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CLINICAL AND HISTOLOGICAL CHARACTERIZATION OF PEMPHIGUS IN PATIENTS WITH DIRECT IMMUNOFLUORESCENCE.

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Abstract:

INTRODUCTION: Pemphigus is a group of life-threatening mucocutaneous autoimmune bullous disease with blister formation. Although the disease is rare but it is associated with high morbidity and mortality, if proper treatment is not taken. It is IgG-mediated autoimmune diseases of stratified squamous epithelium, like skin and oral mucosa, in which acantholysis causes blisters and erosions. The immune reaction breaks down the adhesion components and leads to epithelial cell detachment**.** There are several types of pemphigus; three types are associated with oral mucosa, pemphigus vulgaris (PV), pemphigus foliaceus (PF), and paraneoplastic pemphigus. The diagnosis of pemphigus should be promptly done as clinically it may be difficult to differentiate the different variants leading to delay or wrong treatment and therefore increasing the mortality and morbidity rates. Direct immunofluorescence (DIF) is a very sensitive test for the diagnosis of pemphigus.

MATERIAL AND METHODS: patients attending paediatric age group up to 12-15 years of age group were included in the study.28 clinically suspected cases of pemphigus were observed, screened and were included in the study. Histological and DIF investigations were carried out on all the patients. On the basis of histological, DIF and clinical diagnosis patients were confirmed and correlated for disease activity.

RESULTS: 26 cases were included in the study. Out of 26 cases 12 (46.2%) cases were male and 14 (53.8%) cases were female. Duration of the illness was 3.21 ± 12.14 months. Most of the cases started with mucosal involvement and then presented with oral and cutaneous presentation. 20 (76.9%) cases were diagnosedas Pemphigus vulgaris (PV), 5(19.2%) cases as pemphigus foliaceus (PF) and 1 (3.8%) was IgA pemphigus. In this study, 13 (50%) patients showed acantholytic cells on histopathological examination. In Pemphigus vulgaris (n=20) involvement of whole, lower and upper epidermis was 17 (85%), 2 (10%) and 1(5%) respectively. In Pemphigus foliaceus (n=5) whole epidermis involvement was in 1 (20%). In IgA Pemphigus only upper epidermis was involved. IgG was observed in 8 (60%) of PV cases while IgG + C3 was observed in 12 (40%) patients. In PF IgG was seen in 4 (80%) cases while IgG + C3 were observed in 1(20%) case. IgA was observed in one case.

CONCLUSION: Pemphigus even though a rare disease in children should be diagnosed promptly and reduce morbidity and mortality. DIF is a sensitive test and can be utilized for the diagnosis of pemphigus.

Key Wards: *pemphix, PF, PV, DIF.*

INTRODUCTION

The term pemphigus is derived from the Greek word '*pemphix*', which means blister or bubble. Pemphigus is a group of life-threatening mucocutaneous autoimmune bullous disease with blister formation. Although the disease is rare but it is associated with high morbidity and mortality, if proper treatment is not taken[i].It is IgG-mediated autoimmune diseases of stratified

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squamous epithelium, like skin and oral mucosa, in which acantholysis (the loss of cell adhesion) causes blisters and erosions[ii]. IgG autoantibodies are characteristically directed against desmogleins (desmoglein 1 and desmoglein 3), which are part of the cadherin family of cell–cell adhesion molecules that are found in desmosomes[iii]. The immune reaction breaks down the adhesion components and leads to epithelial cell detachment, which is clinically seen as intraepithelial blisters, erosions or ulcers in the skin and mucous membranes[iv].

There are several types of pemphigus, three types are associated with oral mucosa, pemphigus vulgaris (PV), pemphigus foliaceus (PF), and paraneoplastic pemphigus[v].Pemphigus vulgaris and pemphigus foliaceus are the originally characterized, classic forms of pemphigus. Paraneoplastic pemphigus is associated with malignant neoplasia. Histological analysis shows that paraneoplastic pemphigus is distinguished by the presence of a known-associated or occult-associated neoplasm, usually of lymphoid tissue, pemphigus vulgaris blisters develop deep in the epidermis or oral epithelium above the basal layer, whereas pemphigus foliaceus blisters occur in the superficial layers of the epidermis, mostly in the granular layer. [vi]

The diagnosis of pemphigus should be promptly done as clinically it may be difficult to differentiate the different variants leading to delay or wrong treatment and therefore increasing the mortality and morbidity rates. Direct immunofluorescence (DIF) is a very sensitive test for the diagnosis of pemphigus[vii].

MATERIAL AND METHODS

The present study was carried out in department of dermatology of a Shri Vinoba Bhave Civil hospital, Silvassa. This study was done from 2014 to Aug 2018. Only patients attending paediatric age group up to 14 years of age group were included in the study.28 clinically suspected cases of pemphigus were observed, screened and were included in the study. Written informed consent was taken from all the patients and their parents who were included in the study.

Histological and DIF investigations were carried out on all the patients. On the basis of histological, DIF and clinical diagnosis patients were confirmed and correlated for disease activity. Chi-square test, Fisher's exact tests were used as applicable for statistical analysis and and $P < 0.05$ was considered statistically significant..all data was compiled and entered in Microsoft excel 2013 edition.

RESULTS

Among 28 cases, consent was not given by 2 cases, only 26 cases were included in the study. Out of 26 cases 12 (46.2%) cases were male and 14 (53.8%) cases were female. Of the 26 cases evaluated for pemphigus20 (76.9%) cases were diagnosed as Pemphigus vulgaris (PV), 5(19.2%) cases as pemphigus foliaceus (PF) and 1 (3.8%) was IgA pemphigus. Duration of the illness was3.21 ± 12.14 months. Most of the cases started with mucosal involvement and then presented with oral and cutaneous presentation.

Table 1: characteristics of pemphigus according to mucosal involvement

	Pemphigus vulgaris	**Pemphigus foliaceus**	**IgA Pemphigus**	**Total**	
Total	20 (76.9%)	5 (19.2%)	1 (3.8%)	26 (46.15%)	
Oral involvement	11 (55%)	1 (20%)	0	12 (46.2%)	P<0.0001
Other mucosal	5 (25%)	0	0	5 (19.2%)	

In pemphigus vulgaris group 20 (76.9%) patients were observed of which 11 (55%) showed oral involvement while 5 (25%) showed other mucosal involvement. In pemphigus foliaceus group 1(20%) patient showed oral involvement. No mucosal involvement was seen in IgA group.
In this study, 13 (50%) patients showed acantholytic cells on histopathological examination. Dermal inflammation, consisting of neutrophils, was present in around 80% patients of pemphigus.

Table 2: Direct immunofluorescent findings in patients

Parameter	Pemphigus vulgaris (n=20)	Pemphigus foliaceus (n=5)	IgA Pemphigus (n=1)
Whole epidermis	17 (85%)	1 (20%)	-
Lower epidermis	2 (10%)	-	-
Upper epidermis	1 (5%)	3 (60%)	1 (100%)
Type of Antibody			
IgG	8 (60%)	4 (80%)	-
IgA	-	-	1 (100%)
IgG + C3	12 (40%)	1(20%)	-

In Pemphigus vulgaris (n=20) involvement of whole, lower and upper epidermis was 17 (85%), 2 (10%) and 1(5%) respectively. In Pemphigus foliaceus (n=5) whole epidermis involvement was in 1 (20%). In IgA Pemphigus only upper epidermis was involved.

IgG was observed in 8 (60%) of PV cases while IgG + C3 was observed in 12 (40%) patients. In PF IgG was seen in 4 (80%) cases while IgG + C3 was observed in 1(20%) case. IgA was observed in one case.

DISCUSSION AND CONCLUSION

Pemphigus is a severe bullous autoimmune dermatosis that can show a clinical challenge even if high-dose immunosuppressive therapy due to the therapy-related comorbidities and the lack of long-term control of disease activity. It is a potentially life threatening disease that causes blisters and erosions of the skin and the mucous membrane[viii]. There are 0.5 to 3.2 cases reported each year per lakh population, and the highest incidence is seen in the 5th and 6th decade of life, with male to female ratio of 1:2[ix]. Very rarely it has been reported in children and the elderly[x].

Pemphigus Vulgaris is the most common form which accounts for over 80% of cases[xi]. In our study also pemphigus vulgaris was observed in 20 (76.9%) of cases. In most of the oral lesions are followed by the development of skin lesions[xii]. In our study also same results were observed in most of the cases. All 26 cases that were diagnosed clinically were confirmed by histopathology and immunofluorescence tests. 1 case of pure mucosal PV and 1 case of IgA pemphigus were diagnosed by DIF.

In our study, Out of 26 cases 12 (46.2%) cases were male and 14 (53.8%) cases were female in our study slight female preponderance was noted. It was in accordance with a study by ShafiMet. al[xiii] in which they studied 109 cases.

In our study out of 26 casespemphigus vulgaris (PV) was observed in 20 (76.9%) patients, while PF was observed in 5 (19.2%) cases and one case of IgG pemphigus.similar results was shown in other studies[xiv],[xv].

In PV out of 20 cases IgG was observed in 8 (60%) and IgG + C3 was observed in IgG + C3 patients. DIF study from skin of lesion showed mainly IgG and C3 deposits. In Pemphigus foliaceus (n=5), 4 (80%) patient showed IgG and 1 (20%) was of IgG + C3. histopathology of patients with pure mucosal casesrevealed basal layer budding. An inflammatory infiltrate was present in 15 cases. DIF study from skin showed mainly IgG and C3 deposits.

In our study in Pemphigus vulgaris, involvement of whole, epidermis was 17 (85%),lower was 2 (10%) and upper epidermis was 1(5%) respectively. In Pemphigus foliaceus (n=5) whole epidermis involvement was in 1 (20%). In IgA Pemphigus only upper epidermis was involved. Similar results were observed by Choudhary J et al[xvi].

To conclude Pemphigus even though a rare disease in children should be diagnosed promptly and reduce morbidity and mortality. DIF can be used as a biomarker and histopathology can confirm the diagnosis and it most sensitive test.. Big cohort studies are required in the area to confirm the results and

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