

Examination of histopathological findings in scabies cases: a retrospective analysis of five years of experience

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Abstract. – OBJECTIVE: Scabies is a skin infestation that has been known for hundreds of years and is caused by the ectoparasitism of *Sarcoptes scabiei*. Scabies is a public health problem that can be seen in all age groups, races, genders, socioeconomic groups, and all societies. The aim of this study was to identify the prominent histopathological findings in scabies cases and to guide the clinical approach.

PATIENTS AND METHODS: Scabies cases, which were clinically diagnosed between January 2016 and December 2020 in our hospital, were retrospectively screened, and 3,027 cases were detected. As a result of the screening, a skin punch biopsy-histopathological examination was performed in only 62 cases that were included in the study. Cases without punch biopsy were excluded from the study. After a histopathological evaluation, the cases were divided into two groups: those diagnosed with scabies (n=9) and those diagnosed with nonscabies (n=53). Pathological findings of the groups were statistically compared using Fisher's exact Chi-square test.

RESULTS: After microscopic examination, superficial and deep inflammatory reactions and the presence of lymphocytes were detected in 100% of cases. Furthermore, eosinophils and spongiosis were detected in 55% of cases. Histomorphological findings of the two groups were statistically examined and significant differences were found in spongiosis and eosinophil findings ($p=0.019$, $p=0.025$). There were no statistically significant differences in the other histopathological findings (parakeratosis, vesicle, bullae, intraepidermal pustule, vasculitis, dermal edema, superficial and deep inflammatory reaction, neutrophils, and plasma cells – $p=0.259$, $p=0.266$, $p=0.083$, $p=0.683$, $p=0.557$, $p=0.066$, $p=0.980$, $p=0.290$, and $p=0.083$, respectively).

CONCLUSIONS: In histopathological examination of scabies biopsies, spongiosis and eosinophil findings may be useful in differential diagnosis. Pathological diagnosis can be a decisive stage for controlling scabies, which has epidemic potential, especially in crowded environments such as schools, dormitories, and refugee camps. For pathology science to play an active role in the diagnosis of scabies, more punch biopsies are need-

ed from cases. Large-sample prospective clinical studies comparing histopathological findings and the severity of the disease may contribute to the literature.

Key Words:

Scabies, Infestation, Pathology.

Introduction

Scabies is a skin infestation caused by *Sarcoptes scabiei* ectoparasites, characterized mainly by itching and erythematous lesions¹. It is a public health problem that can be seen in every population. In crowded settings where hygienic conditions are not well controlled, the disease can spread rapidly through contact and cause epidemics². Due to the need for global control, scabies were added to the Neglected Tropical Diseases (NTD) list by the World Health Organization (WHO) in 2017^{3,4}. It is important to know the signs and differential diagnostic criteria involved in the clinical and pathological diagnosis of scabies disease to control and limit it^{5,6}. The International Alliance for the Control of Scabies (IACS) established criteria for the diagnosis of scabies. According to these criteria, the diagnosis of the disease is divided into three categories: definite, clinical, and suspicious. For definitive diagnosis of scabies, mites, egg, or feces samples should be seen with light microscopy, radiological examinations, or dermatoscopy. For the diagnosis of clinical scabies, a clinical examination requires the appearance of typical lesions (cillion, tunnel, vesicle) in the stratum corneum layer of the skin and knowledge of two anamneses. Suspected scabies is diagnosed with the presence of typical scabies-specific lesions in the body and anamnesis information. The anamnesis parameters of scabies are itching and a history of close contact with scabies patients⁴. Detection of histopathological

signs plays an important role in the final diagnosis of clinically suspicious cases. Detection of mites, eggs, and feces under a light microscope makes a definitive diagnosis of scabies.

In this study, we examined the clinical and histomorphological features of scabies cases in the Çorum province of Turkey and aimed to evaluate the characteristic histopathological findings that may contribute to the diagnosis of the disease.

Patients and Methods

Patients diagnosed with scabies at the Erol Olçok Training and Research Hospital of Hitit University between January 2016 and December 2020 were scanned retrospectively. A total of 3,027 cases diagnosed as scabies were detected clinically. Demographic, clinical, and pathology data of these patients were recorded. Out of these 3,027 cases, only 62 (2%) underwent a skin punch biopsy and received a histological diagnosis. A total of 2,965 (98%) cases were diagnosed with scabies only clinically. The clinical examination findings and preliminary diagnoses of 62 patients who underwent biopsies were examined. The types and localizations of the lesions detected in their clinical examinations were determined, and their histomorphological diagnoses were examined by a pathologist by taking new sections. These cases were divided into two groups: diagnosed with scabies ($n=9$) and not diagnosed with scabies ($n=53$). The areas where the reaction was most intense were selected. Parakeratosis in these areas, vesicles, find, intraepidermal pustules, superficial and deep inflammatory cell reaction, dermal edema, and the presence of vasculitis spongios⁷ “yes” or “no” as eosinophils (more than 50, 5-50, less than 5, 0), lymphocytes (more than 300, 100-300 and less than 100, 0), neutrophils (more than 50, 5-50, less than 5, 0), plasma cells (more than 10, 5-10 less than 5, 0) the highest degree in the presence of severe (score 3), moderately severe (score 2), mild to severe (score 1) and non-severe (score 0) were analyzed⁷. The histopathological differences between these two groups with and without scabies were compared statistically.

Histopathological Evaluation

Skin punch biopsies were taken from the lesions of patients with a prediagnosis of scabies. Biopsy materials were placed in plastic sample containers with 10% formaldehyde solution and transferred to the pathology laboratory. Biopsy

materials fixed with formaldehyde for 24 hours were routinely processed with automated tissue processing equipment (Leica ASP300S, Wetzlar, Germany). Then, the biopsy materials were embedded in paraffin and cut with a rotary microtome (Leica RM2255, Wetzlar, Germany) at a thickness of 4 μm . Tissue sections were stained with hematoxylin-eosin (HE). The preparations of the 62 cases were re-evaluated with a Nikon Eclipse Ni-U (Nikon, Tokyo, Japan) microscope. They were imaged with a Nikon Digital DS-Ri2 (Nikon, Tokyo, Japan) camera.

Statistical Analysis

All statistical analyses of the study were performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). A normality test was performed to determine whether the groups were homogeneously distributed. Variables in homogeneously distributed groups were expressed as mean \pm standard deviation, and Student's *t*-test was performed. Independent categorical variables were compared with Fisher's exact Chi-square test in groups that did not show homogeneous distribution. A *p*-value <0.05 was considered significant.

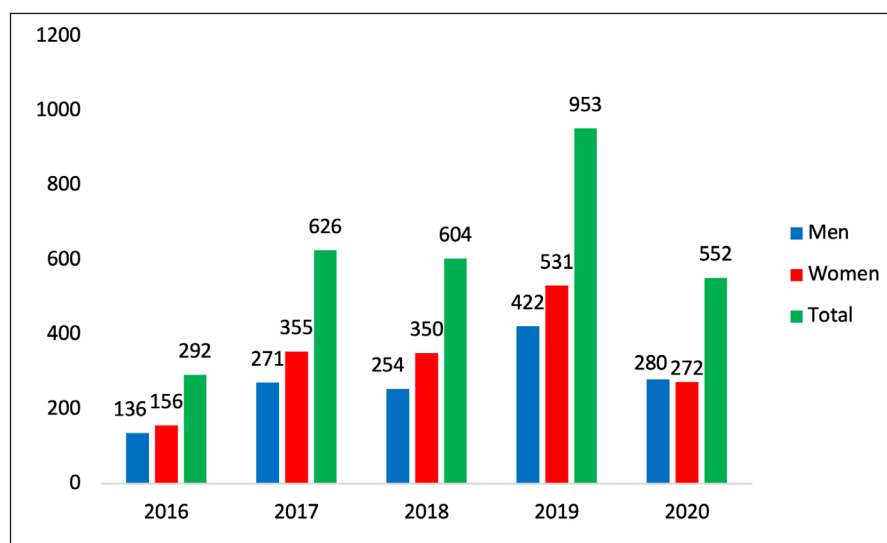
Results

Of the patients, 1,664 (55%) were female, and 1,363 (45%) were male, with a mean age of 38.81 ± 23.08 years. There was no significant difference between the ages of female and male patients ($p=0.659$). Figure 1 shows the distribution of cases with a clinical diagnosis of scabies by year.

Considering the distribution of lesions in the clinical examination, 25 (40.3%) of the cases had lesions on the whole body, 15 (24.1%) had lesions on the trunk, 12 (19.3%) had lesions on the extremities, and 10 (16.1%) had lesions on the trunk, extremities and fingers. Erythematous excoriated papules were detected in 51 (82.2%) cases, plaques in 5 (8.0%), ulcerated lesions in 4 (6.4%), and macular lesions in 2 (3.2%) cases. Figure 2 presents images of these lesions.

Table I shows the histomorphological findings of the cases with and without scabies that were obtained from the pathology reports. The comparison of the histomorphological findings between the two groups showed a significant difference in the spongiosis and eosinophil findings ($p=0.019$, $p=0.025$). There was no statistically significant difference in other histopathological findings (par-

Figure 1. Distribution of 3,027 cases with a clinical diagnosis of scabies by year.



akeratosis, vesicle, bulla, intraepidermal pustule, vasculitis, dermal edema, superficial and deep inflammatory reaction, neutrophil and plasma cell – $p=0.259$, $p=0.266$, $p=0.083$, $p=0.683$, $p=0.557$, $p=0.066$, $p=0.980$, $p=0.290$ and $p=0.083$, respectively). Figure 3 presents microscopic images of the histomorphological findings of the cases.

Discussion

Scabies affects approximately 300 million people a year around the world and approximately 130 million people in any given time period^{5,8}. The literature review globally and in Turkey over

the last decade has indicated that the number of studies on scabies has increased^{3,9,10}. Refugee migration to Turkey, particularly after 2010, could be a reason for the increase in the number of cases. A comprehensive guide¹¹ has been published for arranging the diagnosis and treatment of scabies outbreaks, and a possible scabies outbreak in Germany, a country such as Turkey, which has experienced a very high refugee influx. In this guide, scabies cases are more common in refugees than in the general population in Germany.

In a multicenter study conducted in Turkey by Özden et al¹⁰, the incidence of scabies has significantly increased over the years, leading to the



Figure 2. Itchy lesions of patients with scabies admitted to the dermatology clinic: erythematous lesions on the fingers (A), papular lesions on the front side of the trunk (B), ulcerated dry lesions on the lower extremities (C), common macular lesions on the trunk (D).

Table I. Distribution of histomorphological findings of cases with and without pathological diagnosis of scabies.

Histomorphological Findings	Cases not diagnosed with scabies		Cases diagnosed with scabies		p-value*
	n=53	%	n=9	%	
Parakeratosis	17	32.0	5	55.5	0.259
Vesicle	5	9.4	2	22.2	0.266
Bulla	5	9.4	3	33.3	0.083
Intraepidermal pustule	13	24.5	3	33.3	0.683
Vasculitis	4	7.5	1	11.1	0.557
Dermal edema	17	32.0	6	66.6	0.066
Spongiosis	13	24.5	6	66.6	0.019
Superficial and deep inflammatory reaction	53	100	9	100	-
Superficial	33	62.2	6	66.6	0.980
Deep	20	37.7	3	33.3	0.980
Lymphocyte	53	100	9	100	-
Mild	25	47.2	1	11.1	
Moderate	12	22.6	4	44.4	
Intense	16	30.2	4	44.4	
Eosinophil	14	26.4	6	66.6	0.025
Mild	5	9.4	0	0	
Moderate	7	13.2	3	33.3	
Intense	2	3.7	3	33.3	
Neutrophil	19	35.8	5	55.5	0.290
Mild	3	5.7	0		
Moderate	8	15.1	3	33.3	
Intense	8	15.1	2	22.2	
Plasma cell	5	9.4	3	33.3	0.083
Mild	1	1.9	0	0	
Moderate	2	3.8	1	11.1	
Intense	2	3.8	2	22.2	

*Fisher's exact Chi-square test.

suggestion that it should be accepted as a public health problem. The study by Çetinkaya et al⁶ reported that the cases were mostly between the ages of 24 and 45 years, and the disease was more common among the female population. There are differences in terms of gender, age range, and incidence in scabies cases in other articles¹²⁻¹⁴ published both in Turkey and in the world. In our study, the diagnosis of scabies was more common in women, both clinically and histopathologically. Also, the cases' mean ages were close to each other and were consistent with the literature.

In our study, the number of patients with a clinical prediagnosis of scabies for the last five years has increased every year. The increase in the number of cases in our study was compatible with the literature. However, the decrease in the number of scabies cases in 2020 could be attributed to patients' inability to seek health care due to

the COVID-19 pandemic experienced that year.

When we examine the number of cases in which skin punch biopsy was taken in our study, the 2% biopsy rate of these cases in our hospital is insufficient. In many case reports in the literature^{15,16}, the diagnosis of scabies has been overlooked, correct diagnosis has not been made, patients have applied to different clinical branches and inappropriate treatment protocols have been applied.

Several case reports¹⁵ in the literature reported that patients applied to more than one clinical branch, received different diagnoses and treatments, and the diagnosis was delayed. Hospital records reported that 455 patients with a clinical diagnosis of scabies applied to our hospital recurrently. Of the nine cases diagnosed with scabies histopathologically, five were among the patients who presented with decurrent scabies. This shows

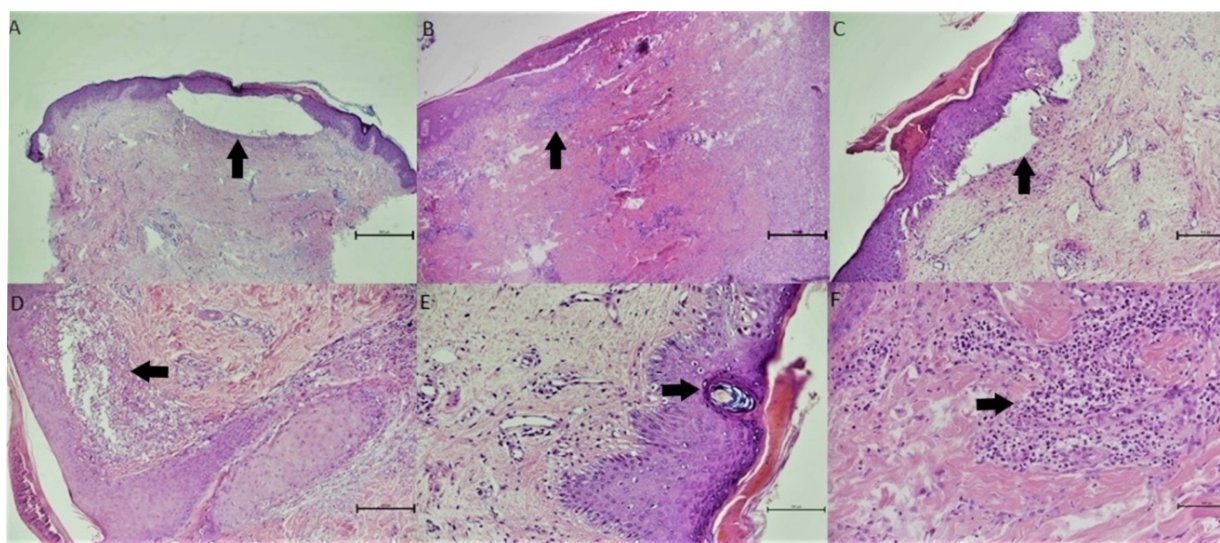


Figure 3. HE-stained histomorphological images of scabies cases. **A**, Subepidermal bulla, spongiosis (magnification: X40). **B**, Intraepidermal vesicle, dense infiltration (magnification: X40). **C**, Crust layer, spongiosis, subepidermal cleft (magnification: X100). **D**, Spongiosis, neutrophil and lymphocyte infiltration, exocytosis (magnification: X100). **E**, Squamous crust, mite nest (magnification: X200). **F**, Dense infiltration with intense eosinophils in the superficial and deep dermis (magnification: X400 – HHKS Archive).

that in cases where it is difficult or ambiguous to diagnose scabies clinically, it would be more effective to take a skin punch biopsy. It further reveals the important role of pathology in reaching a definitive diagnosis. The existence of cases without a preliminary diagnosis of scabies but diagnosed as such during histomorphological examination supports the hypothesis that more skin punch biopsy material should be taken. If the correct diagnosis is not made, the scabies epidemic may continue to spread and threaten public health.

Plaque, erythematous excoriated papules, vesicles, bullae, abscesses, and ulcerated pruritic lesions are observed in the clinic of patients with a diagnosis of scabies¹⁷⁻¹⁹. In our study, the lesions of patients who had complaints for an average of several months and applied to a dermatologist were often in the form of erythematous excoriated papules, some of which were dry lesions. These findings are supported by the literature.

Scabies mites are found in the stratum lucidum and stratum granulosum, and along with life in the burrows they make in the inanimate stratum corneum of the epidermis¹⁸. Although the presence of eggs, larvae, mites, and feces in the stratum corneum are among the histopathological definitive diagnostic criteria of scabies, approximately 80% of the cases where the clinician has difficulty and biopsy consists of biopsy materials that do not meet/contain these criteria^{20,21}. Our

study found nests belonging to scabies in only one case, with no detection of eggs, larvae, mites, and feces.

The saliva, enzymes, hormones, and feces materials that cause the antigenic and pharmacological activities secreted by the mite spread into the intercellular fluid in the epidermis and dermis. These substances also increase vascular permeability and cause inflammation²². For this reason, most cases histomorphologically present with superficial and deep infiltration of lymphocytes, histiocytes, plasma cells, mast cells, Langerhans cells and eosinophils, spongiotic foci, and spongiotic vesicles, bullae, variable numbers of eosinophils and sometimes exocytosis of neutrophils, and rarely atypical mononuclear cells^{7,20,23}. In our study, out of 62 biopsy materials, 9 (14.5%) cases without eggs, larvae, mites, and feces were diagnosed histomorphologically as scabies. The most common histomorphological findings in these cases are superficial and deep inflammatory reactions, lymphocytes, spongiosis, eosinophils, neutrophils, and parakeratosis. When the groups with and without scabies were compared in terms of histomorphological findings, the presence of spongiosis and eosinophils showed a significant difference between the groups. The spongiotic tissue pattern and the presence of eosinophils are common in cases of scabies^{7,20}, are in many other diseases, and are not scabies-specific his-

topathological findings. For this reason, pathologists should approach cases with a spongiotic tissue pattern accompanied by eosinophils more carefully in terms of scabies. Although there are many case reports in terms of the histomorphology of scabies in the literature, histomorphological case-control studies are inadequate. For this reason, it is difficult to statistically highlight any of the histomorphological features of scabies disease. In the study by Elwood et al⁷, who examined the biopsies of scabies patients, eosinophils were reported in 88% of the cases, while spongiosis findings were reported in 76%. However, a statistical comparison of histomorphological findings was not performed⁷. In our study, the presence of lymphocytes, spongiosis, and eosinophils is the most common histomorphological finding. Histomorphologically, both studies presented similar findings. In the case reports²⁴⁻²⁶ of scabies in the literature, the most common histopathological findings of the researchers are the presence of eosinophils in the dermis and spongiosis in the epidermis.

Limitations

The inability to access data such as the duration of patients' complaints and their clinical and laboratory findings can be considered a limitation of our study. Complete blood count (CBC) results can be helpful in diagnosing scabies, which is one of the diseases with high eosinophilia. However, considering the CBC results of 9 patients diagnosed with histopathological scabies, the eosinophil level was $0.79 \times 10^9/L$ (0.03- 0.45) in only one 21-year-old male patient, which was higher than normal limits. The other 8 patients did not have a CBC test. Due to the lack of data, the level of eosinophils could not be evaluated in detail in the study. Although the number of cases with a pre-diagnosis of scabies is high, the number of cases with a definitive diagnosis of scabies is too small to compare the histopathological findings with statistically more powerful tests.

Conclusions

Scabies treatment is provided to both patients and people who have close contact with the patients. The definitive diagnosis of scabies is important in terms of preventing unnecessary treatment costs and possible epidemics. Pathology plays a key role in preventing the epidemic by easily reaching a definitive diagnosis. For

this reason, prospective case-control studies to be carried out jointly by dermatology and pathology branches may contribute to the easier diagnosis of scabies and the simultaneous transition to treatment. Taking more skin biopsies from scabies cases, sending them to pathology, and determining the pathophysiology of histomorphological changes may contribute to the enrichment of the literature and help pathologists gain more experience. Due to the study's small number of scabies cases, it appears that there is a need for multicenter, larger sample, multidisciplinary, and prospective studies, as well as the development of advanced diagnostic methods using molecular methods to differentiate it from other diseases that cause similar histomorphological findings.

Conflict of Interest

The author declares no conflicts of interest.

Informed Consent

Written informed consent was obtained from the study participants.

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Ethics Approval

This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethics Committee Approval was obtained from the Hitit University Faculty of Medicine Clinical Research Ethics Committee (06.01.2021/378).

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Data Availability

Data information can be obtained from the author upon request.

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