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Review Article

Bullous pemphigoid: a 7-year survey on 75 Chinese patients in Hong Kong

大疱性類天疱瘡：7 年期 75 例的研究

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Bullous pemphigoid is the most common immunobullous disease affecting the elderly. It typically presents clinically as well formed blisters and histopathologically shows sub-epidermal blistering. The present study reviewed 75 cases of newly diagnosed bullous pemphigoid at a dermatology clinic in a seven years period. The incidence of bullous pemphigoid was 15.6 per million per year. The average age was 79.6. Forty-eight percent of the patients presented with generalised bulla.

大疱性類天疱瘡是長者最常見的自身免疫性大疱性病。患者臨床上多呈現完整大疱。皮膚組織病理檢查呈現表皮下水疱。本文就一所皮膚科診所在 7 年期間的 75 宗病例進行研究。每年病發率為百萬份之 15 點 6 ，平均年齡為 79.6 歲。 48% 的患者呈泛發性大疱。

Keywords: Bullous pemphigoid

關鍵詞：大疱性類天疱瘡

Introduction

Bullous pemphigoid (BP) is a sub-epidermal disease affecting mainly the elderly. It usually presents as well formed, tense blisters on the lower abdomen, anterior thighs and flexor forearms. It is characterised by the immunopathologic findings of C3 and IgG along the dermo-epidermal junction. The incidence of bullous pemphigoid is estimated to be 7 per million per year in both France[1] and Germany.[2] However, local data on the incidence of bullous pemphigoid are scarce.

The objective of the study was to investigate the epidermiology of bullous pemphigoid seen at a dermatology clinic in Hong Kong.

Patients and methods

The skin biopsy records of all patients at Chai Wan Social Hygiene Clinic from 1st January, 1998 to 31st December, 2004 were reviewed. Patients with the biopsy reported as consistent with bullous pemphigoid, compatible with bullous pemphigoid and suggestive of bullous pemphigoid were included in the study.

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The following data were extracted from the medical records: patients' demographic, associated medical illnesses and investigation results.

Results

Demographics

Seventy-five new cases of bullous pemphigoid were diagnosed during the study period. The female to male ratio was approximately 1.2:1 (41 females and 34 males). The mean age of onset of disease was 80 (range 45-98) (Table 1). Approximately half of patients (52%) lived at home (Table 2).

Clinical presentation

Thirty-six patients had generalised bullous pemphigoid, involving trunk and limbs. Thirty-nine patients had localised bullous pemphigoid, involving only one body part. Only one of them had oral erosion (Table 3).

Duration of symptom onset to the first consultation

The average duration of symptom onset to the first consultation at Chai Wan Social Hygiene Clinic was 45.3 days. The longest duration of symptom onset to the first consultation was 730 days, whereas the shortest one was 1 day. For the generalised bullous pemphigoid, the duration of symptom onset to the first consultation was 31.9 days (Table 4).

Associated medical illnesses

Approximately half of the patients had hypertension. One third of patients had cerebrovascular accident. The other associated medical illnesses were shown in Table 5.

Histology and immunopathology

Histology showed sub-epidermal blistering in all cases. Seventy-one patients showed linear deposits

Table 1. Demographics of patients with bullous pemphigoid

	Male	Percentage	Female	Percentage
Sex	41	45.3	34	54.7
	Min	Mean	Max	S.D.
Age	45	79.6	98	9.8

Table 2. Patients' living conditions

	Home	Percentage	OAH	Percentage
Living environment	39	52	36	48

OAH = old aged home

Table 3. Clinical presentation

	Number	Percentage
Generalised	36	48
Localised	39	52
Oral lesion	1	1.3

Table 4. Duration of symptom onset to the first consultation

	Generalised	Localised
Duration (Days)	31.9	57.7

t test, p = 0.397

Table 5. Associated medical illnesses

	Number	Percentage
Hypertension	35	46.7
Cerebrovascular accident	26	34.7
Ischaemic heart disease	18	24
Dementia	18	24
Diabetes mellitus	18	24
Cancer	7	9.3
Chronic chest condition	4	5.3

of C3 and/or complement at the dermo-epidermal junction. Direct immunofluorescence were absent in four patients because the epidermis was absent. The diagnoses of these cases were based on the clinical features, histology and indirect immunofluorescence. Indirect immunofluorescence were done in 50 patients. Forty-seven of them showed positive indirect immunofluorescence (Table 6).

Discussion

Chai Wan Social Hygiene Clinic provides dermatological services to people living in the Eastern District in Hong Kong Island. Eastern District has a population of 0.689 million. As a result, the incidence of bullous pemphigoid in Hong Kong would be more than 15.6 per million per year. This was the minimum estimate as patients with bullous pemphigoid could consult dermatologists in the private sectors. The figure was much higher than the studies reported from France[1] and Germany.[2] The incidence was twice than that of the figure – 7.6 per million per year, reported from Singapore.[3] This contradicts the belief that bullous pemphigoid is rarer in the Far East than in Western Europe.[4]

Our results showed that bullous pemphigoid was more common in the elderly population, with only a slight female predominance. The results are in keeping with a study from Singapore.[3] The reasons for the higher incidence in the elderly are not known. Some reports showed that altered immune regulation with aging might contribute to the development of bullous pemphigoid.[5] The portion of memory T cells increases with aging and they have a predilection towards the Th2 cytokine profile. These changes in immune system may lead to loss of self-tolerance and contribute to the generation of autoimmune process against the skin basement membrane antigen.[6]

Our study showed no major difference in the incidence of bullous pemphigoid between patients living at home and in the old aged home. This suggests that the incidence of bullous pemphigoid may not be related to the living environment.

Generalised bullous pemphigoid accounted for 48% in our series. Mucosal involvement was rare is our study (~1 %) which was similar to the finding in other study.[5] The longest duration of symptom onset to the first consultation was 730 days. This suggests that bullous pemphigoid may be neglected by patients or overlooked by attending doctors. Bullous pemphigoid should be attended as soon as possible as it is associated with high mortality rates, particularly the elderly population. In one study, the first year mortality rate was 41%.[7] Although patients with generalised disease consulted the doctors earlier than those with localised disease, there was no significant difference in the duration of symptom onset to the first consultation between the two groups.

The most frequently associated medical illnesses were hypertension, cerebrovascular accident, ischaemic heart disease, dementia and diabetes mellitus. A case control study also reported a

Table 6. Immunofluorescence study

Immunofluorescent study	Positive	Percentage	Negative	Percentage	Not done	Percentage
Direct immunofluorescence	71	94.7	4	5.3	0	0
Indirect immunofluorescence	47	62.7	3	4	25	33.3

higher prevalence of diabetes in patients with bullous pemphigoid before prescription of corticosteroids than the controls.[8] The underlying reason was not known. Seven patients (9.3%) in our sample had associated malignancies. This was similar to that of Singapore (6.8%).[3] There is still no consensus on whether bullous pemphigoid is associated with a higher incidence of malignancy. A Japanese Study reported an increased incidence of malignancies, particular the gastric cancer in patients with bullous pemphigoid.[9] However, a Swedish study showed no difference in the incidence of malignancies between patients with bullous pemphigoid and the controls.[10]

The histological findings were classical in all cases. They showed subepidermal blisters with dermal eosinophilic infiltrate. Direct immunofluorescence were positive in almost all cases. Only four cases were negative for direct immunofluorescence. It may be due to the fact that the blisters are biopsied rather than the perilesional skin. Indirect immunofluorescence tests were positive in 94% of patients tested. This may suggest that indirect immunofluorescence could be a useful tool for supporting the diagnosis of bullous pemphigoid if skin biopsy cannot be performed.

Limitations

Our study investigated the epidermiology of patients with bullous pemphigoid living in the Eastern district of Hong Kong Island only. This might not represent the situation in Hong Kong. As the study involved retrospective review of medical records, some of the information are incomplete. Further prospective study with a larger sample is thus recommended.

Conclusion

In conclusion, we reported a relatively high incidence of bullous pemphigoid in Hong Kong. The other epidermiological factors were similar to that of other countries. The duration between the onset of symptom and the first consultation was long. Front line doctors should be more aware of the condition and the possibility should always be considered in elderly presented with blisters. Direct immunofluorescence was important in the diagnosis of bullous pemphigoid. The high positivity of indirect immunofluorescence in our study suggests that indirect immunofluorescence may be a useful tool for supporting the diagnosis of bullous pemphigoid.

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