

A CLINICOPATHOLOGICAL STUDY OF PEMPHIGUS

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Summary

A clinical study of 53 patients suffering from various types of pemphigus is presented. There were 32 males and 21 females. The clinical diagnosis was confirmed by Tzanck test and histopathological studies. Pemphigus vulgaris the commonest type, was seen in 44 patients. Majority of the patients belonged to 30-60 years of age group, of low socioeconomic status. Disease appearing early in life, especially pemphigus foliaceus tended to fatal. With steroids, there was miraculous response in majority of the patients. Some required ACTH and blood transfusion, while a few went downhill, inspite of all treatments. It is our observation that disease is milder in severity in India as compared to Western countries and can be controlled with proportionately lower dosage of corticosteroids.

The term pemphigus was coined by De-Sauvages¹ in 1760 from the Greek word "Pemphix" which means a pustule. Wichman² in 1791, described it as a "Chronic bullous disease", while William in 1808 called it "Pompholyx diutinum".

The classical and most common variety of disease was named pemphigus vulgaris. Several of its variants were described later on. Cazenave³ in 1844 recognised pemphigus foliaceus. Neumann⁴ in 1886 reported the first case of pemphigus vegetans and Seneor and Usher⁵ in 1926 named and described pemphigus-erythematosus. Still another variant "Familial Benign Chronic Pemphigus", was recognised by Hailey and Hailey⁶ in 1939.

Civatte⁷ and Tzanck⁸ outlined the histopathological criteria of intra-epider-

mal splitting and acantholysis for the diagnosis of pemphigus.

Though the disease is not uncommon in dermatological practice and still carries a grave prognosis, inspite of the advent of corticosteroids, only a few reports on this disease have appeared in Indian literature, especially from Northern India. The largest series of 100 patients was reported by Fernandez et al⁹. The earlier series by Desai and Rao¹⁰. Kandhari and Pasricha¹¹ and Ambady et al¹² consisted of 21, 34 and 21 patients respectively. Observations on all the 53 cases of various types of pemphigus, who were admitted in the Skin ward of Irwin Hospital from 1966 to 1970, are presented.

Method

The diagnosis of pemphigus was made on clinical grounds, positivity of the Nikolsky's sign and was confirmed by the demonstration of acantholytic cells by Tzanck test and finally substantiated by the typical histopathological features. Total and differential

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leukocyte count and estimation of haemoglobin, E.S.R., serum proteins, serum electrolytes etc. were done in every case from time to time.

Observations and Discussions

All varieties of pemphigus were seen

Pemphigus vulgaris	... 44 cases
Pemphigus foliaceus	... 6 cases
Pemphigus vegetans	... 1 case
Pemphigus erythematosus	... 1 case
Benign chronic pemphigus of Hailey & Hailey	... 1 case
Total	.. 53 cases

Acantholytic cells by Tzanck test were seen in all the 53 cases (100%). Intra-epidermal bullae at different levels with acantholytic cells were demonstrated in 43 cases (81.3%) on histopathological examinations. Histological studies were non-contributory in 10 patients, either due to inadequate or mutilated biopsy specimens, or bulla was not visualized.

Incidence

This was insignificant as compared to the total number of new cases seen in the Skin O.P.D. of Irwin Hospital :

Year	Total no. of patients	No of pemphigus patients	Percentage
1966	24841	10	0.040
1967	21899	8	0.036
1968	20405	10	0.048
1969	19763	10	0.050
1970	25417	15	0.059

There has been a gradual rise, though not very significant statistically, in the incidence of the disease.

Socio-economic status

Except for one patient, all belonged to the low socioeconomic group. Similar observations have been made by Kandhari and Pasricha¹¹.

Age incidence

The distribution of age is shown in table I. 37 (69.8%) of the patients were in the age group of 30-59 years. 18 patients were in the age group of 20-39 years. Similar observations have also been made by Ambady et al¹²; Kandhari and Pasricha¹¹; Fernandez et al⁹ and is at variance with the findings of western authors (Combes and Canizares¹⁸; Director¹⁴; Lever^{15, 16}; Costello¹⁷; Sanders and Nelson¹⁸; Fernandez et al⁹ and Costello¹⁷ reported cases above 60 years of age as 5% and 80% respectively, while in the present study such cases were only 5 (9.4%). Disease affected 11 patients in the age group of 0-29 years. The youngest patient in the present series was a case of pemphigus vulgaris aged 7 years. Ambady et al¹² have reported a case in which the disease manifested at 5th year of life, probably the youngest patient in the literature. The youngest patient in the series of Kandhari and Pasricha¹¹ and Fernandez et al⁹ were of 9 and 16 years of age respectively. It is our experience that the disease manifests itself at a younger age in Indians.

Sex

Out of a total of 53 patients, 32 (60.4%) were males and 21 (39.6%) were

females. There were 27 males and 17 females with pemphigus vulgaris. In pemphigus foliaceus group, 4 were males and 2 females. There was one case each of pemphigus erythematosus in a female, pemphigus vegetans in a male and chronic benign pemphigus of Hailey and Hailey in a female, as shown in Table I. Similar findings

TABLE I

Type of pemphigus	Sex	Age in years							Total
		0-9	10-19	20-29	30-39	40-49	50-59	60-69	
Pemphigus vulgaris	M	—	—	4	7	5	7	4	27
	F	1	2	1	4	6	3	—	17
Pemphigus foliaceus	M	—	2	—	—	1	1	—	4
	F	—	—	—	—	1	1	—	2
Pemphigus erythematous	M	—	—	—	—	—	—	—	—
	F	—	—	—	1	—	—	—	1
Pemphigus vegetans	M	—	—	1	—	—	—	—	1
	F	—	—	—	—	—	—	—	—
Pemphigus of Hailey and Hailey	M	—	—	—	—	—	—	—	—
	F	—	—	—	—	—	—	—	—
Grand Total		M 32 + F 21 = 53							

Table 1 Age & sex incidence of pemphigus :
Maximum incidence was in the age group of 30-59 years and pemphigus vulgaris was the commonest type.

have been recorded by Ambady et al¹²; Kandhari and Pasricha¹¹ and Fernandez et al⁹. Pilsbury et al¹⁹ and Lever¹⁶ are of the opinion that pemphigus affects both the sexes equally. Higher incidence in males in India could be due to a larger number of male patients attending the hospital.

Symptomatology

In the initial stage of the disease, the subjective symptoms of itching, fever and burning were encountered. Itching was most common symptom present in 34.0% of the cases. Fever and burning sensation was present in 13.2% and 7.5% respectively (Table II). Similar observations have been recorded by Director¹⁴; Costello¹⁷; Perry²⁰ and Fernandez et al⁹. One patient of pemphigus vulgaris presented with clinical

features of dermatitis herpetiformis and on histopathology intra-epidermal bulla with acantholytic cells were classically seen.

Severity of Disease

In order to study the association between the severity of the disease, age and sex, the cases of pemphigus were divided arbitrarily into two groups, severe and moderate, depending upon the extent of involvement, its spread, toxæmia and fever, as under :

Based on above criteria, 16 cases (30.2%) were having severe type and 37 (69.8%) patients were fortunate enough to have the disease of moderate severity as shown in Table III. Out of 44 cases of pemphigus vulgaris, 14 were severe type and 30 were of moderate

Severe	Moderate
1. Rapid spread of disease within 3 months of onset	1. Slow evolution of disease over 6 months
2. Widespread skin involvement	2. Lesser skin involvement
3. Toxæmia & fever present	3. Little or no toxæmia

A CLINICOPATHOLOGICAL STUDY OF PEMPHIGUS

TABLE II

Symptoms	Type of pemphigus					Percentage
	Pemphigus vulgaris	Pemphigus foliaceus	Pemphigus erythematosus	Pemphigus vegetans	Pemphigus of Hailey & Hailey	
Itching	12	3	1	1	1	34.0
Fever	6	1	—	—	—	13.2
Burning	3	—	1	—	—	7.5

Table II. Symptoms associated with pemphigus :
Itching was the most common symptom.

TABLE III

	Pemphigus vulgaris	Pemphigus foliaceus	Pemphigus erythematosus	Pemphigus vegetans	Pemphigus of Hailey & Hailey	Percentage
Severe	14	2	—	—	—	30.2
Moderate	30	4	1	1	1	69.8
Total	44	6	1	1	1	

Table III. Severity of pemphigus cases :
Disease was mostly of moderate severity.

severity. Out of six cases of pemphigus foliaceus, two (33.3%) were of severe form. One case each of pemphigus erythematosus, pemphigus vegetans and chronic benign pemphigus of Hailey and Hailey of moderate intensity were also recorded as shown in Table III. This corroborates the findings of Fernandez et al⁹. It is our observation that pemphigus foliaceus is the severest variety of pemphigus, though its incidence is much less as compared to the pemphigus vulgaris.

Table IV shows the break up of 16 severe cases of pemphigus in relation to total number of cases in the same age group. It is clear from the table that if the disease appears early in life, it is likely to be of severe type especially in pemphigus foliaceus variety. This finding of ours is at variance with Rook and Wilkinson²¹, according to whom pemphigus is likely to run relatively benign course if it appears early in life. There was nothing to suggest that severity of the disease is related to sex.

TABLE IV

Type of pemphigus	Age in years			Total
	0—19	20—39	40 & above	
Pemphigus vulgaris	1(33.3%)	6 (37.5%)	7 (28.0%)	14
Pemphigus foliaceus	1(50.0%)	—	1 (25.0%)	2
Pemphigus erythematosus	—	—	—	—
Pemphigus vegetans	—	—	—	—
Pemphigus of Hailey & Hailey	—	—	—	—

Table IV. Break up of 16 cases of pemphigus in relation to total number of cases in the same age group. Pemphigus foliaceus in younger age between 0-19 years was severe in 50% cases, whereas it was severe in only 25% cases in older age group, 40 years and above.

Site of Onset of Disease

In cases of pemphigus vulgaris, disease first made its appearance on the oral mucous membrane in 16 (30.2%) patients, but oral mucosa was involved at one time or the other during the course of the disease in 34(77.3%) cases as shown in Table V. Similar findings have been reported by Director¹⁴; Lever¹⁵; Sander et al²²; Fernandez et al⁹. Oral mucosa was never involved in all other types of pemphigus in the present series. This finding is at variance with the observations of Lever¹⁵; Perry²⁰; and Kandhari and Pasricha¹¹, according to whom oral mucous membrane is involved in pemphigus foliaceus and erythematous also but to a much lesser extent. Scalp, extremities and trunk were sites of onset of the disease in 14 (26.4%) and 23 (43.4%) respectively.

TABLE V

Site of onset	Number of patients	Percentage
Oral mucous membrane	16	30.2
Scalp	14	26.4
Extremities and Trunk	23	43.4

Table V. Site of onset of pemphigus:

In approximately one third of patients oral mucous membrane was involved simultaneously with or prior to skin involvement.

Relapse

Since pemphigus is a chronic disease punctuated with exacerbations and remissions, inspite of systemic therapy with corticosteroids, an attempt was made to assess the cause of relapse in these patients. Table VI shows the causes of relapse. In 26 patients (78.8%) no obvious cause could be detected; perhaps it was natural course of the disease. In 4 patients (12.1%) relapse occurred because of treatment default.

TABLE VI

Causes of relapse	Number	Percentage
Unknown (Normal course)	26	78.8
Treatment default	4	12.0
Pregnancy	2	6.1
No relapse	1	3.0
Not followed up	20	—
Total	53	100

Table VI. Relapses of pemphigus—causes: In majority of cases, no cause of relapse could be found.

Treatment defaults may lead on to fulminating relapses as reported by Dharani et al²³ but no fulminating relapse due to treatment default was seen in the present series. Pregnancy precipitated relapse in 2 (6.1%) cases. This is in contrast to the findings of Sanitz et al²⁴, who observed the beneficial effect of pregnancy on the course of this disease especially in first and third trimesters of pregnancy. There is no relapse of the disease in one patient for the last 9 years and the patient is on a maintenance dose of one tablet of prednisolone only and is under surveillance. Similar observations have been made by other workers also (Reznick et al²⁵, Stevenson²⁶, Perry²⁰, and Dharani et al²³).

Prognosis

25 out of the total of 53 patients are regularly attending the follow up clinic at present; others have been very irregular.

All these 25 patients are on a maintenance dose of corticosteroids, 5 mg to 20 mg of prednisolone. It is very encouraging that 2 of our patients have been under treatment since the year 1962 and the disease is very much under control with maintenance dose of corticosteroids.

The prognosis of pemphigus has considerably improved with the advent of corticosteroids; mortality rate has

come down to about 30% (Reznick et al,^{2,5}). In our series, the mortality rate was 16.3% (5 deaths out of 30 patients with adequate follow up), which is less than that reported by Reznick et al^{2,5} and Dharani et al^{2,3}. The causes of death were toxæmia (3 patients), secondary infection (1 patient) and unknown (1 patient—he died at his residence).

Treatment

All the patients were treated initially with 40 mg of prednisolone per day, besides the supportive and local therapy. All but 8 patients showed considerable improvement. Initial controlling dose of 40 mg of prednisolone per day is considerably less as compared to a very high dose of prednisolone (120 mg-400 mg) used by the western workers (Reznick et al^{2,5}, Stevenson^{2,6}, Lever^{1,6}, Sanders and Nelson^{1,3}, Cronin and Calnan^{2,7}). Low controlling dose of prednisolone (30-40mg per day) in Indian patients of pemphigus have been reported by other Indian workers also. (Ambady et al^{1,2}, Kandhari and Pasricha^{1,1}, Dharani et al^{2,3}).

The remaining 8 patients who did not respond to 40 mg of prednisolone, were given a higher dose of 60 mg of prednisolone: 2 of them improved, but 6 were still unresponsive. However, 3 were controlled when ACTH (I.M) and blood transfusion were added to the therapy; while the other 3 were refractory to all treatment and further increase in dosage of prednisolone or its analogus and pursued a relentless downhill course and ultimately died. In such refractory cases Cronin and Calnan^{1,7} have reported very good results with ACTH, I.V drip, but the same could not be tried here because of its nonavailability.

Side effects

As corticosteroids are administered for prolonged periods to patients suffering from pemphigus, one expects the side effects in the bargain. The various side effects are given in Table VII. Moon facies, recurrent pyoderma, gastrointestinal disturbances, muscular wastings, acne form lesions, hypertension, diabetes etc. seen in the present series have also been reported by various workers (Reznick et al^{2,5}, Stevenson,^{2,6}, Ambady et al^{1,2}, Lever^{1,6}, and Dharani^{2,3} et al).

TABLE VII

S. No.	Side effects	No. of patients
1.	Pyoderma	26
2.	Monillial infection	6
3.	Lung infection	1
4.	Acute Septic Arthritis	1
5.	Moon facies	12
6.	Buffalo hump	4
7.	Acne form lesions	6
8.	Hirsutism	4
9.	Muscular wasting	7
10.	Gastro-intestinal disturbances	6
11.	Hypertension	3
12.	Diabetes	3
13.	Mental symptoms	2
14.	Odema	3
15.	Alopecia	2
16.	Bleeding disorders	2

Table VII. Side effects of corticosteroid therapy :
Pyodermas and moon facies were the commonest side effects encountered.

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