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Research Article | Araştırma Makalesi

DIFFERENCES IN THE CLASSICAL/NON-CLASSICAL HISTOPATHOLOGICAL FINDINGS OF PSORIASIS PATIENTS ACCORDING TO PSORIASIS SUBTYPE, DISEASE DURATION AND SEVERITY, ANATOMICAL REGION, AND CLINICAL PRESENTATION

PSORİAZİS HASTALARINDA KLASİK/KLASİK OLMAYAN HİSTOPATOLOJİK BULGULARIN PSORİAZİS ALT TİPLERİNE, HASTALIK SÜRESİNE VE ŞİDDETİNE, ANATOMİK BÖLGEYE VE KLİNİK GÖRÜNÜME GÖRE DEĞİŞİMİ

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ABSTRACT

Objective: Although histopathological examination is considered the gold standard in the diagnosis of psoriasis, it has limited usefulness in patients with non-classical histopathological and/or clinical presentations. The aim of this study was to examine the distribution of classical and non-classical histopathological findings according to psoriasis subtype, disease duration, disease severity, biopsy site, and classical/non-classical presentation.

Methods: We retrospectively reviewed the records of 160 patients with histopathologically confirmed psoriasis. Classical and non-classical histopathological features were determined according to dermatopathology textbooks and literature. Patients were categorized according to disease duration (≤12 and >12 months) and disease severity (Psoriasis Area Severity Index [PASI] ≤10 and >10) at presentation, and classical/non-classical presentation (based on morphology, distribution, nail pitting, and family history).

Results: The most common classical histopathological findings were regular acanthosis (99.4%), confluent parakeratosis (96.3%), blood vessels, dilated (93.1%), hyperkeratosis (89.4%), and suprapapillary plate thinning (89.4%). The most common non-classical histopathological findings were superficial perivascular dermal infiltration (81.3%) and spongiosis (53.8%). Hyperkeratosis (p=0.044) and intraepidermal lymphocyte accumulation (p=0.042) were more frequent in patients with a disease duration >12 months. The presence of Munro microabscess (p=0.010) and stratum basale necrotic keratinocytes (p=0.031) were observed more frequently in patients with PASI >10. Significant hyperkeratosis (p=0.024) and suprapapillary plate thinning (p=0.027) were more common in trunk biopsies compared to other locations. Spongiosis (p=0.005) and intraepidermal lymphocytes (p=0.008) were more common in patients with non-classical clinical presentation.

Conclusion: Non-classical histopathological findings can be observed in patients with psoriasis. Clinical features should be considered when evaluating classical/non-classical histopathological findings during diagnosis.

Keywords: Dermatopathology, histopathology, psoriasis, diagnosis

ÖZ

Amaç: Psoriazis hastalığının tanısında histopatolojik inceleme altın standart olarak kabul edilmekle birlikte, klasik olmayan histopatolojik ve/veya klinik bulgulara sahip hastalarda bu yöntemin kullanımı sınırlıdır. Çalışmamızda klasik ve klasik olmayan histopatolojik bulguların psoriazisin klinik alt tiplerine, hastalık süresine, hastalığın şiddetine, biyopsi alınan anatomik bölgeye ve klasik/klasik olmayan klinik görünüme göre dağılımının incelenmesi amaçlanmıştır.

Yöntem: Histopatolojik olarak Psoriazis tanısı doğrulanmış toplam 160 hastanın kayıtları geriye dönük olarak incelendi. Dermatopatoloji ders kitapları ve literatür verilerine göre klasik ve klasik olmayan histopatolojik özellikler belirlendi. Hastalar, başvuru anındaki hastalık süresine (≤12 ve >12 ay) ve hastalık şiddetine (Psoriazis Alan Şiddet İndeksi [PAŞİ] ≤10 ve >10) ve klasik/klasik olmayan klinik görünüme (lezyonların morfolojisi ve dağılımı, tırnaklarda pitting varlığı ve ailede psoriazis öyküsü) göre gruplara ayrıldı.

Bulgular: En sık görülen klasik histopatolojik bulgular düzenli akantoz (%99,4), konfluent parakeratoz (%96,3), kan damarlarının genişlemesi (%93,1), hiperkeratoz (%89,4) ve suprapapiller tabakada incelme (%89,4) idi. Klasik olmayan histopatolojik bulgular arasında en sık yüzeysel perivasküler dermal infiltrasyon (%81,3) ve spongioz (%53,8) görüldü. Hastalık süresi 12 ayın üzerindeki hastalarda hiperkeratoz (p=0,044) ve intraepidermal lenfosit birikimi (p=0,042) daha sık görüldü. Munro mikroabsesi (p=0,010) ve stratum bazalede nekrotik keratinositlerin varlığı (p=0,031) PAŞİ değeri 10'nun üzerindeki hastalarda daha sıktı. Gövdeden alınan biyopsilerde hiperkeratoz (p=0,024) ve suprapapiller tabakada incelme (p=0,027) diğer lokalizasyonlara göre daha belirgindi. Klasik olmayan klinik görünüme sahip hastalarda spongiyoz (p=0,005) ve intraepidermal lenfosit birikimi (p=0,008) daha fazlaydı.

Sonuç: Psoriazis hastalarında klasik olmayan histopatolojik bulgular görülebilmektedir. Tanı sırasında klasik/klasik olmayan histopatolojik bulgular değerlendirilirken klinik özellikler dikkate alınmalıdır.

Anahtar Kelimeler: Dermatopatoloji, histopatoloji, psoriazis, tanı

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Introduction

Psoriasis is a chronic, multifactorial skin disease that affects 2-3% of the global population.[1,2] The diagnosis is usually made clinically. However, biopsy is needed for an accurate diagnosis in subtypes such as erythrodermic psoriasis (EP) and pustular psoriasis (PP), in the eruptive phase of psoriasis, and in patients with scalp, palmoplantar, and intertriginous involvement.[3] Histopathological examination is considered the gold standard in the diagnosis of psoriasis, although it is considered a subjective method.[4]

Characteristic changes seen in psoriatic plaques include: (i) irregular proliferation and maturation of keratinocytes, (ii) increased dermal blood vessels, and (iii) inflammatory cell infiltration in the skin.[5] Classical histopathological findings in the skin biopsies of mature psoriatic lesions include regular (psoriasiform) epidermal hyperplasia, elongation of the rete ridges with a thin suprapapillary epidermis, dilated vessels in the upper dermis, and hyperkeratosis with parakeratotic mounds.[6] However, regardless of the histopathological features described, it has been noted there is no completely characteristic microscopic architecture even in untreated, clinically active psoriatic lesions.[7] Moreover, psoriasis is a dynamic process and its histopathological features may vary according to disease duration and lesion location.[1,3] Establishing a pathological diagnosis of psoriasis is challenging in patients with non-classical features.[5,8]

This study aimed to investigate the distribution of classical/non-classical histopathological findings in psoriasis patients according to 1) psoriasis subtype, 2) disease duration, 3) disease severity, 4) the anatomical site of biopsy, and 5) classical/non-classical clinical presentation.

Methods

We retrospectively analyzed data from 160 patients diagnosed with psoriasis through histopathological examination at our clinic between 2017 and 2023. Patients who had not discontinued all topical and systemic dermatological treatments one month prior to biopsy were excluded. Ethical approval for the study was obtained from the Trakya University, Faculty of Medicine, Non-Interventional Scientific Research Ethics Committee (approval date/number: 09.10.2023/335).

Histopathologically classical and non-classical findings were determined by reviewing dermatopathology textbooks and relevant primary literature.[3,9,10] Biopsy specimens stained with hematoxylin and eosin were re-examined according to the histopathological criteria by two pathologists from the pathology department of Trakya University, Faculty of Medicine who were experienced in dermatopathology.

The sociodemographic (age, gender) and clinical characteristics (psoriasis subtypes, disease duration, lesion morphology and distribution, family history, and fingernail pitting) of the patients participating in the study were recorded retrospectively from electronic medical records. Psoriasis subtypes were classified as psoriasis vulgaris (PV), palmoplantar PP (PPPP), palmoplantar psoriasis, generalized PP (GPP), guttate psoriasis, and EP. The PPPP category included patients with vesiculo-pustular lesions involving the palms and soles of the feet, while the palmoplantar psoriasis category included patients with well-circumscribed erythematous keratotic plaques but few pustular formations.[11]

To enable a comparison with the literature data and identify histopathological data in early-onset psoriasis, disease duration was classified as ≤12 or >12 months and as ≤1 or >1 month.[12] Except for those with PPPP and palmoplantar psoriasis, we retrospectively reviewed all patients' Psoriasis Area Severity Index (PASI) scores, which are used to measure the severity of psoriasis. According to PASI scores calculated at the time of biopsy, the patients were divided into two groups as PASI ≤10 or PASI>10.[13] The anatomical regions biopsied were categorized as trunk, lower extremities, palmoplantar, upper extremities and scalp.

The clinical manifestations of psoriasis patients were classified as classical and non-classical feature using the criteria specified by Chau et al. as a reference.[10] In addition to classical morphology and/or classical distribution, the presence of nail pitting (10 or more on a nail)[14] and/or a history of psoriasis in a first-degree relative were evaluated. Patients who met at least two diagnostic criteria were regarded as having the classical features.

Statistical Analysis

The data were statistically analyzed using IBM SPSS version 26 software. Pearson's chi-square and Fisher's exact test were used for comparisons of categorical variables between the groups. $P < 0.05$ was considered statistically significant.

Results

A total of 160 biopsy sections from 160 patients were included in this study. The sociodemographic and clinical characteristics of the patients are summarized in Table 1.

Table 1. Demographic and clinical characteristics of the study sample (n=160)

	n (%)
Age, years, mean±SD (range)	44.34±14.52 (18-75)
Gender, n (%)	
Female	93 (58.1)
Male	67 (41.9)
Psoriasis subtype, n (%)	
Psoriasis vulgaris	112 (70)
PPPP	25 (15.6)
Palmoplantar psoriasis	8 (5.0)
Generalized PP	6 (3.8)
Guttate psoriasis	5 (3.1)
Erythrodermic psoriasis	4 (2.5)
Disease Duration (months), n (%)	
>12	93 (58.1)
≤12	67 (41.9)
Mean±SD (Min-Max)	65.85±92.07 (1-480)
PASI, n=112 (%)	
PASI ≤10	82 (73.2)
PASI >10	39 (34.8)
Mean±SD (Min-Max)	8.4±8.03 (0.1-43.4)
Clinical diagnostic criteria, n (%)	
Classic morphology*	102 (63.8)
Classic distribution†	86 (53.8)
Nail pitting‡	22 (13.8)
Family history of psoriasis§	38 (23.7)
Classic features	96 (60)
Non-classic features	64 (40)
Anatomical site of biopsy, n (%)	
Trunk	42 (26.3)
Lower extremity	41 (25.6)
Palmoplantar	31 (19.4)
Upper extremity	28 (17.5)
Scalp	18 (11.3)

SD: Standard deviation, Min: Minimum, Max: Maximum, PPPP: Palmoplantar pustular psoriasis, PP: Pustular psoriasis, PASI: Psoriasis Area Severity Index.

* Classical morphology was defined as well-demarcated erythematous papules and plaques accompanied by silvery micaceous scales.[9]

† Classical distribution was defined as scalp, elbows, knees, or gluteal region involvement in psoriasis vulgaris and as palmoplantar region involvement in palmoplantar pustular psoriasis and palmoplantar psoriasis.[9]

‡ A nail with 10 or more pits was considered positive.[13]

§ History of psoriasis in a first-degree relative was considered positive family history.[9]

The mean age of the patients was 44.34 years (range: 18-75 years). Women accounted for 58.1% (n=93) of the study group. Lesion duration was less than ≤12 months in 67 patients (41.9%) and ≤1 month in 8 patients. Classical morphology and classical distribution were observed in 63.8% (n=102) and 53.8% (n=86) of the patients, respectively.

The most common classical histopathological findings were regular acanthosis (99.4%), confluent parakeratosis (96.3%), blood vessels, dilated (93.1%), hyperkeratosis (89.4%), suprapapillary plate thinning (89.4%), thick-walled vessels (83.8%), and hypogranulosis (78.8%). Among the non-classical histopathologic features, the most common were superficial perivascular dermal infiltration (81.3%), spongiosis (53.8%), and the presence of intraepidermal lymphocytic cells (51.3%) (Table 2).

Spongiform pustule of Kogoj was more common in PPPP and GPP patients than in other psoriasis subtypes (64% and 66.7%, respectively). A higher proportion of PPPP patients had intraepidermal neutrophil accumulation (44%). All GPP patients (n=6, 100%) exhibited an increased number of dermal blood vessels, papillary oedema and superficial perivascular dermal infiltration. Among the classical histopathological findings in palmoplantar psoriasis patients, hyperkeratosis and associated vascular pathologies (dermal papillae capillary ectasia, blood vessels, dilated, increased number of vessels, thick-walled vessels) were detected at a rate of 100% (n=8). Irregular acanthosis, stratum basale necrotic keratinocytes, and spongiosis were detected in 100% (n=4) of patients with EP (Table 3).

When the distribution of classical and non-classical histopathological findings was examined according to disease duration, hyperkeratosis and intraepidermal lymphocyte accumulation were more common in patients with disease duration longer than 12 months (p=0.044 and p=0.042, respectively) (Table 4). Dilated blood vessels, papillary edema, and dermal neutrophils were statistically more frequent in patients with a disease duration of less than ≤ 1 month (p=0.031, p=0.011, and p=0.011, respectively) (Table 5).

Analysis of changes in histopathological findings according to disease severity revealed that the presence of Munro microabscess (p=0.010), papillary oedema (p=0.014), stratum basale necrotic keratinocytes (p=0.031) were higher in patients with PASI >10 (Table 6).

In terms of the distribution of histopathological findings according to biopsy site, we determined that spongiform pustule of Kogoj, intraepidermal neutrophils, and vacuolar changes in the basement membrane were more common in biopsies of the palmoplantar region (p=0.003, p=0.002, and p=0.021, respectively). Hyperkeratosis and

suprapapillary plate thinning were more common in trunk biopsies (p=0.024 and p=0.027, respectively) (Table 7).

Table 2. Distribution of histopathological findings in psoriasis patients (n=160)

	n	%
Classical histopathologic features		
Hyperkeratosis	143	89.4
Confluent Parakeratosis	154	96.3
Hypogranulosis	126	78.8
Munro microabscess	50	31.3
Spongiform pustule of Kogoj	51	31.9
Regular acanthosis	159	99.4
Club-shaped rete ridges	101	63.1
Dermal papillae capillary ectasia	126	78.8
Suprapapillary plate thinning	143	89.4
Blood vessels, dilated	149	93.1
Increased number of the vessels	109	68.1
Thick-walled vessels	134	83.8
Papillary oedema	10	6.3
Non-classical histopathologic features		
Irregular acanthosis	35	21.9
Hypergranulosis	6	3.8
Compact orthokeratosis	9	5.6
Stratum spinosum necrotic keratinocytes	2	1.3
Stratum basale necrotic keratinocytes	10	6.3
Spongiosis	86	53.8
İntraepidermal cells		
Lymphocytes	82	51.3
Neutrrophils	27	16.9
Eosinophilis	2	1.3
Neutrophilic spongiosis	6	3.8
Vacuolar change in basement membrane	3	1.9
Dermal infiltration		
Erythrocyte extravasation	1	0.6
Eosinophils	3	1.9
Neutrophils	11	6.9
Lymphocytes	1	0.6
Deep perivascular	6	3.8
Superficial perivascular	130	81.3
Papillary dermal fibrosis	2	1.3

When the histopathological findings of patients with non-classical presentation were evaluated, it was found that spongiosis and intraepidermal lymphocytes were more common than in patients with the classical presentation (p=0.005 and p=0.008, respectively) (Table 8).

Discussion

Psoriasis occurs equally in men and women.[15] However, because psoriasis in men has a more severe course and is more likely to require systemic treatment, male predominance has been mentioned in recent studies.[16] In our study, women were predominant. This may be because psoriasis has a greater impact on quality of life in women than men, leading them to present to the dermatology outpatient clinic more frequently[16,17], and most of the patients in our study have mild PASI scores (≤10 in 59.4% of patients).

The most common and easily recognized subtype of psoriasis is chronic plaques or PV.[18] PPPP is a variant that can affect 11-39% of psoriasis patients,[19] while palmoplantar psoriasis accounts for 3-4% of all cases.[20] Although our findings are generally consistent with the literature, the rate of palmoplantar psoriasis was found to be higher. This may be because palmoplantar psoriasis is difficult to distinguish from contact dermatitis due to both clinical presentation and location, and therefore skin biopsy is more necessary during diagnosis.[1]

Nail pitting is a common nail finding in psoriasis, reported at a rate of 37% in a study by Singh.[21] This rate was similar to that observed in our study. It has been shown that approximately 30% of psoriasis patients have a first-degree relative with a history of psoriasis and that this is associated with early-onset psoriasis (before the age of 40).[22] In our study, 22% of the patients had a positive family history. The fact that the mean age of the patients participating in the study was 44.34 years and patients under the age of 18 were not included in the study may have led to the lower rate of family history positivity.

Consistent with the literature, our study found that acanthosis and parakeratosis were among the most frequently occurring histopathological changes in the epidermis of patients with psoriasis. Studies have reported that the histopathological finding of Munro microabscess is more common than spongiform pustule of Kogoj.[8,10,24] In our study, both were observed at similar rates. This may be due to the higher proportion of PPPP patients in our study compared to other studies.[8,10]

Appukkuttan et al. reported that lymphocytes were the most common dermal infiltrating cells, similar to our findings.[25] Song et al. detected a prominence of dermal neutrophils and noted that they were seen in biopsies of early psoriasis lesions.[8] In our study, the majority of early psoriasis patients (disease duration ≤1 month) had a dominant dermal neutrophil population. This may be explained by the autoinflammation process that is prevalent in early psoriasis lesions.[12]

Tablo 3. Histopathological findings in various clinical subtypes of psoriasis

	Psoriasis subtype					
	PV (n=112)	**PPPP (n=25)**	**Palmoplantar psoriasis (n=8)**	**GPP (n=6)**	**Guttate psoriasis (n=5)**	**Erythrodermic psoriasis (n=4)**
Classical histopathologic features						
Hyperkeratosis	101 (90.2)	22 (88)	8 (100)	4 (66.7)	4 (80)	4 (100)
Confluent Parakeratosis	111 (99.1)	23 (92)	7 (87.5)	5 (83.3)	4 (80)	4 (100)
Hypogranulosis	93 (83)	19 (76)	5 (62.5)	3 (50)	2 (40)	4 (100)
Munro microabscess	34 (30.4)	10 (40)	1 (12.5)	2 (33.3)	2 (40)	1 (25)
Spongiform pustule of Kogoj	25 (22.3)	16 (64)	3 (37.5)	4 (66.7)	1 (20)	2 (50)
Regular acanthosis	112 (100)	25 (100)	8 (100)	6 (100)	5 (100)	4 (100)
Club-shaped rete ridges	69 (61.6)	17 (68)	7 (87.5)	3 (50)	3 (60)	2 (50)
Dermal papilla capillary ectasia	88 (78.6)	21 (84)	8 (100)	4 (66.7)	3 (60)	2 (50)
Suprapapillary plate thinning	102 (91.1)	21 (84)	7 (87.5)	5 (83.3)	5 (100)	3 (75)
Blood vessels, dilated	106 (94.6)	22 (88)	8 (100)	5 (83.3)	4 (80)	4 (100)
Increased number of the vessels	73 (65.2)	17 (68)	8 (100)	6 (100)	2 (40)	3 (75)
Thick-walled vessels	95 (84.8)	22 (88)	8 (100)	5 (83.3)	2 (40)	2 (50)
Papillary oedema	0 (0)	0 (0)	0 (0)	6 (100)	0 (0)	4 (100)
Non-classical histopathologic features						
Irregular acanthosis	22 (19.6)	6 (24)	1 (12.5)	2 (33.3)	0 (0)	4 (100)
Hypergranulosis	3 (2.7)	2 (8)	0 (0)	0 (0)	1 (20)	0 (0)
Compact orthokeratosis	4 (3.6)	5 (20)	0 (0)	0 (0)	0 (0)	0 (0)
Stratum spinosum necrotic keratinocytes	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)	0 (0)
Stratum basale necrotic keratinocytes	5 (4.5)	1 (4)	0 (0)	0 (0)	0 (0)	4 (100)
Spongiosis	54 (48.2)	17 (68)	5 (62.5)	4 (66.7)	2 (40)	4 (100)
Intraepidermal cells						
Lymphocytes	55 (49.1)	12 (48)	6 (75)	3 (50)	2 (40)	4 (100)
Neutrrophils	13 (11.6)	11 (44)	2 (25)	1 (16.7)	0 (0)	0 (0)
Eosinophilis	1 (0.9)	0 (0)	0 (0)	1 (16.7)	0 (0)	0 (0)
Neutrophilic spongiosis	5 (4.5)	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)
Vacuolar change in basement membrane	0 (0)	3 (12)	0 (0)	0 (0)	0 (0)	0 (0)
Dermal infiltration						
Erythrocyte extravasation	1 (0.9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Eosinophils	1 (0.9)	0 (0)	0 (0)	2 (33.3)	0 (0)	0 (0)
Neutrophils	6 (5.4)	1 (4)	0 (0)	3 (50)	0 (0)	1 (25)
Lymphocytes	1 (0.9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Deep perivascular	4 (3.6)	2 (8)	0 (0)	0 (0)	0 (0)	0 (0)
Superficial perivascular	95 (84.8)	19 (76)	3 (37.5)	6 (100)	4 (80)	3 (75)
Papillary dermal fibrosis	2 (1.8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

PV: Psoriasis vulgaris, PPPP: Palmoplantar pustular psoriasis, GPP: Generalized pustular psoriasis.

Table 4. Distribution of classical and non-classical histopathological findings according to disease duration

	Disease Duration (months)		X^2	P value*
	≤ 12 (n=67)	>12 (n=93)		
Classical histopathologic features				
Hyperkeratosis	56 (83.6)	87 (93.5)	4.07	**0.044**
Confluent Parakeratosis	62 (92.5)	92 (98.9)	4402.00	0.083
Hypogranulosis	49 (73.1)	77 (82.8)	2172.00	0.141
Munro microabscess	23 (34.3)	27 (29)	0.51	0.476
Spongiform pustule of Kogoj	24 (35.8)	27 (29)	0.83	0.363
Regular acanthosis	67 (100)	92 (98.9)	0.73	1.000
Club-shaped rete ridges	42 (62.7)	59 (63.4)	0.01	0.922
Dermal papillae capillary ectasia	52 (77.6)	74 (79.6)	0.09	0.765
Suprapapillary plate thinning	59 (88.1)	84 (90.3)	0.21	0.647
Blood vessels, dilated	61 (91)	88 (94.6)	0.779	0.528
Increased number of the vessels	43 (64.2)	66 (71)	0.83	0.363
Thick-walled vessels	57 (85.1)	77 (82.8)	0.15	0.700
Papillary oedema	8 (11.9)	2 (2.2)	3467.000	0.096
Non-classical histopathologic features				
Irregular acanthosis	13 (19.4)	22 (23.7)	0.41	0.521
Hypergranulosis	3 (4.5)	3 (3.2)	0.17	0.695
Compact orthokeratosis	4 (6)	5 (5.4)	0.03	1.000
Stratum spinosum necrotic keratinocytes	1 (1.5)	1 (1.1)	0.06	1.000
Stratum basale necrotic keratinocytes	8 (11.9)	2 (2.2)	6370.00	0.018
Spongiosis	42 (62.7)	44 (47.3)	3703.00	0.054
Intraepidermal cells				
Lymphocytes	28 (41.8)	54 (58.1)	4.128	**0.042**
Neutrrophils	13 (19.4)	14 (15.0)	0.088	0.767
Eosinophilis	1 (1.5)	1 (1.1)	0.06	1.000
Neutrophilic spongiosis	3 (4.5)	3 (3.2)	0.17	0.695
Vacuolar change in basement membrane	3 (4.5)	- (-)	4244.00	0.072
Dermal infiltration				
Erythrocyte extravasation	0 (0)	1 (1.1)	0.73	1.000
Eosinophils	1 (1.5)	2 (2.2)	0.09	1.000
Neutrophils	6 (9)	5 (5.4)	0.78	0.528
Lymphocytes	0 (0)	1 (1.1)	0.73	1.000
Deep perivascular	3 (4.5)	3 (3.2)	0.17	0.695
Superficial perivascular	64 (95.5)	66 (71)	5.30	**0.021**
Papillary dermal fibrosis	1 (1.5)	1 (1.1)	0.06	1.000

*Pearson chi-Square, Fisher's exact test. Bold values denote statistical significance at the p <0.05 level.

Tablo 5. Change of histopathological findings depending on whether the disease duration is less than 1 month or not

	Disease Duration (months)		X^2	P value*
	≤ 1 (n=8)	>1 (n=152)		
Classical histopathologic features				
Hyperkeratosis	5 (62.5)	138 (90.8)	6405.00	**0.040**
Confluent Parakeratosis	7 (87.5)	147 (96.7)	1786.00	0.269
Hypogranulosis	5 (62.5)	121 (79.6)	1329.00	0.368
Munro microabscess	4 (50)	46 (30.3)	1378.00	0.258
Spongiform pustule of Kogoj	3 (37.5)	48 (31.6)	0.12	0.710
Regular acanthosis	8 (100)	151 (99.3)	0.05	1.000
Club-shaped rete ridges	6 (75)	95 (62.5)	0.51	0.711
Dermal papilla capillary ectasia	7 (87.5)	119 (78.3)	0.39	1.000
Suprapapillary plate thinning	6 (75)	137 (90.1)	1832.00	0.203
Blood vessels, dilated	8 (100)	141 (91.5)	5.061	**0.031**
Increased number of the vessels	8 (100)	101 (66.4)	3940.00	0.056
Thick-walled vessels	7 (87.5)	127 (83.6)	0.09	1.000
Papillary oedema	4 (25)	8 (5.3)	12.336	**0.011**
Non-classical histopathologic features				
Irregular acanthosis	2 (25)	33 (21.7)	0.05	1.000
Hypergranulosis	0 (0)	6 (3.9)	0.33	1.000
Compact orthokeratosis	0 (0)	9 (5.9)	0.50	1.000
Stratum spinosum necrotic keratinocytes	0 (0)	2 (1.3)	0.11	1.000
Stratum basale necrotic keratinocytes	1 (12.5)	9 (5.9)	0.56	0.410
Spongiosis	6 (75)	80 (52.6)	1530.00	0.288
Intraepidermal cells				
Lymphocytes	5 (62.5)	77 (50.7)	0.43	0.720
Neutrrophils	2 (25)	25 (16.4)	0.05	1.000
Eosinophilis	1 (12.5)	1 (0.7)	8634.00	0.098
Neutrophilic spongiosis	0 (0)	6 (3.9)	0.33	1.000
Vacuolar change in basement membrane	0 (0)	3 (2)	0.16	1.000
Dermal infiltration				
Erythrocyte extravasation	0 (0)	1 (0.7)	0.05	1.000
Eosinophils	1 (12.5)	2 (1.3)	5167.00	0.143
Neutrophils	3 (37.5)	8 (5.3)	12336.00	**0.011**
Lymphocytes	0 (0)	1 (0.7)	0.39	1.000
Deep perivascular	0 (0)	6 (3.9)	0.33	1.000
Superficial perivascular	8 (100)	122 (80.3)	1067.00	0.599
Papillary dermal fibrosis	0 (0)	2 (1.3)	0.11	1.000

*Pearson chi-Square, Fisher's exact test. Bold values denote statistical significance at the p <0.05 level.

Table 6. Distribution of histopathological findings according to PASI scores (n=121)

	PASI		X^2	P value*
	PASI 10 ≤	PASI 10 >		
Classical histopathologic features				
Hyperkeratosis	73 (89)	36 (92.3)	0.319	0.750
Confluent Parakeratosis	80 (97.6)	39 (100)	0.967	1.000
Hypogranulosis	65 (79.3)	34 (87.2)	1.112	0.292
Munro microabscess	19 (23.2)	18 (46.2)	6.577	**0.010**
Spongiform pustule of Kogoj	17 (20.7)	11 (28.2)	0.830	0.362
Regular acanthosis	82 (100)	38 (97.4)	2.120	0.322
Club-shaped rete ridges	49 (59.8)	25 (64.1)	0.210	0.647
Dermal papillae capillary ectasia	61 (74.4)	32 (82.1)	0.872	0.350
Suprapapillary plate thinning	75 (91.5)	35 (89.7)	0.095	0.745
Blood vessels, dilated	77 (93.9)	37 (94.9)	0.046	1.000
Increased number of the vessels	50 (61)	28 (71.8)	1.351	0.245
Thick-walled vessels	69 (84.1)	30 (76.9)	0.927	0.336
Papillary oedema	2 (2.4)	6 (15.4)	7.174	**0.014**
Non-classical histopathologic features				
Irregular acanthosis	14 (17.1)	12 (30.8)	2.939	0.086
Hypergranulosis	3 (3.7)	1 (2.6)	0.099	1.000
Compact orthokeratosis	3 (3.7)	1 (2.6)	0.099	1.000
Stratum spinosum necrotic keratinocytes	-	-	-	-
Stratum basale necrotic keratinocytes	3 (3.7)	6 (15.4)	5.278	**0.031**
Spongiosis	39 (47.6)	21 (53.8)	0.418	0.518
Intraepidermal cells				
Lymphocytes	38 (46.3)	23 (59)	1.687	0.194
Neutrrophils	7 (8.5)	8 (20.5)	3.491	0.079
Eosinophilis	1 (1.2)	0 (0)	0.480	1.000
Neutrophilic spongiosis	2 (2.4)	4 (10.3)	3.427	0.084
Vacuolar change in basement membrane	-	-	-	-
Dermal infiltration				
Erythrocyte extravasation	1 (1.2)	0 (0)	0.480	1.000
Eosinophils	1 (1.2)	0 (0)	0.480	1.000
Neutrophils	5 (6.1)	2 (5.1)	0.046	1.000
Lymphocytes	0 (0)	1 (2.6)	2.120	0.322
Deep perivascular	2 (2.4)	2 (5.1)	0.598	0.593
Superficial perivascular	68 (82.9)	34 (87.2)	0.361	0.548
Papillary dermal fibrosis	2 (2.4)	0 (0)	0.967	1.000

PASI: Psoriasis Area Severity Index. *Pearson chi-Square, Fisher's exact test. Bold values denote statistical significance at the p <0.05 level.

Table 7. Classical and non-classical histopathological findings according to the anatomical site of the biopsy

	Anatomic site of biopsy						
	Trunk (n=42)	**Lower extremity (n=41)**	**Palmoplantar (n=31)**	**Upper extremity (n=28)**	**Scalp (n=18)**	**X^2**	**P value***
Classical histopathologic features							
Hyperkeratosis	42 (100)	36 (87.8)	28 (90.3)	22 (78.6)	15 (83.3)	10.098	**0.024**
Confluent Parakeratosis	40 (95.2)	41 (100)	29 (93.5)	26 (92.9)	18 (100)	3.786	0.372
Hypogranulosis	31 (73.8)	36 (87.8)	21 (67.7)	22 (78.6)	16 (88.9)	5.793	0.209
Munro microabscess	16 (38.1)	12 (29.3)	10 (32.3)	10 (35.7)	2 (11.1)	4.663	0.324
Spongiform pustule of Kogoj	12 (28.6)	11 (26.8)	19 (61.3)	6 (21.4)	3 (16.7)	16.369	**0.003**
Regular acanthosis	42 (100)	40 (97.6)	31 (100)	26 (92.9)	18 (100)	3.665	0.740
Club-shaped rete ridges	27 (64.3)	23 (56.1)	22 (71)	17 (60.7)	12 (66.7)	1.880	0.758
Dermal papillae capillary ectasia	33 (78.6)	29 (70.7)	27 (87.1)	21 (75)	16 (88.9)	4.002	0.405
Suprapapillary plate thinning	41 (97.6)	33 (80.5)	27 (87.1)	25 (89.3)	17 (94.4)	10.120	**0.027**
Blood vessels, dilated	40 (95.2)	40 (97.6)	29 (93.5)	17 (60.7)	16 (88.9)	4.414	0.320
Increased number of the vessels	32 (76.2)	27 (65.9)	22 (71)	19 (67.9)	9 (50)	4.195	0.380
Thick-walled vessels	34 (81)	33 (80.5)	28 (90.3)	22 (78.6)	17 (94.4)	3.478	0.483
Papillary edema	7 (16.7)	1 (2.4)	1 (3.2)	1 (3.6)	0 (0)	7.504	0.061
Non-classical histopathologic features							
Irregular acanthosis	12 (28.6)	8 (19.5)	6 (19.4)	4 (14.3)	5 (27.8)	2.647	0.624
Hypergranulosis	1 (2.4)	2 (4.9)	1 (3.2)	2 (7.1)	0 (0)	1.825	0.835
Compact orthokeratosis	2 (4.8)	1 (2.4)	5 (16.1)	1 (3.6)	0 (0)	5.957	0.132
Stratum spinosum necrotic keratinocytes	0 (0)	0 (0)	2 (6.5)	0 (0)	0 (0)	4.812	0.083
Stratum basale necrotic keratinocytes	6 (14.3)	1 (2.4)	1 (3.2)	1 (3.6)	1 (5.6)	4.999	0.247
Spongiosis	22 (52.4)	19 (46.3)	20 (64.5)	15 (53.6)	10 (55.6)	2.406	0.661
Intraepidermal cells							
Lymphocytes	21 (50)	20 (48.8)	17 (54.8)	14 (50)	10 (55.6)	0.437	0.979
Neutrrophils	9 (21.4)	1 (2.4)	11 (35.5)	5 (17.9)	1 (5.6)	16.226	**0.002**
Eosinophilis	1 (2.4)	0 (0)	0 (0)	1 (3.6)	0 (0)	2.956	0.658
Neutrophilic spongiosis	3 (7.1)	2 (4.9)	0 (0)	0 (0)	1 (5.6)	3.560	0.441
Vacuolar change in basement membrane	0 (0)	0 (0)	3 (9.7)	0 (0)	0 (0)	6.606	**0.021**
Dermal infiltration							
Erythrocyte extravasation	0 (0)	0 (0)	0 (0)	0 (0)	1 (5.6)	5.311	0.111
Eosinophils	1 (2.4)	2 (4.9)	0 (0)	0 (0)	0 (0)	2.534	0.691
Neutrophils	5 (11.9)	3 (7.3)	1 (3.2)	2 (7.1)	0 (0)	2.962	0.554
Lymphocytes	0 (0)	1 (2.4)	0 (0)	0 (0)	0 (0)	3.665	0.740
Deep perivascular	1 (2.4)	1 (2.4)	1 (3.2)	1 (3.6)	2 (11.1)	2.961	0.554
Superficial perivascular	37 (88.1)	35 (85.4)	22 (71)	24 (85.7)	12 (66.7)	6.434	0.164
Papillary dermal fibrosis	0 (0)	0 (0)	0 (0)	1 (3.6)	1 (5.6)	4.651	0.121

*Pearson chi-square. Bold values denote statistical significance at the $p < 0.05$ level.

Table 8. Distribution of histopathological findings according to classical/non-classical features classification

	Classical feature (n=96)	Non-classical feature (n=64)	X^2	P value*
Classical histopathologic features				
Hyperkeratosis	87 (90.6)	56 (87.5)	0.395	0.530
Confluent Parakeratosis	94 (97.9)	60 (93.8)	1.847	0.219
Hypogranulosis	76 (79.2)	50 (78.1)	0.025	0.875
Munro microabscess	28 (29.2)	22 (34.4)	0.485	0.486
Spongiform pustule of Kogoj	27 (28.1)	24 (37.5)	1.554	0.213
Regular acanthosis	95 (99)	64 (100)	0.671	1.000
Club-shaped rete ridges	62 (64.6)	39 (60.9)	0.219	0.640
Dermal papillae capillary ectasia	78 (81.3)	48 (75)	0.896	0.344
Suprapapillary plate thinning	84 (87.5)	59 (92.2)	0.889	0.346
Blood vessels. dilated	91 (94.8)	58 (90.6)	1.041	0.350
Increased number of the vessels	66 (68.8)	43 (67.2)	0.043	0.835
Thick-walled vessels	76 (79.2)	58 (90.6)	3.705	0.054
Papillary oedema	3 (3.1)	7 (10.9)	4.000	0.091
Non-classical histopathologic features				
Irregular acanthosis	18 (18.8)	17 (26.6)	1.371	0.242
Hypergranulosis	2 (2.1)	4 (6.3)	1.847	0.219
Compact orthokeratosis	5 (5.2)	4 (6.3)	0.078	1.000
Stratum spinosum necrotic keratinocytes	1 (1)	1 (1.6)	0.084	1.000
Stratum basale necrotic keratinocytes	3 (3.1)	7 (10.9)	4.000	0.091
Spongiosis	18 (18.8)	46 (71.8)	7.748	**0.005**
Intraepidermal cells				
Lymphocytes	66 (68.8)	16 (25)	1.839	**0.008**
Neutrrophils	14 (14.6)	13 (20.3)	0.899	0.343
Eosinophilis	2 (2.1)	0 (0)	1.350	0.517
Neutrophilic spongiosis	4 (4.2)	2 (3.1)	0.115	1.000
Vacuolar change in basement membrane	1 (1)	2 (3.1)	0.906	0.564
Dermal infiltration				
Erythrocyte extravasation	1 (1)	0 (0)	0.671	1.000
Eosinophils	0 (0)	3 (4.7)	4.586	0.062
Neutrophils	5 (5.2)	6 (9.4)	1.041	0.350
Lymphocytes	1 (1)	0 (0)	0.671	1.000
Deep perivascular	2 (2.1)	4 (6.3)	1.847	0.219
Superficial perivascular	78 (81.3)	52 (81.3)	0.000	1.000
Papillary dermal fibrosis	2 (2.1)	0 (0)	1.350	0.517

*Pearson chi-Square, Fisher's exact test. Bold values denote statistical significance at the p <0.05 level.

In a study by Fülle et al., intraepidermal eosinophilia was observed at a rate of 2.6% (n=2), eosinophilic spongiosis at 1.3% (n=1), and dermal eosinophilia at 21.3% (n=16).[3] Chau et al. reported the frequency of eosinophilic spongiosis and dermal eosinophilia as 4.6% and 25.4%, respectively.[10] In our study, the rate of intraepidermal eosinophilia was 1.3% (n=2) and that of dermal eosinophilia was 1.9% (n=3), while eosinophilic spongiosis was not observed in any patient. Pathology textbooks and primary sources state that eosinophils are typically rare or absent in psoriasis patients.[26] Chau et al. considered that their higher levels of eosinophilia may be attributable to the presence of coexisting contact dermatitis or atopic dermatitis in the psoriasis lesions of their patients.[10]

Histopathological findings in patients with GPP include the classic histopathological findings (hyperkeratosis, confluent parakeratosis and regular acanthosis) that accompany spongiform pustule of Kogoj.[27] In contrast to PV, papillary oedema and superficial perivascular dermal infiltration are more common.[2] In our study, we observed that the histopathological finding of spongiform pustule of Kogoj was more common in GPP patients, while an increased number of dermal blood vessels, papillary edema, and superficial perivascular dermal infiltration were observed in all patients.

Palmoplantar psoriasis is often accompanied by fissures and hyperkeratosis, making it difficult to differentiate from contact dermatitis.[1] Aydın et al. emphasized that focal parakeratosis and associated moderate hyperkeratosis are important in the diagnosis of palmoplantar psoriasis.[28] In addition, dilated and tortuous capillaries are not seen in contact dermatitis.[1] Although there was no control group in our study, we believe that because hyperkeratosis, orthokeratosis, and vascular changes are more common in palmoplantar psoriasis compared to other psoriasis subtypes, these findings will be especially helpful in the diagnosis of palmoplantar psoriasis.

In EP, Munro microabscesses and parakeratosis are not histopathologically evident because highly accelerated cell turnover causes loss of the stratum corneum layer.[1,29] In addition to other non-classical histopathological findings, apoptotic keratinocytes are also seen in EP.[29] Recently, it has been emphasized that necrotic keratinocytes can be seen in psoriasis and are mostly located in the upper epidermis. However, psoriasis subtyping was not performed in this study.[30] During erythrodermic drug eruptions, the epidermis shows vacuolar alteration and necrotic keratinocytes at all levels of the epidermis.[31] Although we noted no drug-associated EP in our retrospective data analysis, it is noteworthy that stratum basale necrotic keratinocytes were observed in our EP patients.

Psoriatic histopathological changes in the dermis precede histopathological changes in the epidermis. The earliest histopathological changes include dilated vessels in the papillary dermis and congestion with mild perivascular lymphocytic infiltration.[25,32] In our study, early histopathological findings were pronounced in lesions with a short duration. However, the histopathological findings of early psoriasis are nonspecific.[32] In addition, patients' clinical characteristics should be known in order to better evaluate these histopathological findings, because the classical histopathological findings accompanying epidermal changes are seen in well-established lesions.[1] Although there are no clear data on early psoriasis lesions and lesion duration in the literature, Fanoni et al. described patients with early psoriasis as presenting with papular lesions or actively emerging pustular/papulopustular lesions.[12] However, the retrospective nature of our study resulted in data loss, and the characteristics defined by Fanoni et al. could not be evaluated.

It has been reported in the literature that there is no correlation between histopathological findings and PASI scores.[33,34] In their quantitative computer-aided study, Kim et al. observed a relationship between histopathological findings and the three components of the PASI score (erythema, thickness, and desquamation).[35] In our study, stratum basale necrotic keratinocytes were observed at higher rates only in patients with high PASI values. The fact that this histopathological finding is mostly seen in patients with EP may be related to the higher PASI scores in this group. In order to more clearly evaluate the relationship between PASI and histopathological findings, we think it would be more appropriate to determine PASI component scores separately and calculate PASI scores at the lesion level.

Similar to the study by Chau et al., the lower extremities and trunk were among the most commonly biopsied anatomical regions in our study.[10] The list of differential diagnoses for psoriasis is long and includes inflammatory, infectious, and neoplastic diseases with papulosquamous lesions.[18] These diseases are mostly localized to the limbs and trunk.[36] As clinicians have difficulty in the differential diagnosis of psoriasis lesions on the lower extremity and trunk, more biopsies are needed for lesions located in these regions.

Patients with PP exhibit intraepidermal pustules at various stages of development.[1] The histopathologic features in acute PP differ from those seen in PV because neutrophil exocytosis occurs before the typical epidermal

hyperplastic changes take place.[24] In our study, these histopathological findings were more frequent in patients with PPPP compared to other localizations, consistent with clinical findings.

Ackerman et al. emphasized that histopathological findings in patients with leg psoriasis were less psoriasiform and that this was more pronounced in patients with psoriasis and concomitant stasis dermatitis.[37] Fülle et al. reported that regular hyperplasia and suprapapillary thinning were less common in psoriasis patients with leg involvement compared to trunk involvement.[3] The same authors stated that stasis dermatitis did not alter the histopathological findings in patients with leg psoriasis. In our study, these histopathological changes were more common in patients with trunk involvement. As a result, when evaluating histopathological findings in psoriasis patients, attention should be paid to the location of the biopsy site.

The appearance of different clinical pictures at different times in psoriasis patients creates a dilemma both for the clinician and the diagnostic value of the histopathological findings used in diagnosis.[4] In this respect, psoriasis should be distinguished histopathologically from psoriasiform dermatitis.[4,38] The histopathological findings of psoriasiform dermatitis should include spongiosis, irregular acanthosis, and the absence of Munro microabscesses and Kogoj abscesses.[4] In the study of Chau et al., irregular acanthosis and spongiosis were among the most common non-classical histopathological findings.[10] In our study, the spongiosis and intraepidermal lymphocytes were more common in psoriasis patients with non-classical clinical features. The appearance of intraepidermal lymphocytes may be related to mild spongiosis.[1] Mehta et al. found that the presence of intraepidermal lymphocytic cells was significantly associated with the diagnosis of psoriasiform dermatitis.[4] In conclusion, it should be noted that the presence of spongiosis and intraepidermal lymphocytes seen in psoriasis vulgaris histopathology can also be seen histopathologically in patients with non-classical clinical features, and pathognomonic signs such as the presence of Munro's microabscess and Kogoj's spongiform pustules should be sought to distinguish it from psoriasiform dermatitis.[7]

In the study by Chau et al., vacuolar changes in the basal layer were among the second most common non-classical histopathological findings, observed at a rate of 1% in palmoplantar psoriasis.[10] Vacuolar changes in the basal layer are known as a sign of interface/lichenoid dermatitis associated with necrotic keratinocytes.[39] In our study, vacuolar changes in the basal layer and stratum spinosum necrotic keratinocytes were observed in palmoplantar region involvement. Psoriasiform dermatitis encompasses a wide-ranging group of diseases with similar clinical and histopathological features. It is classified into two main categories: the pure psoriasiform pattern and combination patterns (psoriasiform lichenoid, spongiotic psoriasiform, spongiotic psoriasiform lichenoid).[40] In our study, histopathological changes in the psoriasiform lichenoid pattern were observed in palmoplantar region involvement. Although these findings are among the non-classical histopathological findings of psoriasis, it should not be forgotten that they can be seen in the palmoplantar location.

Eczematized psoriasis is seen in 10-15% of psoriasis patients. The most common findings in these patients were found to be spongiosis, the presence of eosinophils, and serum crusts.[41] Although spongiosis was a prominent histopathological finding in our study, eosinophils were not detected. Psoriasis, especially in the early stages, can manifest with minimal spongiosis in certain locations (e.g., mucosal and flexural involvement) and in the presence of severe eczema.[1] However, in patients who present with non-classical clinical findings, the diagnosis of eczematized psoriasis should also be considered. A limitation of our study is that spongiosis severity was not evaluated.

There are a few limitations of this study that should be considered. Due to its retrospective design, it was not possible to clearly evaluate patients' existing lesions and whether psoriasis was in the active phase. Moreover, studies recommend performing multiple biopsies in one session for some patients to confirm a psoriasis diagnosis.[24] In our study, single biopsies from the patients were examined. Finally, this study did not include a control group representing other inflammatory skin diseases.[8]

In conclusion, when evaluating histopathological findings in psoriasis patients, important factors are the disease duration, the anatomical sites biopsy, and the clinical features of the disease. Patients may present both classical and non-classical histopathological findings, and all histopathological findings should be considered together in the diagnosis of psoriasis.

Compliance with Ethical Standards

Trakya University, Faculty of Medicine, Non-Interventional Scientific Research Ethics Committee approved this study (approval date/number: 09.10.2023/335). Informed consent was obtained from all participants.

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Conflict of Interest

The authors declare no conflicts of interest.

Author Contribution

YGÜ, GK, NC: Study design; YGÜ, GK, NC and MAM: Material preparation, data collection and analysis; YGÜ and GK: Writing first draft of the article; YGÜ and NC: Critical review of the article, finalization and publication process. All authors read and approved the final version of the manuscript.

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