



Evaluation of PLEVA and PLC Patients: Two Decades of Clinical Experience

PLEVA ve PLK Hastalarının Değerlendirilmesi: Son 20 Yıllık Deneyimlerimiz

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ÖZET

AMAÇ: Bu çalışmanın amacı, pityriasis likenoides tanısı alan hastaların klinik ve demografik özellikleri ile histopatolojik bulgularını değerlendirmek; pediatrik ve erişkin hasta grupları arasındaki farklılıkları analiz etmektir.

GEREÇ VE YÖNTEM: 01.08.2004-01.08.2024 tarihleri arasında Ankara Eğitim ve Araştırma Hastanesi Dermatoloji Polikliniği'nde takip edilen 47 pityriasis likenoides hastasının verileri retrospektif olarak incelendi. Hastalar pityriasis likenoides kronika ve pityriasis likenoides et varioliformis akuta olarak sınıflandırıldı. Klinik, demografik ve histopatolojik özellikler ile tedavi yanıtları değerlendirildi. Hastalar pediatrik (<18 yaş) ve erişkin (≥18 yaş) gruplarına ayrılarak karşılaştırıldı. İstatistiksel analizlerde p<0.05 anlamlı kabul edildi.

BULGULAR: Hastaların %66'sı kadın, %34'ü erkek olup yaş ortalaması 35.28±18.96 yıl idi. Medyan hastalık süresi 14 ay, medyan tanı süresi 3 ay olarak belirlendi. En sık etkilenen bölgeler gövde ve ekstremitelerdi (%68.1). Hastaların %42.6'sında relaps görüldü. En sık saptanan histopatolojik bulgular perivasküler lenfosit infiltrasyonu (%87.8) ve lenfosit ekzositozu (%80.5) idi. Hastaların tümüne topikal kortikosteroid tedavisi verildi; %95.7'sine dar bant UVB fototerapisi uygulandı. Tam yanıt %40.4, kısmi yanıt %51.1 olup %8.5'inde tedaviye yanıt alınmadı. Pediatrik hastalarda hastalık süresi erişkinlere göre anlamlı olarak daha kısa iken (p=0.026), tanıya kadar geçen süre erişkinlere kıyasla anlamlı derecede kısa bulundu (p=0,039).

SONUÇ: Pityriasis likenoides hastalığının erişkinlerde daha uzun sürdüğü, pediatrik hastaların daha erken tanı aldığı saptandı. Topikal kortikosteroid ile dar bant UVB fototerapisi kombinasyonu ve gerekli olgularda tedaviye antibiyoterapi eklenmesi, hem çocuk hem erişkinlerde etkili bir tedavi seçeneğidir. Pityriasis likenoides yönetimi için daha fazla prospektif çalışmaya ihtiyaç duyulmaktadır.

Anahtar Kelimeler: Pityriasis likenoides, fototerapi, doksisisiklin

ABSTRACT

AIM: The aim of this study is to evaluate the clinical and demographic characteristics, as well as the histopathological findings, of patients diagnosed with pityriasis lichenoides, and to analyze the differences between pediatric and adult patient groups.

MATERIAL AND METHOD: The data of 47 patients with pityriasis lichenoides, followed up at the Dermatology Clinic of Ankara Training and Research Hospital between 01.08.2004 and 01.08.2024, were retrospectively analysed. The patients were classified as pityriasis lichenoides chronica and pityriasis lichenoides et varioliformis acuta. Clinical, demographic, and histopathological characteristics, as well as treatment responses, were evaluated. The patients were divided into pediatric (<18 years) and adult (≥18 years) groups for comparison. In statistical analyses, a p-value of <0.05 was considered significant.

RESULTS: Sixty-six percent of the patients were female, and 34% were male, with a mean age of 35.28±18.96 years. The median disease duration was 14 months, and the median time to diagnosis was 3 months. The most commonly affected areas were the trunk and extremities (68.1%). Relapses were observed in 42.6% of the patients. The most frequently detected histopathological findings were perivascular lymphocytic infiltration (87.8%) and lymphocytic exocytosis (80.5%). All patients were treated with topical corticosteroids, and 95.7% received narrow-band UVB phototherapy. The complete response rate was 40.4%, the partial response rate was 51.1%, and no response was observed in 8.5% of the patients. In pediatric patients, the disease duration was significantly shorter than in adults (p=0.026) and time to diagnosis was significantly shorter compared to adults (p = 0.039).

CONCLUSION: Pityriasis lichenoides has a longer duration in adults, while pediatric patients are diagnosed earlier. The combination of topical corticosteroids with narrowband UVB phototherapy, along with the addition of antibiotic therapy when necessary, is an effective treatment option for both children and adults. More prospective studies are needed for the management of pityriasis lichenoides.

Keywords: Pityriasis lichenoides, phototherapy, doxycycline

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INTRODUCTION

Pityriasis lichenoides (PL) is the broad term given to a group of papulosquamous skin diseases which includes pityriasis lichenoides chronica (PLC) and pityriasis lichenoides et varioliformis acuta (PLEVA). PLC presents with multiple erythematous-brownish papules with mica-like scale, which often heal with postinflammatory hypopigmentation. The trunk, buttocks and proximal extremities are the most common sites of involvement. Although PLC is usually asymptomatic, pruritus may occur in some cases. Patients with PLC follow a relapsing and remitting course lasting for months to years 1. PLEVA generally presents with acute erythematous papules and papulovesicles with haemorrhagic or necrotic crusts. In PLEVA, lesions are symmetrically distributed on the trunk, buttocks and proximal extremities. Varioliform scars and post-inflammatory hyper- and hypopigmentation may form after healing. Patients may describe burning and pruritus as symptoms. Both PLC and PLEVA tend to affect children and young adults 2. Infectious agents, inflammatory response to an underlying T-cell dyscrasia and immune-complex mediated hypersensitivity are proposed theories for pathogenesis 2,3. Treatment options include topical corticosteroids, oral antibiotics including erythromycin, azithromycin, clarithromycin, minocycline and tetracycline, phototherapy, and systemic immunosuppressants such as methotrexate and cyclosporine 2,4. When the present literature was examined, most of them were determined to be limited to case reports and reviews. Only a few retrospective studies were detected, and there was no prospective studies evaluating the clinical course and treatment strategies for the disease 4-7. In this retrospective study, the clinical and demographic characteristics, histopathological findings, and the treatment agents given to PL patients over the last 20 years will be discussed. Additionally, the characteristics of the disease in different age groups and treatment responses will be evaluated. The main purpose of the study was to contribute to the clinical diagnosis and treatment approach of the disease, including clues for the clinicians in their clinical practice.

MATERIAL AND METHOD

The study included 47 PL patients, who presented to the Dermatology Outpatient Clinic of the Ankara Training and Research Hospital between 01.08.2004 and 01.08.2024. The institutional ethics committee of Ankara Training and Research Hospital approved the study (E-24-215). The study was performed following the latest version of the Helsinki Declaration and Guidelines for Good Clinical Practice. The study included all of the patients' data who were diagnosed as PLEVA or PLC during the past 20 years. Age, sex, accompanying diseases, drug usage, clinical features, duration of the disease, time to diagnosis, detailed analysis of histopathological findings, and treatment agents were investigated and recorded. The patients under 18 years of age were categorized as the pediatric group, and the remaining as adult group. The clinical presentation was detailed in terms of distribution of the lesions such as trunk and extremity involvement. Histopathological findings of 41 patients were classified and examined in detail. Major histopathological findings included parakeratosis, hyperkeratosis, acanthosis, lymphocyte exocytosis, basal vacuolar degeneration and perivascular lymphocyte infiltration. The diagnosis of PL was established based on both clinical presentation and histopathological findings. Treatment agents were analyzed, including topical steroids, systemic antibiotics and phototherapy. Treatment responses were categorized as complete, partial and no response. As the disease may have a relapsing course, the history of relapse was also evaluated. All data obtained were compared in terms of any significant differences between pediatric and adult patients.

Statistical Analysis

All analyzes were performed using IBM SPSS Statistics for Windows, Version 20.00 (IBM Corp.), and a p-value of less than 0.05 was considered statistically significant. The normality of the data was tested with the Kolmogorov Smirnov test. Continuous variables were expressed as mean ± standard deviation and median (minimum-maximum), interquartile range (IQR) with parametric and non-parametric distribution, respectively. Categorical variables were expressed as numbers and percentages. Mann-Whitney U test was used to compare independent samples. Pearson's chi-square test was applied for categorical variables, and if any cell had an expected count below 5, Fisher's Exact test was used instead.

RESULTS

A total of 47 patients were included in this study. Thirty-one (66%) of them were female and 16 (34%) were male. The age of the patients ranged from 6 to 78 years old, and the mean age was 35.28±18.96 years. The median duration of the disease was 14 months (IQR=16), and the median time to diagnosis was 3 months (IQR=3). Thirty seven (78.7%) patients had no additional disease while 10 (21.3%) patients had other accompanying diseases. Forty patients (85.1%) were diagnosed with PLC and 7 patients (14.9%) with PLEVA. The disease was located mostly on both trunk and extremities (68.1 %). While 27 patients (57.4 %) had no relapse, 20 of them (42.6 %) had a relapsing course. The demographic and clinical characteristics of patients with PLC and PLEVA are presented in Table 1.

Table 1. The demographic and clinical features of patients with PLC/PLEVA

	PLC/PLEVA group (n=47)
PLC/PLEVA (n/%)	
PLC	40 (85.1%)
PLEVA	7 (14.9%)
Sex (n/%)	
Female	31 (66%)
Male	16 (34%)
Age [Mean±SD, years]	35.28±18.96
Duration of disease [Median, (IQR), months]	14 (16)
Time to diagnosis [Median, (IQR), months]	3 (3)
Medical History (n/%)	
None	37 (78.7%)
Present	10 (21.3%)
There were 15 disease diagnoses in 10 patients with PLC/PLEVA	
Hypertension	5 (10.6%)
Diabetes mellitus	3 (6.4%)
Coronary artery disease	2 (4.3%)
Asthma	2 (4.3%)
Hypothyroidism	2 (4.3%)
Multiple sclerosis	1 (2.1%)
Locations of involvement (n/%)	
Trunk	11 (23.4%)
Extremities	4 (8.5%)
Trunk&Extremities	32 (68.1%)
History of relapse (n/%)	
None	27 (57.4%)
Present	20 (42.6%)
PLC: Pityriasis lichenoides chronica, PLEVA: Pityriasis lichenoides et varioliformis acuta IQR: interquartile range, SD: standard deviation, Data were expressed as mean±SD or median and IQR in continuous variables and n (%) in categorical variables.	

Although the study included 47 patients, histopathological findings of 6 patients were inaccessible since they received their diagnoses at external healthcare institutions. Therefore, histopathological examination results of 41 (87.2%) patients were examined. Perivascular lymphocyte infiltration (n=36, 87.8%) and lymphocyte exocytosis (n=33, 80.5%) were the most frequently reported histopathological findings. Histopathological findings of the patients are summarized in Table 2.

Table 2. Histopathological features of patients with PLC/PLEVA

	PLC/PLEVA group (n=41)
Histopathological findings (n/%)	
Parakeratosis	22 (53.7%)
Hyperkeratosis	23 (56.1%)
Acanthosis	18 (43.9%)
Lymphocyte exocytosis	33 (80.5%)
Basal vacuolar degeneration	16 (39%)
Perivascular lymphocyte infiltration	36 (87.8%)
PLC: Pityriasis lichenoides chronica, PLEVA: Pityriasis lichenoides et varioliformis acuta Data were expressed as n (%) in categorical variables.	

All of the 47 patients had received topical corticosteroid treatment. In addition to topical steroids, 11 (23.4%) patients were given systemic antibiotic treatment while 45 (95.7%) patients received narrow-band UVB phototherapy. Doxycycline was the most frequently preferred systemic antibiotic therapy followed by erythromycin. The median total cumulative dose of phototherapy was 16.55 Joule/ cm2. While 19 (40.4%) patients had a complete response, 24 (51.1%) had a partial response. Only 4 (8.5%) of the patients had no response to the treatment. Of the four patients who did not respond to treatment; two were adults, two were from the pediatric group, and all were patients who received phototherapy. The treatment agents administered to the patients and treatment response are given in Table 3.

Table 3. Treatment history of patients and their response to these agents

	PLC/PLEVA group (n=47)
Treatment history (n/%)	
Topical corticosteroid	47 (100%)
Systemic antibiotics	11 (23.4%)
Doxycycline	9 (19.1%)
Erythromycin	2 (4.3%)
Narrow-band UVB Phototherapy	45 (95.7%)
Total cumulative dose of phototherapy [Median, (IQR), Joule/cm ²]	16.55 (36.63)
Treatment Response (n/%)	
Complete response	19 (40.4%)
Partial response	24 (51.1%)
No response	4 (8.5%)
PLC: Pityriasis lichenoides chronica, PLEVA: Pityriasis lichenoides et varioliformis acuta	
Data were expressed as n (%) in categorical variables.	

Patients under 18 years of age were categorized as pediatric, over or equal to 18 years of age were categorized as adult group. Eleven patients were pediatric and 36 were classified as adult patients. Among the 11 pediatric patients, 7 (63.6%) were diagnosed with PLC and 4 (36.4%) with PLEVA. Of the 36 adult patients, 33 (91.7%) were diagnosed with PLC and 3 (8.3%) with PLEVA. The proportion of PLEVA cases was significantly higher in the pediatric group compared to the adult group ($p = 0.042$). The median disease duration was 8 months (IQR=17) for pediatric patients and 16 months (IQR=14) for adult patients. Disease duration for pediatric patients was statistically significantly lower compared to adult patients ($p=0.026$). The median time to diagnosis was 2 months (IQR = 2) for pediatric patients and 3 months (IQR = 4) for adult patients. This difference was statistically significant ($p = 0.039$), indicating that pediatric patients received an earlier diagnosis compared to adults. Histopathological examination revealed that parakeratosis was statistically significantly more common in adult patients (64.5%) compared to pediatric patients (20%) ($p=0.026$). No statistically significant difference was detected between the two groups in the remaining parameters. Comparison of the demographic and disease characteristics, treatment modalities and histopathological results between patients under 18 years and adult patients are demonstrated in Table 4.

Table 4. Comparison of the demographic and disease characteristics, treatment modalities and histopathological results between patients under 18 years and adult patients

	Patients under 18 years of age (n=11)	Adult patients (n=36)	p
PLC/PLEVA			
PLC	7 (63.6%)	33 (91.7%)	0.042*
PLEVA	4 (36.4%)	3 (8.3%)	
Sex (n/%)			
Female	7 (63.6%)	24 (66.7%)	0.853 ^s
Male	4 (36.4%)	12 (33.3%)	
Duration of disease (Median, (IQR), months)			
	8 (17)	16 (14)	0.026**
Time to diagnosis (Median, (IQR), months)			
	2 (2)	3 (4)	0.039**
Locations of involvement (n/%)			
Trunk	1 (9.1%)	10 (27.8%)	0.556 ^f
Extremities	1 (9.1%)	3 (8.3%)	
Trunk&Extremities	9 (81.8%)	23 (63.9%)	
History of relapse (n/%)			
None	8 (72.7%)	19 (52.8%)	0.310 ^f
Present	3 (27.3%)	17 (47.2%)	
Treatment history (n/%)			
Topical corticosteroid	11 (100%)	36 (100%)	1
Systemic antibiotics	3 (27.3%)	8 (22.2%)	0.056 ^f
Doxycycline			
Erythromycin			
Narrow-band UVB Phototherapy	10 (90.9%)	35 (97.2%)	0.417 ^f
Treatment Response (n/%)			
Complete response	6 (54.5%)	13 (36.1%)	0.523 ^f
Partial response	4 (36.4%)	20 (55.6%)	
No response	1 (9.1%)	3 (8.3%)	
Histopathological findings (n/%)			
	Patients under 18 years of age (n=10)	Adult patients (n=31)	P
Parakeratosis	2 (20%)	20 (64.5%)	0.026*
Hyperkeratosis	6 (60%)	17 (54.8%)	1 ^f
Acanthosis	3 (30%)	15 (48.4%)	0.467 ^f
Lymphocyte exocytosis	8 (80%)	25 (80.6%)	1 ^f
Basal vacuolar degeneration	4 (40%)	12 (38.7%)	1 ^f
Perivascular lymphocyte infiltration	10 (100%)	26 (83.9%)	0.310
PLC: Pityriasis lichenoides chronica, PLEVA: Pityriasis lichenoides et varioliformis acuta			
UVB: Ultraviolet B			
IQR: interquartile range, SD: standard deviation.			
Data were expressed as mean±SD or median and IQR in continuous variables and n (%) in categorical variables. *p<0.05. **Mann-Whitney U test. ^s Chi-Square test. ^f Fisher's Exact Test			

DISCUSSION

PL is the general term for a group of disorders with PLEVA and PLC regarded as two ends of the same disease spectrum, sharing overlapping clinical and histopathological features while differing in their presentation and course. PLEVA is characterized by acute, inflammatory papules, vesicles, and necrotic crusts, often accompanied by pruritus or burning. In contrast, PLC typically presents with chronic, scaly, and erythematous-brownish papules that evolve slowly and may heal with post-inflammatory pigmentary changes. Despite these differences, both conditions are thought to arise from a similar underlying pathogenesis, potentially involving immune dysregulation, T-cell-mediated inflammation, infections or hypersensitivity reactions 2.

The sex distribution among PL patients has shown considerable variability in the literature. In a randomised study involving 15 PLC patients, 53% of the patients were male while 47% were female 8. In another retrospective study involving 25 PLC patients, 56% were male and 44% were female 4. In a review involving pediatric PL cases, a slight (61%) male predominance was noted out of a total of 393 patients 3. On the other hand, in an observational retrospective study including 20 PL patients, more than half (55%) of the patients were female 5. In a retrospective study investigating the differences between pediatric and adult PL, male: female ratio was 1.5 : 1 for children and 1 : 1 for adults with no statistically significant difference in sex distribution between two groups 7. In this study, the majority of the patients was female (66% vs 34%) with no significant difference in sex distribution between pediatric and adult patients.

The age distribution of PL patients has been widely documented in the literature, with varying median and mean ages reported across different studies. In a retrospective study with 75 PL patients, the median age was found 16 and 26 years for PLEVA and PLC, respectively 9. In another retrospective study including PL patients collected during a 8-year period, the median age was 8 years for children (age range: 2-18 years) and 40 years for adults (20-65 years) 7. Agaoglu et al reported a mean age of 30.3 years in their retrospective study on 20 PL patients 5. In this study, the mean age was 35.28 years, and the proportion of PLEVA patients was higher in the pediatric group compared to adults, consistent with findings in the literature.

The duration of disease in PL patients has been a subject of interest in the literature, with studies reporting varying disease durations across different patient populations. In a retrospective review with 24 PL patients, median disease duration was reported as 11 months 6. Ersoy-Evans et al reported a median duration of 18.5 months in their retrospective study involving 124 PL patients 10. Wahie et al compared pediatric and adult PL patients and found that 80% of pediatric cases had active disease after a median duration of 30 months while 78% of adult patients had achieved remission by this time 7. In this study, the median disease duration was 14 months which was similar to the results in the literature. In contrast to the literature, the median disease duration of adults was significantly longer when compared with the pediatric patients.

The duration from symptom onset to diagnosis is highly variable. In a retrospective study on 75 PL patients, the median time to diagnosis was 5 weeks for PLEVA patients and 12 weeks for PLC patients 9. In a study by Fatturi et al, the mean time from symptom onset to diagnosis was 5 months with a maximum delay of up to 10 years 11. Similarly, a previous series reported a mean diagnostic delay of 1 year, with some cases taking as long as 3 years 12. Wahie et al reported 6 months and 24 months as the median time until consultation in children and adults, respectively 7. In our study, the median time to diagnosis was 3 months with children getting a diagnosis significantly earlier than adults.

Numerous studies have reported the coexistence of diseases in patients with PL. For instance, febrile tonsillitis was reported in a 3-year-old male patient diagnosed with PLEVA 13. Tsai et al reported accompanying alopecia areata in a 5-year-old male patient with PL while Saltik-Temizel et al reported autoimmune hepatitis in a 13-year-old male patient with PLC 14,15. Moreover, granulomatous chronic variable immunodeficiency was reported in a 8-year-old female patient with PL 16. Hodgkin's lymphoma, mitochondrial disorder, asthma, hereditary hemorrhagic telangiectasia and atopic dermatitis were reported in pediatric PL patients whereas hypertension, rheumatoid arthritis, ischemic heart disease, psoriasis, atopic dermatitis, immune thrombocytopenic purpura and hepatitis B were reported in adult patients 7. In our study, the majority of the patients (78.7%) had

no additional disease. The remaining patients had diseases such as hypertension, diabetes, coronary artery disease, asthma, hypothyroidism and multiple sclerosis, with hypertension being the most common associated disease.

PL typically affects trunk and proximal extremities. However, involvement of the face and inguinal regions have also been reported. For example, in a retrospective study by Agaoglu et al., involvement of the face, trunk, and inguinal region was classified as central, involvement of the extremities as peripheral, and whole-body involvement as diffuse. The study reported that the majority of patients exhibited diffuse involvement, followed by central and acral involvement, respectively 5. Ersoy-Evans noted that peripheral and diffuse involvement was noted in 48% and 44% of PL patients while only 8% had trunk involvement 4. In our study, the majority of patients had involvement of both the trunk and extremities, followed by those with only trunk involvement and those with only extremity involvement, respectively; with no significant difference in location of involvement between children and adults.

Both PLC and PLEVA have relapsing and remitting disease course and highly variable relapse rates have been reported so far, ranging from 18.9% to 42.8% 17,18. In a prospective study, relapse occurred in 43% of PLC patients within the first six months after narrowband ultraviolet B phototherapy 18. Conversely, research involving pediatric PL patients treated with oral erythromycin reported a relapse rate of 12.5% 6. In our study, relapse was observed in 42.6% of the patients. No difference was observed in relapse rates between pediatric and adult patients.

Histopathology of PLEVA and PLC has some overlapping features as well as certain differences. In PLEVA, parakeratosis, spongiosis, acanthosis, basal layer vacuolization, lymphocyte exocytosis and epidermal necrosis are observed. Perivascular lymphohistiocytic infiltrate, dermal edema and subepidermal vesicles can also be found as well as vascular dilation, erythrocyte extravasation and vasculitis. In PLC, focal parakeratosis, mild acanthosis, spongiosis, mild epidermal necrosis, and mild dermal edema with perivascular infiltration, occasional erythrocyte extravasation and vessel dilation are observed. Vasculitis is not an expected finding of PLC 2. In our study, parakeratosis and hyperkeratosis were present in over half of the patients, while lymphocyte exocytosis and perivascular infiltrate were noted in the majority of the patients. Notably, spongiosis, erythrocyte extravasation, epidermal necrosis, subepidermal vesicles, vascular dilation, vasculitis, and dermal edema were not detected. Parakeratosis was noted significantly more common in adult patients compared to pediatric patients.

Different treatment approaches for PL are available, with topical corticosteroids, oral antibiotics, and phototherapy being the most commonly used modalities, demonstrating differing rates of efficacy and response among pediatric and adult patients. Wahie et al. reported that 64% of pediatric and 56% of adult cases received topical corticosteroids, with symptom relief in 50% and 56%, respectively. Oral antibiotics were used in 32% of children and 13% of adults, resulting in full/partial resolution in 25% and 75% of children and adults, respectively. Phototherapy was administered to 32% of children and 64% of adults, with improvement observed in 88% and 71%, respectively 7. Ozdol et al. reported that 17%, 29%, and 23% of PLEVA patients received topical corticosteroids, oral antibiotics, or phototherapy, compared to 15%, 15%, and 55% of PLC patients, respectively 9. In our study, all patients received topical corticosteroid treatment, nearly a quarter underwent systemic antibiotic therapy, and all except two patients were treated with narrowband UVB phototherapy with a median cumulative dose of 16.55 Joule/cm². More than half of the patients achieved a partial response, 40% achieved complete resolution, while 8.5% showed no response to treatment. No significant difference was noted in the treatment history and response rates between pediatric and adult patients. It can be concluded that narrow-band UVB therapy is a safe, well-tolerated treatment option in both pediatric and adult patients, with high rates of treatment success.

Limitations

This study has a few limitations. Firstly, there may be potential biases in data collection. Since the study was retrospective, patients with PL could not be prospectively evaluated regarding treatment responses over a period of time. Additionally, treatment responses for individual

treatment options (topical corticosteroids, narrow band UVB, systemic antibiotics) could not be assessed, which is a drawback of this study.

CONCLUSION

In conclusion, PL tends to have a longer duration in adults, while pediatric patients are typically diagnosed earlier. The combination of topical corticosteroids, narrowband UVB phototherapy and antibiotic therapy, when indicated, has proven to be an effective treatment approach for both children and adults. However, further prospective studies are essential to refine and optimize management strategies for PL.

Yazarlık Katkıları:

Author Contributions: Concept and design: NK, Data collection: BD, İY, ZA, Data analysis: PÖÇ, Literature research and collection: NK, İK, Writing: NK, İK, Review and assessment: NK, İK, BD, ZA, İY, PÖÇ

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