A clinico-pathological analysis of pemphigus from Teaching Hospital Kandy

M Dissanayake[1], W M Tilakaratne[2]

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Abstract

Pemphigus has been largely studied in developed countries (North America and Europe), Brazil and South Africa. Relatively little is known about pemphigus in most other parts of the world. We report a study of 33 cases of pemphigus observed at Teaching Hospital Kandy. Our cases of pemphigus were diagnosed on the basis of clinical, histological and direct immunofluorescence studies. We estimated the annual incidence in Central Province of Sri Lanka to be 0.64 per 100,000 inhabitants. The disease was more common in women (60.6%), with a mean age of 45 years. Our study group was composed of pemphigus vulgaris (PV) (94%); one case of pemphigus foliaceus (PF) and another case of subcorneal type of Ig A pemphigus. These data suggest that central parts of Sri Lanka has a low incidence of pemphigus foliaceus compared to other regions of the world.

Introduction

Pemphigus is an autoimmune intraepidermal blistering disease, which has a worldwide distribution. Pemphigus affects all races and both sexes[1,2]. Adults in their middle age are the mainly affected group[1]. Pemphigus affects children rarely, but with regard to the age of presentation, younger cases have been reported in India compared to the Western countries[3]. It is the most common immunobullous disease in Asian countries such as India, Malaysia, China and Sri Lanka[2-4]. Pemphigus is less common in North America, Europe and Israel; with an annual incidence rate varying from 0.3 cases per 100,000 to 1.62 per 100,000[1,2,4]. Pemphigus vulgaris (PV) accounts for 80% of all cases of pemphigus. Pemphigus foliacesus (PF) is less common in most parts of the world[1,2]. It accounts for 10-20% of all pemphigus cases in some areas of the world[1,2]. Endemic PF (fogo selvegem) which is common in rural Brazil may be triggered off by some environmental factors[1,2]. The incidence rate of this type can be as high as 5 cases per 100,000[1,2]. PF is more common than PV in some of the African countries such as Mali, Libya and Tunisia[2,3]. Pemphigus in South Asia is under-reported and thus it has been under-studied. This is a study of 33 cases of pemphigus diagnosed at Teaching Hospital Kandy (THK) over a period of 2 years from August 1999 to July 2001. In this prospective study we aimed to define the spectrum of pemphigus seen at the Teaching Hospital Kandy and to compare their clinico-pathological and epidemiological features with the reports from Sri Lanka and other regions.

Materials and methods

The study sample consisted of 33 cases of pemphigus clinically diagnosed at Teaching Hospital Kandy. The diagnoses were confirmed by histopathology and immunofluorescence at the Department of Oral Pathology, Faculty of Dental Sciences, University of Peradeniya. The criteria for inclusion of cases into the study were as follows;

i. a clinical history and signs compatible with autoimmune pemphigus.

ii. presence of intraepidermal acantholytic blisters on skin biopsy

iii. direct immunofluorescence (DIF) on perilesional skin showing deposition of immunoglobulins and/or complement 3 between keratinocytes.

A comprehensive case history was obtained from each patient. This included geographical and ethnic origin and examination for clinical signs. Skin biopsies were done in all the cases included in the study. According to the clinicopathological classification of pemphigus, patients were classified into PV (large denuded erosions and suprabasal acantholytic blister), and PF (clinically superficial blister, erythrodermic or localized in seborrhoeic areas, and superficial blister on biopsy). Perilesional biopsies were performed and they were frozen for direct immunofluorescence. All the specimens were assessed for the presence of IgG, IgM, IgA and C3.

[1] *Consultant Dermatologist, Teaching Hospital, Kandy.*
[2] *Senior Lecturer and Consultant in Oral Pathology, Faculty of Dental Sciences, University of Peradeniya.*
Corresponding author M. Dissanayake.

Results

During the study period, pemphigus was found to be the most frequent autoimmune bullous disease presented to our Institution. Patients were from both rural and urban areas. The incidence rate of pemphigus in the Central Province of Sri Lanka was estimated. 33 cases came from this region during a 2-year period. Since the estimated population in the Central Province for the year 2001 is 2.4 million, the estimated annual incidence rate was found to be 0.64 per 100,000.

There were 13 men and 20 women (male to female ratio 1:1.5). The main ethnic groups of Sri Lanka (Sinhalese, Sri Lankan Tamils, Indian Tamils and Muslims) was well represented in the study group. The most common ethnic group was Sinhalese (23 of 33). All patients belonged to low and middle socioeconomic classes.

In this study group consisting of 33 patients, PV was found to be the commonest (31 patients). One patient had PF and another patient had subcorneal type of IgA pemphigus. Age range for this group was from 8 to 83 years (mean 45). An eleven year old girl had PF. The lesions had small flaccid bullae, scales and crusts were mainly limited to the trunk. A 42-year-old male previously diagnosed as subcorneal pustular dermatosis was subsequently diagnosed as IgA pemphigus by DIF on perilesional skin. Five patients of PV had only oral lesions. PF patient and subcorneal type IgA pemiphigus patient did not have any oral lesions.

Histopathological findings

Acantholysis was always prominent. All the lesions were classified according to the level of split. PV showed supra basal clefts and PF lesion had clefts in superficial layers of the epidermis (under the granular cell layer). Subcorneal acantholytic pustules containing neutrophilic polymorphonuclear cells were seen in the lesion of subcorneal type of IgA pemphigus patient. Eosinophils in the dermis were a frequent feature. Histological subtype agreed with the clinical classification.

All patients with PV and PF showed depositions between keratinocytes of IgG and/or C3. In addition deposits of IgA were present in two patients and IgM in one patient with PV. The patient with subcorneal of IgA pemphigus showed IgA deposition in the upper layer of epidermis.

Course and treatment

The follow up period varied from 3 months to 2 years. All patients were treated with oral corticosteroids (prednisolone) with initial doses ranging from 30mg to 75mg per day. Four patients with PV and patients with PF and IgA pemphigus were also put on dapsone 50-100mg/day. 13 had adjuvant therapy with azathiaprin (50-100mg/day). 12 patients had adjuvant therapy with cyclophosphamide of which 7 had dexamethasone/cyclophosphamide pulse therapy. Up to date, 25 patients with PV were in partial remission i.e. requiring a prednisolone dose of less than 15 mg for control for more than 1 month. At the time of writing PF patient was on remission with 50mg of dapsone. Four cases of PV had active disease requiring a prednisolone dose of 15mg/day or more.

If a patient had new bullae formation and/or erosions after a period of remission requiring an increased dose of corticosteroids, to stop new blister formation or if steroid therapy had to he reinstituted upon discontinuation to control blister formation; the situation was regarded as a "relapse". Thus 11 patients (34%) with PV were reported as relapses after initial disease remission.

Side effects of corticosteroids were seen in 14 patients. These included diabetes mellitus, hypertension, heart failure, oesophageal candidiasis and phychosis. One patient in the study group developed hepatitis following azathiaprin and another developed fever due to cyclosphosphamide. A 75-year-old ischaemic heart disease patient died during the study.

Among the patients with PV in this study one had ocular myasthenia without any evidence of thymoma. One patient had grand mal epilepsy and was treated with phenytoin sodium. One had pre-existing hypertension and another patient had pre existing ischaemic heart disease. One had chronic plaque type psoriasis. There were no patients with pemphigus-associated malignancy.

Discussion

Our study showed that pemphigus in Sri Lanka was apparently as frequent as that in North America or Europe. Data on incidence were difficult to analyse as the Teaching Hospital Kandy is the only institution having a specialized unit in dermatology for the Central Province and it is likely that some patients of pemphigus could have been undiagnosed or treated by other practitioners. Thus the annual incidence rate of 0.6 cases per 100,000 was probably an underestimation. However this incidence was more comparable with that from North America than that from endemic areas of Brazil, where it was reported to be upto five cases per 100,000[1,2]. As our patients were from all over the province without any familial cases, an epidemiological pattern more of the North American/European type can be suggested rather than Brazilian type. In a previous study in Sri Lanka, Sirimanna has reported

that 59% of all autoimmune bullous diseases were due to pemphigus with 86% of pemphigus cases being due to pemphigus vulgaris. Sirimanna has estimated an annual incidence of 0.3 per 100,000 population[4].

The male to female ratio, which was 1:1.5 in our study, differed from the usual ratio 1:1 encountered in Europe and in Brazil[1,2]. A previous Sri Lankan study too had recorded a high female preponderance[4]. Two studies with similar male to female ratio have been reported from Europe[6]. Very high incidence of PF (54%) with a male to female ratio of 1:1.7 had been reported in South Africa[5]. Pemphigus patients in our study consisted mainly of PV (94%). Incidence of PF in this study was very low (3%). Mean age of onset of symptoms of our study was 45 years. There were two children aged 8 and 11 years. The 8 year old patient had severe disease with extensive oral ulceration. Patient was treated with prednisolone 45mg daily, cyclophosphamide 50mg daily and dapsone 50mg daily. The other patient had mild disease mainly confined to the trunk without any mucosal lesions with a histology suggestive of PF. Patient was treated initially with prednisolone 30mg daily and subsequently disease was controlled on dapsone 30 mg daily. One patient presented at 83 years of age. He was treated intially with prednisolone 5mg on alternative days. In most previous studies PV has shown to be a disorder of middle to late life and rare in juvenile patients and after the eighth decade[6]. In the present study one patient had myasthenia gravis. PV may be associated with other autoimmune disorders such as rheumatoid arthritis, myasthenia gravis, lupus erythematosus or pernicious anaemia, drugs with active thiol groups in the molecule, such as penicillamine and captopril and even garlic can induce PV[6]. The average duration of illness at the time of diagnosis was 4 months. The delay in diagnosis probably reflects a low index of suspicion among primary care practitioners leading to consequent late referral to the dermatologist.

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