4
51-60	3	1	4
61-70	1	3	4
71-80	1	1	2
Total	7	11	18

Bullous pemphigoid

Among the 18 patients diagnosed as having sub epidermal diseases, 8 were diagnosed as bullous pemphigoid. Prodromal urticarial and figurate erythemas and tense large blisters were common in our patients (Figure 3A). Histology showed sub epidermal bullae with eosinophils (Figure 3B). DIF showed IgG, C3 along BMZ as shown in Table 8 and Figure 3C.

Dermatitis herpetiformis

4 cases were diagnosed as dermatitis herpetiformis. The histology showed mixed and neutrophilic infiltrate in 3 and one patients respectively and DIF showed features of bullous pemphigoid and LABD as seen in Table 8.

Table 7: Clinical diagnosis of sub epidermal diseases.

Diagnosis	Number of cases
Bullous pemphigoid	8
Dermatitis herpetiformis	4
Linear IgA bullous dermatosis	2
Chronic bullous disease of childhood	1
Lichen planus pemphigoides	2
Epidermolysis bullosa acquisita	1

Linear IgA dermatosis

Among 18 patients with sub epidermal disease, 2 were diagnosed as linear IgA dermatosis. Based on the clinical finding of cluster of jewel appearance of lesions (Figure 4); histopathological and DIF findings however did not correlate with the clinical diagnosis as is shown in are given in Table 8.

Epidermolysis bullosa acquisita

Clinical diagnosis was made in 1 out of 18 patients; histopathological and DIF findings and salt split skin DIF confirmed the diagnosis (Table 8).

Chronic bullous disease of childhood

One patient was diagnosed as chronic bullous disease of childhood; histopathological study showed subepidermal bulla with neutrophils; DIF study was that of LABD (Table 8).

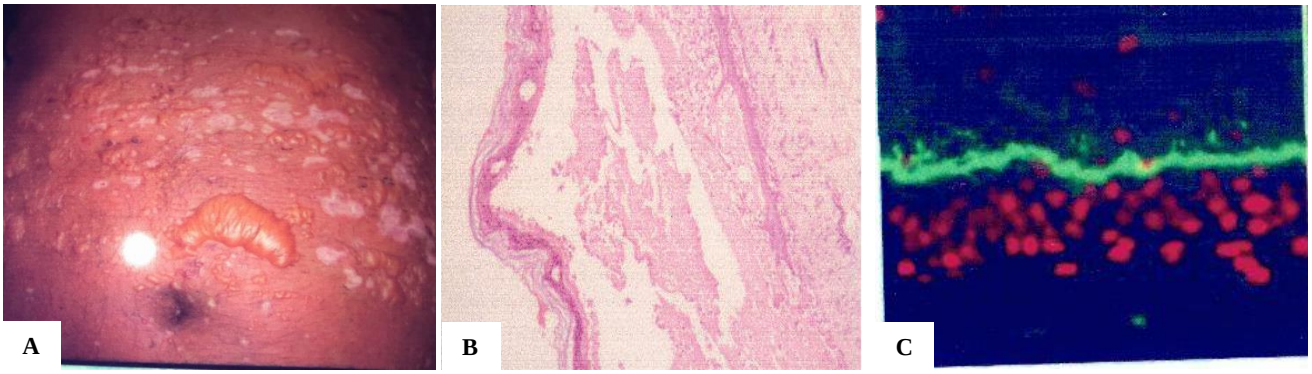

Figure 3: (A) Bullous pemphigoid; (B) Bullous pemphigoid with sub epidermal bulla (H&E 10X); (C) DIF: linear immunofluorescence in the basement membrane zone (bullous pemphigoid).

Table 8: Histology and DIF in patients clinically diagnosed as sub epidermal disease.

Clinical diagnosis	Cases (n)	Histology	DIF
Bulloous pemphigoid	8	Sub epidermal bulla- 8 Eosinophils-6, mixed infiltrate -2	Strong IgG and C3 band in BMZ Suggestive of bullous pemphigoid
Dermatitis herpetiformis	4	Sub epidermal bullae with mixed infiltrate in 3 neutrophil predominance in 1	Ig G, C3 linear BMZ band with negative IgA, IgM and fibrinogen : consistent with bullous pemphigoid- 3 patients Linear IgA, BMZ band with negative IgG, IgM and C3 diagnosed as LABD- 1 patient
Linear Ig A bullous dermatoses	3	Sub epidermal bullae with plenty of eosinophils- 1 Normal epidermis, dermal oedema, mononuclear infiltrate around blood vessels, suggesting diagnosis of Erythema multiforme- 2 patients	Strong C3 BMZ band, discontinuous IgG BMZ band-diagnosed as bullous pemphigoid- 1 Fibrinogen around blood vessels with negative IgA, IgG/IgM and C3. Consistent with diagnosis of Erythema multiforme
Epidermolysis bullosa acquisita	1	Sub epidermal bullae with absence of infiltrate	IgG and IgG and C3 on the floor of the split- diagnosed as EBA C3 BMZ band
Chronic bullous disease of childhood	1	Sub epidermal bullae with neutrophils	Linear IgA BMZ band– diagnosed as CBDC
Lichen planus pemphoigoides	2	LP like lesions- hyperkeratosis, hypergranulosis, basal cell degeneration, pigment incontinence and band like mononuclear dermal infiltrate- suggestive of lichen planus- 2 Bullous lesion-sub epidermal bulla with mixed infiltrate	IgG and C3 linear BMZ band –diagnosed as bullous pemphigoid- 2

Lichen planus pemphigoides

Two cases were clinically diagnosed as lichen planus pemphigoides; histology showed features of lichen planus and DIF showed features of bullous pemphigoid (Table 8).

Among the 18 cases clinically diagnosed as sub epidermal diseases one case was diagnosed as erythema multiforme by histology and DIF. In the remaining 17 cases, histology of all cases showed sub epidermal bullae with variable infiltrate. The diagnosis of the variants was possible by DIF in all 17 patients (Table 9).

Immunofluorescence is valuable in confirming a diagnosis of vesiculobullous disease that is suspected by clinical and histological examination. This is specifically true of sub epidermal diseases that often have a overlap in the clinical and histological findings.

Table 9: Correlation between the clinical, histopathological and immunofluorescence pattern in sub epidermal vesiculobullous disorders.

Clinical diagnosis	No. of cases (n)	Histological diagnosis	DIF	Final diagnosis
Bullous pemphigoid	8	Sub epidermal bullae with Eosinophils- 5 Neutrophils- 2 Mixed- 1	Bullous pemphigoid- 8	Bullous pemphigoid- 8
Dermatitis herpetiformis	4	Sub epidermal bulla with mixed infiltrate- 3 Neutrophils- 1	Bullous pemphioid- 3 Linear IgA bullous disease- 1	Bullous pemphigoid- 3 LABD- 1
Linear IgA bullous disease	2	Sub epidermal bullae with eosinophils- 1 Erythema multiforme- 1	Bullous pemphioid- 1 Erythema multiforme- 1	Bullous pemphigoid- 1 Erythema multiforme- 1
Epidermolysis bullosa acquisita	1	Sub epidermal bulla without infiltrate	Epidermolysis bullosa acquisita- 1	Epidermolysis bullosa acquisita- 1
Chronic bullous disease of childhood	1	Sub epidermal bulla with neutrophils- 1	Chronic bullous disease of childhood- 1	Chronic bullous disease of childhood- 1
Lichen planus pemphigoides	2	Lichen planus and sub epidermal bulla with mixed infiltrate- 2	Bullous pemphigoid- 2	Lichen planus pemphigoides- 1

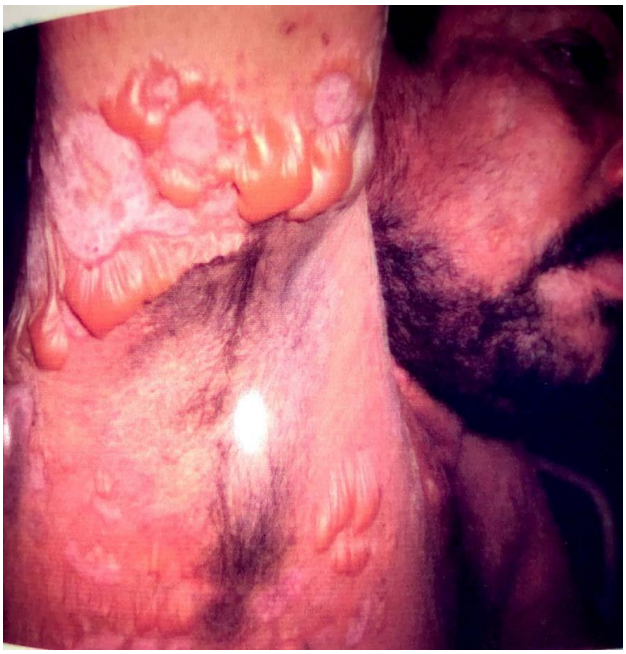

Figure 4: Linear IgA bullous dermatosis.

DISCUSSION

Blistering diseases are a heterogenous group of dermatological disorders. In many cases the bullous diseases cannot be differentiated clinically and need the help of histological and Immunofluorescence study.[1]

A total of 40 patients were included in the study of which 22 (55%) were intraepidermal diseases and 18 (45%) were sub epidermal.

In our study among 22 patients in the intra epidermal (pemphigus) group, 13 patients (59.09%) were females and 9 males (40.09%), in contrast to the studies by Ambadi et al which showed a male preponderance.[2] In another study by Fernandez et al, both sexes were equally affected.[3] In our study maximum patients were seen in the age group 50-70 years and 31-50 years (8 patients each). Maximum cases were in the fourth and fifth decade in a study by Kabir et al.[4]

Pemphigus vulgaris was the commonest sub type in our study (16 out of 22 cases) as seen in the study by Fernandez et al.[3] There was a slight female preponderance. Pemphigus vulgaris showed initial lesions involving the mucus membrane in 37.2% of patients. Flaccid bullae were present in 100%. Histologically salient features were intra epidermal blisters, acantholysis and row of tomb stone appearance; there was 100% clinico histological correlation. Study by Arya et al showed 95% correlation.[5] In our study histology showed neutrophil predominance in 9 cases and eosinophils in 7. According to Lever, inflammation is rare in pemphigus and it varies with the age of the blister.[6] DIF pattern for pemphigus is IgG and C3 throughout the epidermis; the fluorescence may be limited to or most intense in the level of epidermis involved with blister formation; that is

lower epidermal level for pemphigus vulgaris and pemphigus vegetans and superficial epidermal layer in pemphigus foliaceus.[1,7] DIF showed IgG and C3 throughout the epidermis which made the diagnosis of pemphigus possible. The positive predictive value of DIF in the diagnosis of pemphigus is extremely high and approaches 100%.[1]

Pemphigus foliaceus

The three cases of pemphigus foliaceus blisters presented with flaccid vesicles, crusted lesions and erosions. Histologically all cases showed sub corneal blisters with acantholytic cells (100%). According to lever the main histological features of pemphigus foliaceus are sub corneal blister, acantholysis and bullae with inflammatory cells.[6] A study by Arya et al showed presence of acantholysis in 24 and subcorneal bullae in 15 out of 25 cases of pemphigus foliaceus.[5] In our study DIF showed uniform fluorescence throughout epidermis suggestive of pemphigus in 2 cases; one patient had fluorescence limited to superficial epidermal layer confirming the diagnosis of pemphigus foliaceus (33.33%).

Pemphigus erythematosus

Aclinical diagnosis of pemphigus erythematosus was made in one patient. Histology showed separation of epidermis in the upper layers with acantholytic cells in accordance with the study by Amerian and Ahmed.[8] DIF showed IgG in upper epidermis amd IgM, IgA and fibrinogen in BMZ. According to Black et al and Mohan et al preferential localization of immunoreactants in the upper epidermis is more in favour of pemphigus erythematosus. Immunoreactants may be deposited in the BMZ in sun exposed areas.[9,10]

Paraneoplastic pemphigus

Two cases diagnosed as paraneoplastic pemphigus presented with highly variable cutaneous lesions which included target lesions on palms and soles, papules, vesicles and erosions on trunk and limbs in accordance with the criteria of Anhalt et al.[11] Painful stomatitis was also present. A study by Horn and Anhalt showed suprabasal acantholysis, satellite cell necrosis, basal cell vacuolation, interface dermatitis, spongiosis and epidermal exocytosis of inflammatory cells in the histology of paraneoplastic pemphigus.[12] DIF in the study showed IgG and C3 in the intercellular spaces in perilesional skin and mucosa and IgM, IgG and C3 in the BMZ. Our study showed similar findings.

In our study a diagnosis of pemphigus was made in all 22 cases by histology (100%). The diagnosis of pemphigus sub types could be made in all cases. By DIF a diagnosis of pemphigus could be made in the intrepidermal group (100%). Different sub types of pemphigus could be made out in 5 out of the 22 cases (22.72%). In our study group there was no statistical significance between diagnosis of pemphigus subtypes by histology or DIF. Although DIF is the gold standard for the diagnosis of pemphigus the exact pemphigus subtype can be determined by histology of early vesicles.[7,9,10] A previous study by Diya et al found positive predictive value of 100% by DIF in the pemphigus group of disorders and negative predictive value of 85-90%.[1] In our study a positive predictive value of 100% and negative predictive value of 100% was found.

Sub epidermal blistering diseases

Among the 40 patients in our study group 18 patients were diagnosed to have sub epidermal diseases.

Bullous pemphigoid

In our study bullous pemphigoid was the commonest affecting 8 out of 18 patients (44.44%). Maximum number of patients belonged to the age group of 41-70 years as also seen in the study by Luiz et al.[14] Clinically patients had prodromal urticaria, figurate erythemas and tense bullae on normal or inflammed skin. Histology showed sub epidermal bulla with eosinophilic infiltrate in 5 cases; 3 cases showed mixed infiltrate. The presence of sub epidermal bullae with mixed infiltrate is a non specific finding and in such cases DIF is invaluable in confirming the diagnosis.[13,17] The DIF in all 8 patients diagnosed as bullous pemphigoid showed IgG and C3 in a thick linear band in the BMZ. According to Diya et al deposition of C3 with significantly higher intensity than IgG favours pemphigoid group of diseases.[1] If the intensity of IgG is higher than C3 EBA and bullous SLE is more likely.

Dermatits herpetiformis

Four cases were clinically diagnosed as dermatitis herpetiformis. No history of gluten sensitive enteropathy could be elicited in any of the patients. The extensor surface of limbs, buttocks, shoulders, axillary folds, face and scalp showed pruritic erythematous papules, grouped vesicles and erythematous plaques in accordance with the study by Duhring et al.[15] Histology in 3 cases showed sub epidermal bullae with variable infiltrate. One case showed predominance of neutrophils; neutrophilic micro abscesses were absent. In DIF 3 cases showed IgG and C3 bands in the BMZ with absence of other immunoreactants suggesting a diagnosis of bullous pemphigoid. DIF of one patient showed IgA band diagnostic of linear IgA dermatosis. LABD closely resembles DH clinically. DIF helped in reaching a final diagnosis.

Linear IgA bullous dermatosis

Two cases clinically diagnosed as LABD had a morphology resembling cluster of jewel appearance as described in chronic bullous disease of childhood.[16] In

one patient histology showed papillary edema and mononuclear infiltrate around blood vessels with occasional keratinocyte necrosis, diagnostic of erythema multiforme. DIF showed fibrinogen with absence of other immune reactants suggestive of erythema multiforme. In the second patient histology showed sub epidermal bullae with eosinophils suggesting a diagnosis of bullous pemphigoid. DIF showed IgG and C3 deposits in the BMZ consistent with BP. In these 2 cases histological diagnosis correlated with DIF.

Epidermolysis bullosa acquisita (EBA)

In a patient clinically diagnosed as EBA, histopathology showed sub epidermal bullae with absence of infiltrate. According to Klausf et al absence of infiltrate is suggestive of EBA.[17] DIF showed absence linear IgG band and weak IgA band and absence of C3.Increase in the number of immunoglobulins at the BMZ is suggestive of EBA.[1] Salt split immunofluorescence can confirm the diagnosis of EBA.[18.]

Chronic bullous disease of childhood

One patient presented with urticated annular lesions and targetoid lesions with subsequent development of classic cluster of jewel lesions of grouped small blisters around the edge of the lesion. Histology showed subepidermal bullae with neutrophils which is a nonspecific finding. According to Black and Bhoghal histology may be identical to dermatitis herpetiformis or resemble bullous pemphigoid.[9] DIF confirmed the diagnosis in our patient.

Lichen planus pemphigoides

Two patients presented with generalized lichen planus followed by sudden appearance of large bullae both on the lichen planus lesions as well as on normal looking skin. Such clinical features were described by Archer et al.[19] Histopathology in these cases showed hyper-keratosis, hypergranulosis, basal cell degeneration with pigment incontinence and band like mono nuclear infiltrate which is suggestive of lichen planus as described by Kaposi et al.[20] After correlating the clinical, histological and immunofluorescence findings a diagnosis of lichen planus pemphigoides was made.

In 18 cases belonging to the sub epidermal group, 17 cases (94.44%) showed a sub epidermal bulla. One case diagnosed was diagnosed as eythema multiforme. The nature of the infiltrate did not contribute much to the diagnosis of the variants belonging to the sub epidermal group. In the sub epidermal group DIF helped to arrive at the diagnosis in all cases.

The positive and negative predictive value of DIF in patients with sub epidermal diseases approaches 100%. In our study the positive and negative predictive value was 100%. As sub epidermal diseases overlap clinically and histologically, immunofluorescence is invaluable in confirming the diagnosis in this group.

Small sample size, expensive technique and inability to do indirect immunofluorescence were the limitations of our study.

CONCLUSION

In the above study, clinico histopathological correlation was 100% in all cases of pemphigus vulgaris and its clinical variants. The correlation between clinical diagnosis of pemphigus and DIF was 93.75%; it was 22.7% in the clinical variants of pemphigus. The positive and negative predictive value by DIF was 100% in pemphigus group. Bullous pemphigoid was the commonest sub epidermal disease in this study. A specific diagnosis could be made in all patients with sub epidermal disease (100%) by DIF. Gluten sensitive enteropathy an unreported finding was noted in a case of chronic bullous disease of childhood. Cluster of jewel appearance characteristically described in CBDC was found in a case of bullous pemphigoid and a case of erythema multiforme. Our study found that although DIF is the gold standard for the diagnosis of pemphigus the exact pemphigus subtype can be determined by histology of early vesicles. DIF was an invaluable tool in diagnosing different diseases belonging to the sub epidermal group of vesiculobullous diseases, it was not of much help in sub classifying the variants of pemphigus.

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