ORIGINAL ARTICLE

Histological differentiation between palmoplantar pustulosis and pompholyx

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Abstract

Background Palmoplantar pustulosis (PPP) is a chronic and intensely inflammatory skin disease with pustules, erythema and scaling localized to the palms and soles. Pompholyx is characterized by recurrent crops of vesicles on the lateral aspects of the fingers and the palms and soles. Because both PPP and pompholyx share similar clinical and histological features, it is difficult to differentiate between these two diseases even for dermatologists.

Objective To compare the histological features of PPP and pompholyx and to analyse their clinical characteristics.

Methods The clinical history from 45 patients with PPP and 42 with pompholyx was evaluated. Among these patients, the punch biopsies from acute lesions of 40 PPP patients and 35 pompholyx ones were analysed, blind to the clinical diagnosis.

Results There was no sexual predilection in either group, and 65.5% of PPP patients had smoking history. About half of the patients had concomitant palmoplantar lesions in PPP and pompholyx respectively. In histological evaluation, loss of granular layer, suprapapillary plates thinning, eosinophils in the pustules or vesicles, tortuous capillaries, capillaries touching the undersurface of epidermis and extravasated erythrocytes were statistically significant features of PPP. Confluent parakeratosis, psoriasiform epidermal hyperplasia, clubbing and anastomosing of the rete ridges favoured PPP. Meanwhile, multiple foci of parakeratosis, irregular epidermal hyperplasia and thinning of rete ridges were more often observed in pompholyx. However, dyskeratotic cells, papillary dermal oedema, dilated capillaries and acrosyringium were not significantly different between the two diseases.

Conclusions Several histological features could serve as useful 'clues' to differentiate between PPP and pompholyx.

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Conflict of interest

None declared.

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Introduction

Palmoplantar pustulosis (PPP) is a chronic, sometimes disabling condition characterized by pustules, erythema and scaling on the soles and palms.[1] Meanwhile pompholyx or palmoplantar dyshidrosis is a chronic relapsing form of vesicular palmoplantar dermatitis of unknown aetiology. Dyshidrotic eczema is characterized by the formation of small, fluid filled vesicles or bullae that appear suddenly in the affected areas, most commonly the edges of the fingers, toes, palms and soles.[2] Both PPP and pompholyx commonly present as palmoplantar vesicles or pustules. Moreover, these two diseases share similar histological features as well as similar clinical features. Pustules may be present in pompholyx in early stage or within a few days, and PPP may present with pruritus at onset.[3] Moreover, both diseases have common histological features such as epidermal hyperplasia, parakeratosis and spongiosis. Therefore, the differential diagnosis of these two diseases can be quite frustrating even for dermatologists. Since untreated pompholyx and PPP can easily result in infection and impede quality of life, early recognition and proper management is critical. Because the effective treatment for each disease is quite different, differential diagnosis is important.

The aim of our study was to analyse the histological features of PPP and pompholyx which may be of benefit in their differentiation.

Materials and methods

Patients

The patients, who presented with vesicles or pustules on palm(s) and/or sole(s) in our outpatient clinic from January 1 2006 to June 30 2011 were taken in the study group. Medical records of

each patient were reviewed retrospectively. The clinical photo and patient's information were collected about age, gender, disease onset, duration, treatment, recurrence, smoking history and other diseases, etc. The patients were divided into PPP group and pompholyx group based on clinical information such as location and size variation of lesions, severity of itching sense and responses to treatment. The similar-sized lesions which responded well to oral vitamin A and topical vitamin D agent were diagnosed as PPP. On the other hand, vesicular lesions of variable sizes with itching sense throughout the disease process, and with involvement of digital area as well as palmoplantar area were diagnosed as pompholyx. Presumptive dermatophyte infection was eliminated by direct examination with KOH. A total of 87 patients grouped into 45 cases of PPP and 42 cases of pompholyx were included to our study. Among these patients, the 3-mm or 4-mm punch biopsies were taken from acute vesicular lesions of 40 PPP patients and 35 pompholyx ones. Biopsies were fixed in 10% formaldehyde and embedded in paraffin. Five millimetre-thick serial sections from each biopsy were taken and stained with haematoxylin-eosin (HE).

Evaluation of the histopathological findings

According to the checklist of histological parameters (Table 1), HE-stained sections were studied by two dermatopathologists (Cho, Yoon), blind to clinical diagnosis. The histological parameters were established according to the features that were considered helpful in the diagnosis of psoriasis in literature.[4] These parameters had been also used to differentiate non-pustular palmoplantar psoriasis from eczematous dermatitis.[5]

Statistical analysis

Chi-square and Fisher's exact tests were performed to check whether or not any of these histological parameters were useful in the differential diagnosis. Multivariate logistic regression analysis with stepwise selection procedure was done using statistically significant parameters in Chi-square and Fisher's exact test. All data were analysed using SPSS 18.0K for window. A *P*-value less than 0.05 was considered statistically significant.

Based on the sample size and result of Chi-square and Fisher's exact test, power analysis was conducted and appeared as 95.8%.

Table 1 The histological features of PPP and pompholyx

Histological features	Palmoplantar pustulosis *N* (%)	Pompholyx *N* (%)	*P*-values
Presence of parakeratosis	34/40 (85.0)	17/35 (48.6)	<0.001
Multiple foci of parakeratosis*	5/34 (14.7)	10/17 (58.8)	<0.001
Confluent parakeratosis*	29/34 (85.3)	7/17 (41.2)	<0.001
Vertical alternation of parakeratosis and orthokeratosis*	7/34 (20.6)	5/17 (29.4)	0.503
PNL at the summits of parakeratosis*	0/34 (0.0)	1/17 (5.9)	0.333
Only plasma in the parakeratotic foci*	1/34 (2.9)	1/17 (5.9)	1.000
Plasma and PNL in the parakeratotic foci*	18/34 (52.9)	6/17 (35.3)	0.234
Loss of granular layer	31/40 (77.5)	15/35 (42.9)	0.002
Psoriasiform epidermal hyperplasia	30/40 (75.0)	12/35 (34.3)	<0.001
Irregular epidermal hyperplasia	9/40 (22.5)	23/35 (65.7)	<0.001
Thinning of rete ridges	1/40 (2.5)	6/35 (17.1)	0.045
Clubbing and anastomosing of the rete ridges	39/40 (97.5)	27/35 (77.1)	0.010
Full-thickness spongiosis	5/40 (12.5)	23/35 (65.7)	<0.001
Spongiosis at the lower part of the epidermis	3/40 (7.5)	1/35 (2.9)	0.618
Spongiotic vesicle	2/40 (5.0)	20/35 (57.1)	<0.001
Dyskeratotic cells	6/40 (15.0)	4/35 (11.4)	0.742
Thinning of the suprapapillary plates	18/40 (45.0)	5/35 (14.3)	0.004
Oedema of the papillary dermis	2/40 (5.0)	1/35 (2.9)	1.000
Tortuous capillaries in the papillary dermis	25/40 (62.5)	8/35 (22.9)	<0.001
Capillaries touching the undersurface of epidermis	31/40 (77.5)	17/35 (48.6)	0.009
Dilated capillaries in the papillary dermis	37/40 (92.5)	27/35 (77.1)	0.100
Extravasated erythrocytes	18/40 (45.0)	7/35 (20.0)	0.022
Eosinophils in the upper dermis	11/40 (27.5)	10/35 (28.6)	0.918
Eosinophils in the pustule or vesicle†	6/13 (46.2)	2/18 (11.1)	0.043
Presence of acrosyringium	21/40 (52.5)	25/35 (71.4)	0.093

*Histological feature evaluated in the cases of 'presence of parakeratosis' (34 cases of PPP and 17 cases of pompholyx).
†Histological feature evaluated in the cases of existence of pustule or vesicle (13 cases of PPP and 18 cases of pompholyx).
PNL, polymorphonuclear leucocytes.

Results

Clinical findings

Of the 45 patients with PPP included in the study, 24 were men and 21 women, with mean age of 51.5 years (range 20–81 years). Among the 42 pompholyx patients, there were 21 men and 21 women, with a mean age of 45.7 years (range 7–77 years). The onset age was 48.5 years (range 20–79 years) in PPP and 43.6 years (range 7–76 years) in pompholyx.

Some patients were asked about smoking history and 65.5% (19/29cases) of PPP and 53.1% (17/32cases) of pompholyx were past or current smokers. There was no statistically significant difference between the two diseases ($P = 0.326$).

We also evaluated the localization and symmetry of the lesions. Lesions were 48.9% palmoplantar (22/45), 15.6% palmar (7/45) and 35.6% plantar (16/45) in PPP patients. In pompholyx cases, they were 59.5% palmoplantar (25/42), 21.4% palmar (9/42) and 19.0% plantar (8/42) (Fig. 1). In addition, 80.0% (36/45) of PPP patients and 88.1% (37/42) of pompholyx patients had bilateral skin lesions. However, there was no statistical significance in localization and symmetry of lesions.

Histological findings

Histological features of both PPP and pompholyx are shown in Table 1. The parakeratosis was seen more frequently in PPP [85.5% (34/40)] compared with pompholyx [48.6% (17/35), $P = 0.001$]. Confluent parakeratosis (Fig. 2a) was found to be more common in PPP whereas parakeratosis presenting in multiple foci (Fig. 3a) was significantly more common in pompolyx. However, vertically situated multiple foci of parakeratosis alternating with orthokeratosis, were not different between two diseases. Furthermore, presence of neutrophil and/or plasma at the summits of parakeratosis was not significantly different. Loss of granular layer (Fig. 2a) was seen in the majority of PPP patients [77.5% (31/40)], whereas it was present in 42.9% of the patients with pompholyx (15/35). Psoriasiform epidermal hyperplasia (Fig. 2b) was more frequent in PPP than in pompholyx [75.0% (30/40) and 34.3% (12/35), respectively, $P = 0.000$]. However, irregular epidermal hyperplasia (Fig. 3a) was detected in pompholyx more often than in PPP [65.7% (23/35) and 22.5% (9/40), respectively, $P = 0.000$]. When the width of rete ridges became narrower going down into the deeper dermis, it was considered as thinning of rete ridges (Fig. 3b). Thinning of rete ridges was only seen in one patient with PPP and six patients with pompholyx. Clubbing and anastomosing of rete ridges (Fig. 2b) were a frequent finding in both PPP [97.5% (39/40)] and pompholyx [77.1% (27/35)] but there was statistically significant difference ($P = 0.010$). In more than half of the pompholyx cases, full-thickness spongiosis (65.7%) and spongiotic vesicles (57.1%) (Fig. 3b) could be found. Thinning of suprapapillary plate was detected only in half of the cases with PPP [45.0% (18/40)] but it was a significantly different feature compared with pompholyx [14.3% (5/35), $P = 0.004$]. On the other hand, dyskeratotic cells and papillary dermal oedema were seen in similar ratio in both groups. With regard to vascular change, presence of tortuous capillaries in the papillary dermis (Fig. 2c) was more frequent in patients with PPP [62.5% (25/40)] than in patients with pompholyx [22.9% (8/35), $P = 0.001$] and capillaries touching the undersurface of epidermis was also seen more often in PPP [PPP: 77.5% (31/40), pompholyx: 48.6% (17/35), $P = 0.009$]. Dilated capillaries in the papillary dermis were seen in almost all cases of PPP [92.5% (37/40)] but it was a quite common finding in pompholyx as well [77.1% (27/35)]. Extravasated erythrocytes [45.0% (18/40)] and eosinophils in the pustules or vesicles [46.2% (6/13)] were detected more often in PPP. Eosinophils in the upper dermis were almost in equal ratios in both groups [27.5% (11/40) in PPP and 28.6% (10/35) in pompholyx group]. Moreover, the presence of acrosyringium was not significantly different between the two diseases, with 52.5% in PPP vs. 71.4% in pompholyx.

In multivariate analysis (Table 2), PPP was more likely to reveal loss of granular layer (OR, 6.583; $P = 0.006$). On the other hand, histological features of 'irregular epidermal hyperplasia' and 'spongiotic vesicle' were negative for PPP, which means more association with pompholyx ($P = 0.027$, $P < 0.001$ respectively).

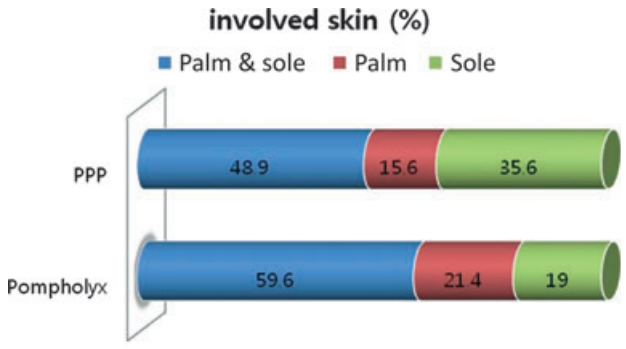

Figure 1 Lesions were 48.9% palmoplantar (22/45), 15.6% palmar (7/45) and 35.6% plantar (16/45) in PPP patients. In pompholyx cases, they were more often palmoplantar [59.5% (25/42)] and palmar [21.4% (9/42)], and less often plantar [19.0% (8/42)].

Discussion

Palmoplantar pustulosis is a chronic and intensely inflammatory skin disease with pustules, erythema and scaling localized to the palms and soles. In our study, the demographic and clinical characteristics were analysed. The onset age was 48.5 years (range 20–79 years) in PPP. It is consistent with previous medical literature.[6] The greater frequency of women among PPP patients was observed before in other occidental studies with ratios between 3.3 and 19 to one male patient.[7] However, the gender incidence was not so marked in Japanese and Arab studies because women's smoking habit was less frequent in these cultures. In our PPP

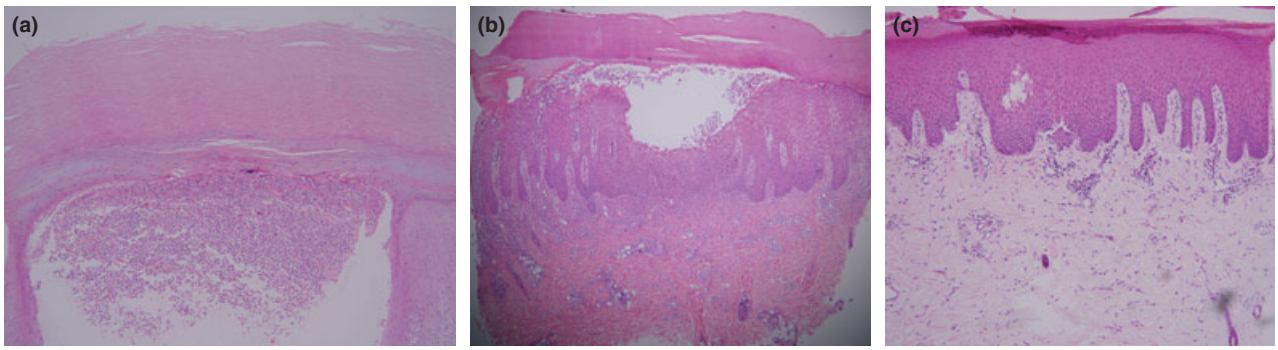

Figure 2 Histological features of PPP. (a) confluent parakeratosis and loss of granular layer (×100) (b) psoriasiform epidermal hyperplasia with clubbing and anastomosing of rete ridges (×40) (c) dilated and tortuous capillaries in the papillary dermis (×100).

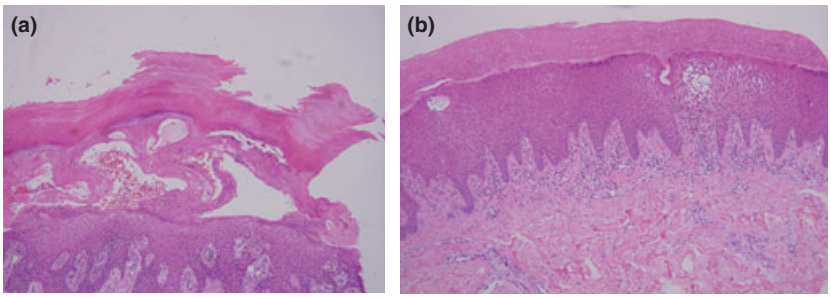

Figure 3 Histological features of pompholyx. (a) multiple foci of parakeratosis and irregular epidermal hyperplasia (×100) (b) thinning of rete ridges and spongiotic vesicles (×100).

Table 2 Multivariate logistic regression for PPP (reference group: pompholyx)

Histologic features	Odds ratio	95% CI	*P*-values
Loss of granular layer	6.583*	(1.720–25.204)	0.006
Irregular epidermal hyperplasia	0.232†	(0.064–0.846)	0.027
Spongiotic vesicle	0.031†	(0.005–0.185)	<0.001

*Histological feature favoured PPP more than pompholyx.
†Histological features favoured pompholyx more than PPPx.

patients, M : F ratio was 1.14:1 and it may be attributed to smoking habit difference. In Korea, 39.0% of men were smokers but only 1.8% of women were in 2011. PPP patients have been reported to smoke more than healthy subjects. In our study 65.5% (19/29 cases asked about smoking history) patients were smokers or ex-smokers at the onset of the PPP disease. In Korea, mean smoking ratio was 20.2% in 2011. Similar figures were reported by Eriksson *et al.*[6] In countries where the frequency of smoking in the general population is less than 25%, the occurrence of 50% of smokers in the PPP group could be as significant as finding incidences of 95%–100% in the European PPP group, where over 40% of the population are smokers.[8,9] These associations may be explained by nicotinic receptors and enzyme choline acetyltransferase overexpressed in lesional skin. The expression of both can be significantly upregulated by smoking.[10,11] In the present study, the skin lesions involved palm and sole in 48.9% (22/45cases). Eriksson *et al.*[6] also documented that 27 of 39 (69.2%) PPP patients had concomitant palmoplantar lesions.

Pompholyx is a common disorder characterized by recurrent crops of vesicles or bullae on the lateral aspects of the fingers and the palms and soles. It has been reported that the peak age of pompholyx is between the ages of 30 and 40 years and the female–male ratio was 1.18 in 120 patients.[12] In the present study, the onset age was slightly older (43.6 years) than that reported in previous literature and the female–male ratio was 1:1. Concerning smoking in the present study 53.1% (17/32 cases asked about smoking history) of patients smoked. This is quite high compared with the mean smoking ratio in Korea, 20.2%. It is consistent with the epidemiological observations of Edman.[13] In other studies, 48.3% of the 120 pompholyx patients had smoked, compared with 28.0% of the controls. The smoking may act as an aggravating factor or is related to pathogenesis, and further studies will be needed. Guillet *et al.* demonstrated that lesions were palmar (70.0%), plantar (10.0%), or palmoplantar (20.0%).[12] However, more than half of the cases involved both palms and soles in our study.

There have been few studies on histological difference between PPP and pompholyx. The differentiation is particularly difficult when there are pustules in pompholyx patients because of secondary infection, or when the PPP patients have mild itching sense. The characteristic histological features of a PPP lesion are represented by a large intra-epidermal unilocular pustule due to intense accumulation of neutrophils and also eosinophils below the stratum corneum.[6] The surrounding skin shows the epidermal changes seen in psoriasis vulgaris such as parakeratosis, loss of granular layer, psoriasiform epidermal hyperplasia, thinned suprapapillary plate and spongiform pustule at the upper epidermis.[4] It was also stated that the features helpful in differentiating pompholyx from PPP were spongiosis and intraepidermal vesiculation in acute phase and acanthosis and parakeratosis in chronic phase.[3] Since histological features change in the life of each lesion in both diseases, we took skin samples from only fresh acute vesicular lesions.

Parakeratosis is common to many diseases where there are changes within the epidermis, but several patterns of parakeratosis may be helpful clues in differential diagnosis. For example, confluent parakeratosis is frequently seen in psoriasis and Bowen's disease whereas focal parakeratosis is seen in most of the 'eczemas'.[14] In the present analysis, confluent parakeratosis was found to be more common in PPP (PPP: 85.3%, pompholyx: 41.2%, $P = 0.001$) whereas parakeratosis in multiple foci was displayed in 58.5% of pompolyx but in 14.7% of PPP. Therefore, the pattern of parakeratosis is also a helpful feature in the differential diagnosis.

Hypogranulosis is a general finding in psoriasis. Seventy-seven per cent of our PPP patients revealed loss of granular layer. Although 'hyper'granulosis was the expected feature in the eczematous dermatitis, in 42.9% of pompholyx patients, absence of granular layer was detected. Consequently, we should be cautious in interpretation.

Clubbing and anastomosing of the rete ridges were detected in 97.5% of PPP patients, and these features were significantly common findings. However, pompholyx cases also had them in 77.1%, especially in chronic phase.

Presence of acrosyringium was also evaluated, but there was no statistical significance (52.5% of PPP vs. 71.4% of pompholyx). In a previous report, the acrosyringium was not detectable in any of the specimens from 22 patients with PPP but was present in all the nine control persons.[6] A more recent study demonstrated involvement of acrosyringium in PPP vesicle formation using EMA staining of horizontal sections.[15] Therefore acrosyringium was considered a main site of the vesicle and pustule formation in PPP. On the other hand, pompholyx has been reported as primarily a spongiotic dermatitis and the intraepidermal eccrine ducts were spared from spongiosis and exocytosis.[16] Regarding acrosyringial involvement in the two diseases, no direct comparison has been performed using vertical sections, and our results indicate primary or secondary acrosyringial involvement in both diseases.

In conclusion, according to our findings, several histological features could serve as useful 'clues' to differentiate between PPP and pompholyx. In PPP patients, some characteristics such as confluent parakeratosis, psoriasiform epidermal hyperplasia, clubbing and anastomosing of the rete ridges, loss of granular layer, tortuous capillaries in the papillary dermis, capillaries touching the undersurface of epidermis and extravasated erythrocytes were found to be statistically significant in favour of PPP. On the other hand, multiple foci of parakeratosis, irregular epidermal hyperplasia, full-thickness spongiosis, spongiotic vesicle and thinning of rete ridges were more often observed in pompholyx. Absence of acrosyringium is not a useful diagnostic clue of PPP. Additional research is needed to elucidate pathophysiology and origin of vesicles and pustules in pompholyx and PPP.

Acknowledgement

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