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Pityriasis lichenoides: a university department long-term follow-up study

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Abstract

Introduction: Pityriasis lichenoides (PL) predominantly affects children and young adults. Its etiology is unclear, and the condition ranges from a harmless inflammatory disease to possible progression or pre-manifestation of cutaneous T-cell lymphoma.
Methods: A long-term cohort included 242 patients with PL of all age groups diagnosed and treated at our department from 2009 to 2019. Follow-up lasted until 2024. We analyzed the disease duration, demographic and clinical features, and outcomes in our patients.
Results: The cohort of PL patients studied included 107 adults and 135 children. A total of 221/242 (91%) patients were followed for 5 to 15 years (the median follow-up period was 9.9 years). No statistically significant difference ($p > 0.05$) in disease duration or lesion distribution was found between different PL forms in children or adults. The results show a male-to-female ratio of 1.7:1 for pediatric patients and 0.6:1 for adults, with a higher incidence of male patients among children ($p < 0.01$). During the follow-up period, no progression to cutaneous T-cell lymphoma was established.
Conclusions: PL encompasses a spectrum of papulosquamous disorders with male predominance among children and female predominance in adults. In addition, the study results underscore the benign course of PL.

Keywords: inflammatory disease, pityriasis lichenoides, polymorphous inflammatory disease, pruritus, rare skin disease

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Introduction

Pityriasis lichenoides (PL) is a spectrum of histopathologically and clinically overlapping dermatological conditions presenting as pityriasis lichenoides et varioliformis acuta (PLEVA), pityriasis lichenoides chronica (PLC), or a mixed form of PL (MPL) characterized by both PLEVA and PLC lesions (1–4). A separate, potentially life-threatening form is febrile ulceronecrotic Mucha–Habermann disease (FUMHD) (5, 6). In PL, the terms *acute* and *chronic* refer to the clinical features of lesions, not to the disease course (5). PLEVA manifests as erythematous papules that evolve into necrotic lesions, often leaving atrophic scars. In contrast, PLC presents with persistent, flat, red-brown papules with mica-like scaling. In MPL both types of lesions are present, whereas FUMHD is characterized by widespread purpuric and ulceronecrotic plaques associated with fever/systemic involvement. Lesions in PLEVA, PLC, and MPL may resolve spontaneously or persist or reappear for months to years. Other forms of PL are of a benign nature, but the FUMHD mortality rate may be up to 19% (6).

The results of a retrospective cohort study are presented below, with the characteristics of 242 PL patients followed for 5 to 15 years and comprehensive insights into the demographic and clinical characteristics of this rare spectrum of cutaneous disorders.

Methods

This 15-year-long retrospective longitudinal study included all in-patients and outpatients with PL treated at the Dermatology Clinic of the University Clinical Center in Belgrade, Serbia. From January 1st, 2009, to December 31st, 2019, 242 patients (107 adults and 135 children) were diagnosed and treated. Follow-up lasted until December 31st, 2024 (5 years for patients diagnosed in 2019 and 15 years for patients diagnosed in 2009).

The study was planned in accordance with the ethical standards defined in the Helsinki Declaration (revised version from 1983) and in accordance with the rules of the Ethics Committee of the University Clinical Center of Serbia (approval no. 1051/17).

Diagnosis of PL was made based on typical clinical findings for PLC, PLEVA, MPL, or FUMHD, and histopathology findings in all adults and in cases with prolonged disease duration in the pediatric patient group. The parameters recorded included the patients' age at the onset of the disease, the PL type, the patients' sex, the distribution of lesions, and treatment modalities. The initial evaluation and subsequent checkups included a complete clinical examination. Treatment options included topical mid-potency corticosteroids and calcineurin inhibitors, oral H1 antihistamines, antibiotics, prednisolone, and methotrexate, as well as phototherapy. We summarized all the data and contacted the patients for checkup.

Statistical analyses were conducted using IBM SPSS Statistics for Windows (IBM, New York, USA), version 21.0. A p-value of < 0.05 was considered statistically significant.

Results

Of the 242 PL patients diagnosed, 107 were adults and 135 were children. Among them, 148 patients (61.2%) had PLC, 43 patients (17.8%) had PLEVA, 45 patients (18.6%) had MPL, and six patients (2.4%) had FUMHD (Table 1).

The male-to-female ratio was 1.7:1 for pediatric patients and 0.6:1 for adults, with a statistically significant higher incidence of

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male patients among children ($p < 0.01$). Among the PLC patients, 54% were younger than 18 and 46% were adults. In the PLEVA group, 47% of patients were children and 53% were in the adult group. In patients with MPL, 67% were children and 33% were adults. FUMHD was diagnosed in six patients: two boys and three girls among children, and one adult woman. The median ages of patients in all groups are presented in Table 1.

All follow-up data are summarized in Table 1. Each group of patients (PLC, PLEVA, MPL, or FUMHD) was analyzed separately (Table 1).

Skin biopsies and histopathology were performed in all adults and 60.7% of children. Histopathology demonstrated typical features of PL.

A viral infection preceded PL in 36 out of 242 patients (15%). We examined the immunization history in children, as well as influenza and COVID-19 vaccinations in adults, but found no association between these events and the onset or relapse of PL.

The anatomical distribution of PL lesions was assessed by categorizing affected areas into four regions: 1) face/head, 2) extremities, 3) trunk, and 4) intertriginous/genital areas. No statistically significant differences were observed in lesion distribution among the different clinical forms of PL ($p > 0.05$) when analyzing the entire cohort (Fig. 1). Similarly, comparison between pediatric and adult patients revealed no significant variation in lesion localization ($p > 0.05$).

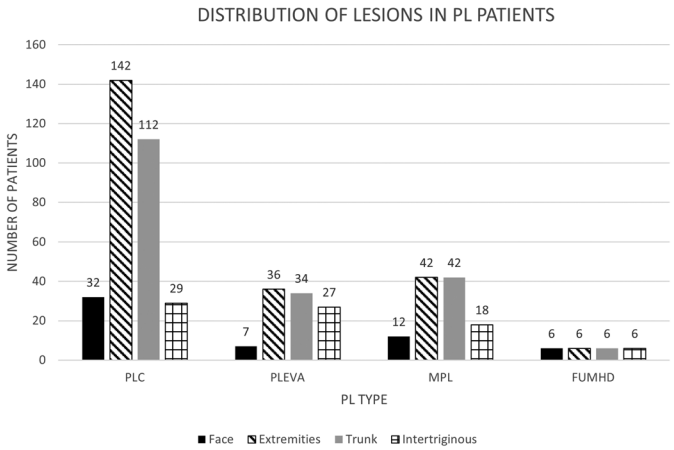

Figure 1 | Distribution of lesions in patients with pityriasis lichenoides chronica, pityriasis lichenoides et varioliformis acuta, mixed form of pityriasis lichenoides, and febrile ulceronecrotic Mucha–Habermann disease.
PL = pityriasis lichenoides, PLC = pityriasis lichenoides chronica, PLEVA = pityriasis lichenoides et varioliformis acuta, MPL = mixed form of pityriasis lichenoides, FUMHD = febrile ulceronecrotic Mucha–Habermann disease.

The proportion of patients with the involvement of only one anatomical region was highest in those with PLC (32%), followed by PLEVA (7%) and MPL (3%; data not shown). All patients diagnosed with FUMHD exhibited involvement of all the anatomical regions defined. Oral mucosal involvement was observed in 100% of FUMHD cases, whereas erythema and small erosions of oral mucosa were identified in 4% of patients with PLEVA. They were absent in those with PLC and MPL. The percentages of patients with involvement of more than one anatomical region were as follows: 78.38% in the PLC group, 83.72% in the PLEVA group, 93.33% in the MPL group, and 100% in the FUMHD group.

Therapy included mid-potency topical corticosteroids in 96% of patients, topical calcineurin inhibitors in 40%, UV light treatment in 63%, low dose prednisolone in 33%, oral erythromycin in 54%, azithromycin in 14%, antihistamines in 51%, and methotrexate in 3% (data not shown).

A total of 221/242 (91%) patients were followed for 5 to 15 years (15 years for patients diagnosed in 2009 and 5 years for patients diagnosed in 2019); the median follow-up period was 9.9 years. Twenty-one patients (9%) were lost from the follow up. The median disease duration of each PL subtype for the pediatric and adult groups is presented in Table 1. No statistically significant difference ($p > 0.05$) in disease duration was found between different PL forms in children or adults (Table 1).

At the end of the follow-up period, scars were present in all six FUMHD patients and in 36% of PLEVA and 22% of MPL patients. There were no residual pigmentary lesions.

Discussion

Pityriasis lichenoides is a group of inflammatory diseases with diverse clinical presentations (2). The precise incidence of PL is

Table 1 | Characteristics of patients with pityriasis lichenoides ($n = 242$).

	PLC	PLEVA	MPL	FUMHD	Total
Total, *n* (%)	148 (100.0%)	43 (100.0%)	45 (100.0%)	6 (100.0%)	242 (100.0%)
Pediatric					
Median age, years (range)	9 (1–18)	7.5 (1–16)	9 (2–17)	8 (6–15)	9 (1–18)
0–5 years, *n* (%)	19 (12.5%)	8 (18.6%)	9 (20.0%)	0 (0.0%)	36 (14.9%)
6–12 years, *n* (%)	47 (31.8%)	8 (18.6%)	14 (31.1%)	4 (66.7%)	73 (30.2%)
13–18 years, *n* (%)	14 (9.5%)	4 (9.3%)	7 (15.6%)	1 (16.7%)	26 (10.7%)
M/F, *n* (ratio)	47/33 (1.4:1)	12/8 (1.5:1)	25/5 (5.0:1)	2/3 (0.7:1)	86/49 (1.7:1)*
Adult					
Median age, years (range)	42 (19–76)	36 (23–74)	51 (23–79)	47 (47)	42 (19–79)
19–35 years, *n* (%)	30 (20.3%)	10 (23.3%)	6 (13.3%)	0 (0.0%)	46 (19.0%)
36–64 years, *n* (%)	32 (21.6%)	11 (25.6%)	7 (15.6%)	1 (16.7%)	51 (21.1%)
65+ years, *n* (%)	6 (4.1%)	2 (4.6%)	2 (4.4%)	0 (0.0%)	10 (4.1%)
M/F, *n* (ratio)	23/45 (0.5:1)	13/10 (1.3:1)	4/11 (0.4:1)	0/1 (0:1)	40/67 (0.6:1)*
Follow-up, *n* (%)	134 (90.5%)	39 (90.7%)	42 (93.3%)	6 (100.0%)	221 (91.3%)
Pediatric, M/F, *n* (ratio)	45/30 (1.5:1)	12/8 (1.5:1)	22/5 (4.4:1)	2/3 (0.7:1)	81/46 (1.8:1)
Adult, M/F, *n* (ratio)	22/37 (0.6:1)	10/9 (1.1:1)	4/11 (0.4:1)	0/1 (0:1)	36/58 (0.6:1)
Lost to follow-up, *n* (%)	14 (9.5%)	4 (9.3%)	3 (6.7%)	0 (0.0%)	21 (8.7%)
Pediatric, M/F, *n* (ratio)	2/3 (0.7:1)	0/0	3/0	0/0	5/3 (1.7:1)
Adult, M/F, *n* (ratio)	1/8 (0.1:1)	3/1 (3.0:1)	0/0	0/0	4/9 (0.4:1)
Median disease duration, months (range)	4.5 (0–144)	3.0 (0–36)	3.0 (0–84)	5.5 (1–8)	4.0 (0–144)
Pediatric, median (range)	4.0 (0–66)	3.25 (0–36)	3.0 (0–84)	6.0 (1–8)	4.0 (0–84)
Adult, median (range)	5.0 (0–144)	2.0 (0–10)	3.0 (1–12)	5.0 (5–5)	4.0 (0–144)

*$p < 0.01$.
PLC = pityriasis lichenoides chronica, PLEVA = pityriasis lichenoides et varioliformis acuta, MPL = mixed form of pityriasis lichenoides, FUMHD = febrile ulceronecrotic Mucha–Habermann disease, M/F = male/female.

unknown, but the disease is rare and more commonly affects children (8) and young adults around age 30 (5, 7). All races are affected (5, 7). The profile of the patients studied concurs with the literature data, although the adult population's median age was slightly higher than that typically reported in the literature (1–9).

According to previous studies, the male-to-female ratio for PL ranges from 1.4:1 to 2:1 (1, 3, 5, 7–9). In our study, there was an observable female predominance among the adult patients and a statistically significant male predominance among the pediatric patients.

The percentages of various PL forms vary across studies: PLC was present in 37% to 76%, PLEVA in 12% to 57.3%, and MPL in 4% to 12% of reported PL patients (2, 5, 10). Data for FUMHD is sparse because it is sometimes considered a severe form of PLEVA and in some cases a separate form of PL (2, 5, 6). Of 242 patients included in the study, 61% had PLC, 18% had PLEVA, 19% had MPL, and 2% had FUMHD.

PL may last from several weeks up to 15 years (5, 7, 11). PLC typically lasts several months, but some cases can wax and wane for years (1, 5, 7, 8, 14). PLEVA typically resolves within weeks, but this can vary, and it may evolve into PLC and vice versa (5, 7, 10). Most studies to date either lack follow-up data or include follow-up periods shorter than 1 year (10). In our study, the median follow-up time was 9.9 years (min–max: 5–15 years).

According to the literature data, PL ranges from a harmless inflammatory disease to possible progression or pre-manifestation of cutaneous T-cell lymphoma (CTCL) (4, 5, 7, 11, 12). In our study, none of the patients progressed to lymphomatoid papulosis or CTCL during the follow-up period. In addition, no association with other diseases was found during the follow up.

The reported mortality rate in FUMHD can reach 19% (5, 6, 13). All our patients with FUMHD survived. Rare small scars were detectable in PLEVA and MPL. In one patient, FUMHD left significant scarring with functional disabilities.

Published studies report that viral infections preceded skin lesions in 4% to 22% of PLC, PLEVA, and MPL patients (2, 8). Upper respiratory tract infection preceded skin lesions in 15% of our patients. They included all six patients with FUMHD, which is usually associated with a viral infection (5). Available data suggest that in 4% of PL patients vaccination may precede skin lesions (2), but in our research no association was found between immunization schedule and disease appearance or relapse. In line with the literature (2, 6, 14), our patients were treated with phototherapy, mid-potency corticosteroids, and topical calcineurin inhibitors. In patients with disseminated lesions or a long-lasting or recurrent course of PL, systemic treatment was initiated. It included erythromycin, azithromycin, antihistamines, low-dose prednisone, and methotrexate. Low-dose prednisone treatment lasted up to 3 weeks, and methotrexate (0.2 mg/kg/week) was reserved for cases with a severe or prolonged course of disease. Methotrexate treatment lasted from 6 weeks to several months, with slow dose tapering. In relapsing forms, treatment with topical agents and phototherapy was initiated. The next step in treating persistent relapsing forms was the consecutive initiation of erythromycin or azithromycin, antihistamines, low-dose prednisone, and methotrexate.

Conclusions

This large retrospective study, encompassing a 15-year follow-up of 242 PL patients, provides comprehensive insights into the demographic and clinical characteristics of this rare spectrum of cutaneous disorders. Our findings show that PL predominantly affects males in the pediatric population, and females in adulthood.

Despite the broad clinical variability, lesion distribution patterns and disease duration did not significantly differ among the PL subtypes or age groups. Notably, a preceding viral infection was observed in 15% of cases, but no association was established between immunizations and disease onset or relapses.

Long term follow-up revealed no progression to lymphoproliferative disorders, and all FUMHD patients recovered without systemic complications.

The results of this PL study underscore the generally benign course of PL, even in its more severe forms, highlighting the importance of long-term follow-up studies.

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