

Retrospective Evaluation of Misdiagnosed Scabies Cases: Clinical and Epidemiological Features and Resemblance to Other Dermatological Conditions

ZOR TANINAN SKABİYEZ OLGULARININ RETROSPEKTİF DEĞERLENDİRİLMESİ: KLİNİK VE EPİDEMİYOLOJİK ÖZELLİKLER VE DİĞER DERMATOLOJİK DURUMLARLA BENZERLİĞİ

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ABSTRACT

Background and Aim: Diagnosing scabies, a skin condition caused by mites, can be challenging due to its resemblance to other skin problems. Avoiding misdiagnoses could result in a significant reduction in treatment delays and complications. Our objective was to investigate scabies cases that initially posed diagnostic challenges.

Methods: This retrospective study focused on scabies patients who were initially misdiagnosed despite routine clinical examinations and underwent histopathological examinations with different preliminary dermatological diagnoses. Inclusion criteria were in accordance with the 2020 International Alliance for the Control of Scabies Diagnosis Criteria. The study retrospectively compiled clinical, histopathological, and demographic characteristics, providing data on the challenges and delays in diagnosing scabies cases that mimic other dermatological conditions.

Results: In a cohort of 27 scabies cases with diagnostic challenges, the majority were females (63%) with a mean age of 64.8±15.9 years. Pre-admission, 66.7% of the patients used systemic antihistamines, 52.4% used immunosuppressants, and 42.9% used topical scabies treatment. Secondary xerosis cutis and contact dermatitis were noted in 11.1% and 7.4% of cases. The most frequently considered differential diagnoses by dermatologists included prurigo subacuta (29.6%), dermatitis herpetiformis (18.5%), lymphomatoid papulosis (14.8%), and vesicular/bullous pemphigoid (11.1%).

Conclusion: Previous treatments; prolonged infestations leading to severe secondary dermatological problems including prurigo subacuta, contact dermatitis, and xerotic eczema; atypical distribution of lesions; female prurigo; and elderly with prolonged pruritic atypical dermatoses or vesicular/bullous presentations should be kept in mind as clinical scenarios that may contribute to a delay in the diagnosis of scabies.

Keywords: Scabies, pruritus, differential diagnosis, histopathological analysis, immunofluorescence microscopy

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ÖZ

Arka Plan ve Amaç: Akarların neden olduğu bir deri hastalığı olan skabiyezin (uyuz) tanısı, diğer dermatolojik hastalıklara benzemesi nedeniyle zor olabilir. Yanlış teşhislerden kaçınmak, tedavi gecikmelerinde ve komplikasyonlarda önemli bir azalmaya neden olabilir. Amacımız başlangıçta tanısız zorluklar yaratan uyuz vakalarını araştırmaktır.

Yöntem: Bu retrospektif çalışma, rutin klinik muayenelere rağmen başlangıçta yanlış tanı konulan ve farklı dermatolojik ön tanılarla histopatolojik inceleme yapılan uyuz hastalarına odaklandı. Dahil etme kriterlerinde, 2020 Uluslararası Uyuz Kontrolü Birliği Tanı Kriterlerine uyuldu. Çalışma klinik, histopatolojik ve demografik özellikleri retrospektif olarak derleyerek, diğer dermatolojik durumları taklit eden uyuz vakalarının teşhisindeki zorluklara ve gecikmelere veri sundu.

Bulgular: Tamı güçlüğü çeken 27 uyuz vakasından oluşan bir kohortta çoğunluğu kadın (%63) ve yaş ortalaması 64,8±15,9 yıl idi. Başvuru öncesi hastaların %66,7'si sistemik antihistaminik, %52,4'ü immüsupresan ve %42,9'u topikal uyuz tedavisi kullanmıştı. Vakaların sırasıyla %11,1'inde ve %7,4'ünde sekonder kserozis kutis ve kontakt dermatit kaydedildi. Dermatologlar tarafından en sık dikkate alınan ayırıcı tanıları prurigo subakuta (%29,6), dermatitis herpetiformis (%18,5), lenfomatoid papüloz (%14,8) ve veziküler/büllöz pemfigoid (%11,1) idi.

Sonuç: Önceki tedaviler; prurigo subakuta, kontakt dermatit ve kserotik egzama gibi şiddetli sekonder dermatolojik sorunlara yol açan uzun süreli enfestasyonlar; lezyonların atipik dağılımı; kadın prurigosu; ve uzamış kaşıntılı atipik dermatozları veya veziküler/büllöz prezentasyonları olan yaşlılar, skabiyezin tanısının gecikmesine katkıda bulunabilecek klinik senaryolar olarak akılda tutulmalıdır.

Anahtar Kelimeler: Skabiyezin, pruritus, ayırıcı tanı, histopatolojik analiz, immünfloresan mikroskopisi

Scabies is a cutaneous infestation caused by the *Sarcoptes scabiei* mite, characterized by intense pruritus and a variety of skin manifestations (1). Scabies is not merely a skin condition but also is a global public health concern, with a substantial impact on both individuals and communities (2). Its prevalence spans the globe, and cases continue to be reported across various demographic groups, underscoring its clinical and epidemiological relevance.

While the diagnosis of classic scabies, characterized by the presence of burrows, vesicles, and papules, may appear straightforward, the reality is confounded by the existence of other dermatological maladies that can manifest with similar clinical features (3). This diagnostic challenge necessitates a meticulous approach to evaluating

patients with pruritus (4-6). In cases where the diagnosis of scabies is significantly delayed, this condition can lead to bacterial infections of skin lesions, resulting in contagious impetigo, ecthyma, erysipelas, furuncles, abscesses, lymphadenitis, and even serious complications such as bacteremia, septicemia, heart disease, and kidney problems (7,8). According to a study, almost 45% of the patients presenting to the dermatology office with scabies had been misdiagnosed before (9).

The importance of distinguishing scabies from its imitators goes beyond clinical curiosity; it is crucial for guiding therapeutic decisions, preventing potential outbreaks, and avoiding misdiagnoses that could result in the side effects of unnecessary treatments, a significant decline in patient quality of life, increased medical costs,

and complications (10,11). Atypical presentations of scabies not only occur in immunosuppressed individuals, but also, for the early recognition of these challenging cases, it would be beneficial to extensively characterize in the literature scabies scenarios that deviate from the "classical in morphology and/or distribution" which are less commonly observed at the clinical level.

In this study, our objective was to investigate scabies cases with clinical features resembling other dermatological conditions, that initially posed diagnostic challenges. We conducted a retrospective evaluation of scabies cases referred for histopathological examination with alternative dermatological diagnoses. In these cases, the diagnosis of scabies was ultimately confirmed by both compatible histopathological findings, and additional clinical and dermoscopic features that became apparent during follow-up, along with the treatment response.

METHODS

This retrospective descriptive study was conducted in accordance with ethical guidelines and received approval from the institutional review board (Approval Number: 2023/26-05).

All patients with an ICD-10 diagnosis code for scabies, as recorded in our electronic patient information system, were examined in this retrospective study. Among these patients, we focused on cases where scabies could not be diagnosed during their initial presentation despite routine examinations, which included clinical and dermoscopic assessments. For these individuals, skin biopsies and histopathological examinations were performed with different preliminary diagnoses for their pruritic dermatoses. However, during their follow-up visits, they were ultimately diagnosed with scabies.

The inclusion criteria encompassed cases in which the accuracy of scabies diagnosis was determined according to the "Summary of the 2020 International Alliance for the Control of Scabies Consensus Criteria for the Diagnosis of Scabies" (12). Accordingly, all cases included in the study were required to exhibit histopathological findings distinguishing them from other dermatological diagnoses, along with the visualization of mites through follow-up dermoscopy or skin specimen

examination under light microscopy, the development of scabies burrows, and a successful response to scabicial treatment. Data on successful treatment outcomes, follow-up information, and clinical notes were sought in cases where histopathological examination findings could be accessed. Exclusion criteria were implemented to ensure the specificity and relevance of the study cohort. Cases presenting with conditions other than scabies, as well as those exhibiting histopathological findings indicative of alternative dermatological disorders, were excluded from the study. Instances where a successful response to scabicial treatment was absent, or where follow-up information, clinical notes, and data on treatment outcomes were unavailable, were also excluded.

The clinical, histopathological, and demographic characteristics of cases experiencing diagnostic challenges and delays were retrospectively compiled from electronic patient records. Other dermatological diseases considered or evaluated in the differential diagnosis were also documented. The findings of this study were interpreted to gain insights into the extent and nature of scabies cases that can mimic other dermatological conditions and the associated diagnostic challenges.

Data Analysis

SPSS software package version 29.0 was employed for comprehensive data analysis. The comparison of variables between two groups involved the application of the Pearson chi-square test for categorical variables and the independent samples t-test for continuous variables. Throughout all analyses, two-tailed tests were employed, and a significance threshold of 0.05 was established for the p-value.

RESULTS

In this study, we included 27 scabies patients who sought histopathological sampling with different dermatological pre-diagnoses. This group comprised 17 females (63%) and 10 males (37%). The mean age of the patients was 64.8 ± 15.9 years, ranging from the 25 to 94 years. Detailed sociodemographic and clinical diagnostic characteristics of the study participants are outlined in Table 1.

Table 1. Sociodemographic and Clinic Features of Patients

Parameter		n	%
Age, years, Mean ± SD (min-max)		64.8 ± 15.9	(25-94)
Gender	Female	17	63.0%
	Male	10	37.0%
Itching/Pruritus	Present	27	100%
Clinical Presentation	Widespread	19	70.4%
	Atypical Local Distribution	8	29.6%
Erythematous Papules		13	48.2%
Excoriations		10	37.0%
Seropapules		9	33.3%
Erythematous Nodules		4	14.8%
Pustules		1	3.7%
Complications	None	22	81.5%
	Xerosis Cutis	3	11.1%
	Contact Dermatitis	2	7.4%
History of itching in the patient's close surroundings	Unknown	25	92.6%
	Family/Close relatives	1	3.7%
	Shared living environment	1	3.7%
Duration of itching, days, Mean ± SD (min-max)		178 ± 27	(7-1.080)
Previous Medication Use	None	6	22.2%
	Scabies treatment	11	40.7%
	Systemic immunosuppressives (including corticosteroids)	9	33.3%
	Systemic Antihistamine	1	11.1%

All patients (n: 27, 100%) presented with complaints of itching, and the average duration of itching was approximately 6 months (178 days). One patient reported intermittently increased and decreased itching over a period of up to 3 years.

The majority of patients (92.6%) reported no history of itching in their family or close contacts. Only one patient had a connection to a close relative who experienced itching at some point, while another individual attributed their condition to a shared living environment, concerning the suspected sources of infection.

Until a definitive diagnosis of scabies was established, a percentage of patients sought various treatments in different centers, with this breakdown: 66.7% received systemic antihistamines, 52.4% were administered systemic immunosuppressants, including corticosteroids, and 42.9% underwent unsuccessful topical scabies treatments. Notably, none of the patients exhibited crusted scabies or any condition or drug use associated with immunosuppression, except for those specifically prescribed immunosuppressants for their pruritus-related clinical conditions.

There were noticeable xerosis cutis in 11.1% of cases and contact dermatitis in 7.4%. Erythematous papules were present in 48.2% (n=13) of cases, excoriations in 37.0% (n=10), seropapules in 33.3% (n=9), erythematous nodules in 14.8% (n=4), and pustules in 3.7% (n=1).

The sample for this study comprised scabies cases that initially presented diagnostic complexities, prompting the exploration and histopathological examination of alternative diagnoses. The most frequently considered differential diagnoses by dermatologists were prurigo subacuta (29.6%), dermatitis herpetiformis (18.5%), lymphomatoid papulosis (14.8%), and vesicular/bullous pemphigoid (11.1%), and, in individual cases, differential diagnoses included xerotic eczema, pityriasis lichenoides et varioliformis acuta (PLEVA), erythema multiforme, mycosis fungoides, pseudo-lymphoma, ichthus, acute generalized exanthematous pustulosis (AGEP), atopic dermatitis, prurigo nodularis and drug eruption (3.7% each).

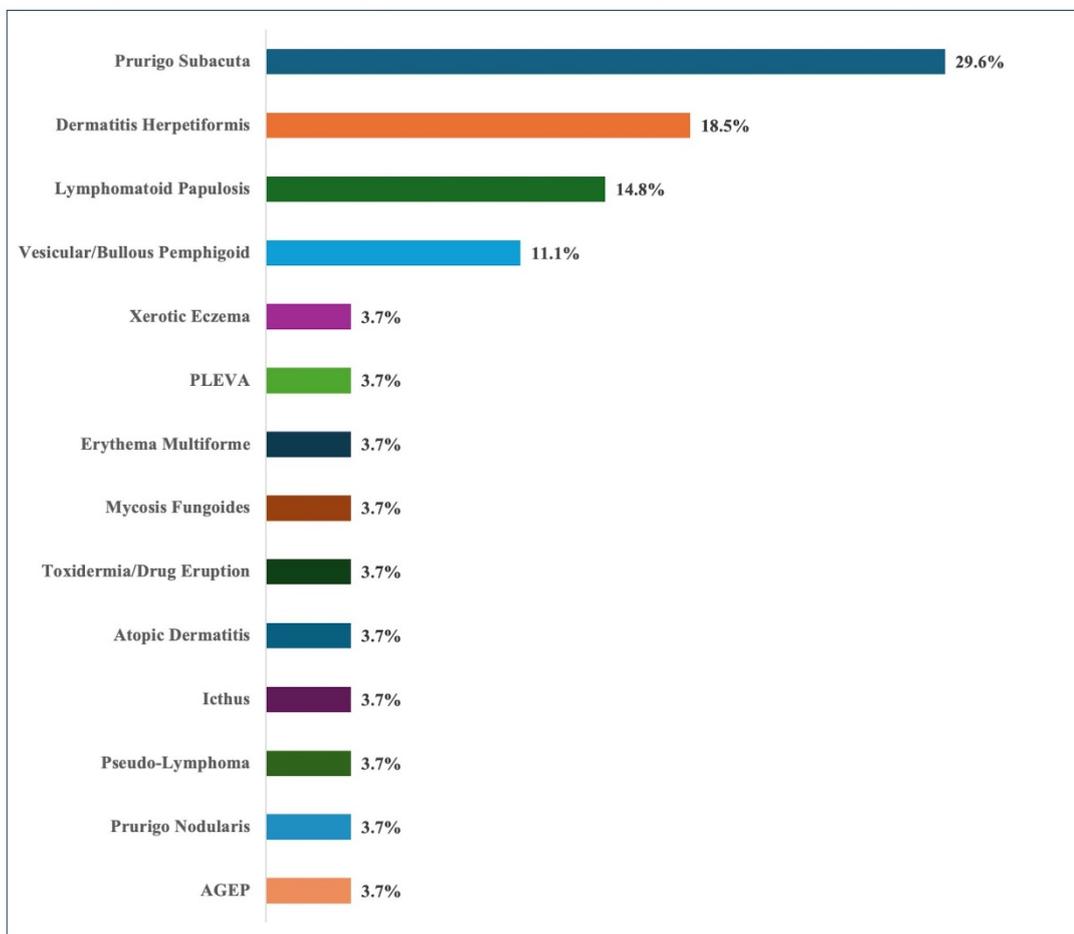
Pruritus and the dermatological lesions exhibited generalized involvement in 70.4% of cases (n=19), while 29.6% (n=8) presented an atypical local distribution, deviating from the typical scabies distribution pattern. The areas preferred for histopathological examinations, where the rash and lesions were pronounced, included the back (22.2%), arm (18.5%), abdomen (18.5%), leg (18.5%), torso (11.1%), gluteal region (7.4%), and chest (3.7%). Among those who underwent direct immunofluorescence (DIF) examination (n=12, 44.4%), the arm, back, leg, and chest were the most common sampling sites. DIF accumulation was not observed in 50% of cases, while fibrinogen, IgG,

and IgM were present in 33.3%, 8.3%, and 8.3%, respectively. The histopathological features supported the diagnosis of scabies in 77.8% (n=21) of cases, nodular scabies in 11.1% (n=3), and prurigo subacuta in 11.1% (n=3). In the histopathology of scabies patients, findings consistent with arthropod bite reaction were observed in 51.9% (n=14) of cases, while a lymphocytic vasculitis pattern was identified in 29.6% (n=8). Detailed information on diagnostic processes, including differential, pathological, and clinical diagnoses, is presented in Table 2 and Figure 1.

Table 2. Diagnostic and Differential Diagnostic Parameters of Study Participants

Parameter		n	%
Biopsy area for routine histopathology	Back	6	22.2%
	Arm	5	18.5%
	Abdomen	5	18.5%
	Leg	5	18.5%
	Torso	3	11.1%
	Gluteal Region	2	7.4%
	Chest	1	3.7%
	Features in routine histopathology	Arthropod Bite Reaction	14
Lymphocytic Vasculitis Pattern		8	29.6%
Prurigo Subacuta		3	11.1%
Scabies		1	3.7%
Post-Scabies Papules		1	3.7%
Biopsy area for direct immunofluorescence (DIF)	Not obtained	15	55.6%
	Back	3	11.1%
	Arm	3	11.1%
	Leg	2	7.4%
	Chest	2	7.4%
	Gluteal Region	1	3.7%
	Abdomen	1	3.7%
Direct Immunofluorescence (DIF) Findings (For patients have DIF examination, n: 12)	No accumulation	6	50.0%
	Fibrinogen	4	33.3%
	IgG	1	8.3%
Pathological Diagnosis	IgM	1	8.3%
	Scabies	21	77.8%
	Prurigo Subacuta	3	11.1%
Final Diagnosis	Nodular Scabies	3	11.1%
	Scabies	27	100%

Figure 1. Frequency of differential diagnoses considered in scabies patients.



Vesicular bullous pemphigoid was observed to be significantly more frequently considered as an initial diagnosis in older scabies patients ($p= 0.008$), and as the duration of itching, therefore the duration of scabies disease, increases, the rate of considering vesicular bullous pemphigoid in the differential diagnosis significantly increases ($p=0.047$). No significant relationship was found between age and other differential diagnoses.

Categorizing by gender, the consideration of prurigo as a potential diagnosis was significantly more frequent in women with scabies ($p=0.026$). Similarly, dermatitis herpetiformis was notably more frequently pondered in female scabies patients ($p=0.037$). Conversely, lymphomatoid papulosis featured significantly higher in men ($p<0.001$), with none of the women having this pre-

diagnosis. No other noteworthy relationships between gender and specific differential diagnoses were identified.

DISCUSSION

In this retrospective study, 27 scabies cases that pose diagnostic difficulties were evaluated. Of the cases, 63% were female and 37% were male, with a mean age of 64.8 ± 15.9 years. This demographic distribution contrasts with the findings of a meta-analysis involving 1544 patients, where the mean age was reported as 41.8, and the female ratio ranged between 19-86% (13). The higher mean age and proportion of female patients in our series may be attributed to the increased diagnostic challenges in this demographic group for scabies. Especially in the elderly, additional dermatological conditions are more frequently

considered in the differential diagnosis. Factors such as cognitive impairment, the prevalence of multiple systemic treatments, and the widespread occurrence of pruritus complaints in older and female patients could contribute to these challenges (9). The literature documents atypical scabies presentations in elderly patients, often characterized by diffuse pruritus or nonspecific eczematous eruptions. These manifestations can contribute to diagnostic delays, sometimes persisting even after partial scabies treatment (14). In our series, vesicular bullous pemphigoid was observed to be significantly more frequently considered as an initial diagnosis in older scabies patients, while prurigo and dermatitis herpetiformis were significantly more frequently considered in female scabies patients.

In this study, pruritic erythematous papules, vesicles, and, in some cases, nodules with excoriations were frequently observed. While these findings are anticipated in typical scabies cases, they are not pathognomonic (3). Approximately one-third of our patients (29.6%) exhibited an atypical distribution of rash and itching, and a significant majority (77.8%) had previously received topical and systemic treatments that might have impacted the manifestation of scabies symptoms. The secondary conditions such as prurigo subacuta, contact dermatitis, and xerotic eczema was observed in approximately one-third of cases (29.6%). Consistent with our findings, a case series investigating misdiagnosed scabies patients revealed that all individuals had a history of previous treatment, including antihistamines and corticosteroids (15). These treatments were believed to have delayed the accurate diagnosis by suppressing symptoms. Additionally, the clinical manifestation of eczema in these patients also led to initial dermatological misdiagnoses (15). Consistent with the literature, the findings presented in this study suggest an association between challenging scabies diagnoses. It is important to be aware that conditions such as subacute prurigo, contact dermatitis, and xerosis may be secondary and potentially obscure an underlying parasitic disease, particularly when manifested in a generalized form with diverse dermatological lesions, encompassing papules, seropapules, and eczematized areas. A history of previous immunosuppressive therapy may also be a clue. These

patients should be re-evaluated after initial treatment to avoid any delay in the diagnosis of scabies and its associated complications.

In our study, dermatologists most commonly considered the following initial differential diagnoses in scabies patients: prurigo subacuta, dermatitis herpetiformis, lymphomatoid papulosis, vesicular/bullous pemphigoid, xerotic eczema, PLEVA, erythema multiforme, mycosis fungoides, toxidermia/drug eruption, atopic dermatitis, ichthus, pseudo-lymphoma, prurigo nodularis and AGEF (9).

In a recent study, the challenges in recognizing scabies by physicians were explored, emphasizing its frequent misdiagnosis due to its similarity with various dermatoses and eczema, urticaria, atopic dermatitis, and allergic contact dermatitis (15), similar to our results. Cases of scabies presenting with secondary impetiginization resembling kerion-type tinea capitis (16), scabies mimicking systemic lupus erythematosus (17), insect bites (18), and prurigo nodularis (19) have also been documented in the literature as initial preliminary diagnoses for scabies patients. The findings underscored the importance of considering and excluding scabies in the diagnostic process for these dermatological conditions. Doing so can minimize delays in achieving an accurate diagnosis and, consequently, timely treatment.

Despite atypical clinical manifestations or previous treatments, including corticosteroids and antihistamines, all scabies patients in this study continued to experience itching. However, contrary to expectations for parasitic diseases, prolonged itching up to an average of 6 months and, in some cases, extending to 3 years, was observed. Itching is a major symptom of scabies, and is consistently reported in the literature in all scabies patients (20). However, the prolonged duration of itching up to years and no reported itching in close family members can contribute to diagnostic challenges for physicians, as in our cases. The results suggest that despite years of unsuccessful scabies treatment, there may not be transmission to family members, deviating slightly from widely known information.

In our study, direct immunofluorescence (DIF) testing revealed no accumulation in 50% of the 12 patients who underwent the procedure. Among the tested patients, fibrinogen, IgG, and IgM were present in 33.3%, 8.3%, and 8.3%, respectively. A separate study, which included 5 patients with bullous scabies subjected to DIF examination, reported IgG positivity in 3 patients, while 2 showed negative results. Bullous scabies typically manifests in the elderly, particularly in patients over the age of 70 years (21). Similarly, our study identified a significant correlation between older age and prolonged pruritus and the consideration of vesicular/bullous pemphigoid in the differential diagnosis.

CONCLUSION

Patients using topical or systemic corticosteroids, as well as those taking antihistamines, individuals with prolonged infestations leading to severe secondary dermatological problems such as prurigo subacuta, contact dermatitis, and xerotic eczematous changes, cases displaying atypical clinical distribution of lesions, female prurigo, and elderly individuals with prolonged pruritic atypical dermatoses or pronounced vesicular/bullous presentations should be kept in mind as clinical scenarios that may contribute to a delay in the diagnosis of scabies.

It may be beneficial to be aware of other dermatological diseases that dermatologists initially consider in the differential diagnosis of reported scabies cases in this study. It is important to bear in mind that these diseases may closely mimic scabies, potentially causing diagnostic delays. Conducting additional diagnostic tests, especially for patients with less typical clinical presentations, and implementing follow-up examinations after prescribed treatment for all patients can be valuable in addressing this concern.

This study contributes to our understanding of the diagnostic challenges associated with scabies and its differentials, providing valuable insights for early diagnosis and treatment to prevent serious complications and community spread.

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