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Ultrastructural Alterations in the Epidermis of Patients with Tinea Pedis

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ABSTRACT

Objective: Tinea pedis is the most common superficial fungal infection of the foot. Although light microscopic characteristics of tinea pedis have already been described and are well known, electron microscopic data is still lacking. In this study, we aimed to examine the ultrastructural changes in the epidermis of patients diagnosed with tinea pedis.

Material and Methods: Biopsies were taken from the lesions between the toes of patients with untreated tinea pedis and from healthy volunteers with no fungal infections. The materials obtained were prepared for electron microscopy and examined by transmission electron microscope.

Results: The ultrastructural examination revealed the following changes: (1) Disturbances in the form and organization of keratinocytes; (2) Irregular distribution and interlacing of tonofilament bundles in keratinocytes; (3) Disruption of desmosomes and detachment of adjoining keratinocytes; (4) Excessive widening of intercellular spaces between keratinocytes; (5) Dilatation of intercellular spaces between basal cells; (6) Degranulation of melanocytes in the stratum basale; (7) Migration of lymphocytes and polymorphonuclear leukocytes between keratinocytes in the stratum spinosum; (8) Degradation of basal lamina; (9) Pericapillary edema in the apillary dermis.

Conclusion: The ultrastructural findings in tinea pedis are described and related to the clinical symptoms and histopathologic features of the disease.

Key Words: Tinea pedis, transmission electron microscopy, epidermis, keratinocyte

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Introduction

Tinea pedis (athlete's foot) is the most common superficial fungal infection of the foot. Studies conducted worldwide and in Turkey have shown that superficial fungal infections are among the most common skin diseases (1-4). Some of the fungi in nature are known to be pathogenic in humans and animals. These microorganisms do not exist in the deep tissues of the human body but tend to be localized in the epidermis and cause infections in superficial keratinized tissues such as skin, hair and nail (5-7).

Feet carry body weight and are exposed to various environmental effects. Fungal infection of the feet (tinea pedis) is a health problem caused by poor foot hygiene (3, 7, 8). Even though these types of dermatophyte infections do not cause very serious complications, they can adversely affect daily activities, social lives and esthetic appearance and can even require medical intervention (9, 10). They may lead to secondary infections and disorders like cellulitis, erysipelas, lymphangitis, asthma, urticaria and atopic dermatitis, which can cause serious problems as they progress (11-14).

Clinically, tinea pedis is characterized by maceration, slight desquamation, erythema and sometimes vesicles and fissures between toes. These characteristics were examined in many studies histopathologically or using other techniques (2-4, 11, 15). In our study, the structure of the epidermis between toes of patients diagnosed with tinea pedis was evaluated ultrastructurally.

Patients and Methods

In the study, biopsies of 10 male patients between the ages of 30 and 35 years diagnosed with tinea pedis who were sent to the Electron Microscopy Laboratory of the Department of Histology and Embryology at the Department of Dermatology of Istanbul Faculty of Medicine were examined by electron microscopy.

Biopsies were taken from the lesions between the toes of patients with untreated tinea pedis. Normal skin biopsies were taken from 3 healthy volunteers with no fungal infections and used as controls. All patients provided written informed consent before enrollment in the study. Each sample of skin was cut into smaller pieces of 1 cubic mm, fixed in 2.5% glutaraldehyde in phosphate buffer (pH 7.4) and post-fixed in 1% OsO_4. Specimens were dehydrated in ethanol and embedded in Epon. Semithin sections were stained with toluidin blue for orientation of the area of interest. Ultrathin sections were stained with uranyl acetate and lead citrate and examined with the JEOL 1011 transmission electron microscope.

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Results

When compared to normal skin, various ultrastructural changes were found in all epidermal layers of patients with tinea pedis.

Basal cells in the stratum basale of normal skin had a columnar shape and large oval nuclei rich in euchromatin. The cytoplasm of the keratinocytes contained abundant ribosomes, a small Golgi apparatus, mitochondria and rough endoplasmic reticulum cisternae. Regularly distributed tonofilament bundles were noted in the cytoplasm of basal cells showing intact intercellular junctions (Fig.1). Stratum basale in normal epidermis formed interdigitations with papillary dermis. Basal lamina was aligned parallel to these interdigitations between these two layers. The papillary layer was composed of loose connective tissue with irregularly distributed collagen fibers (Fig. 1).

Keratinocytes in the stratum spinosum of normal skin had large nuclei and distinct nucleoli. The tonofilaments in the cytoplasm of these cells formed bundles which were generally aligned parallel to nucleus. The size of intercellular spaces was within normal limits and keratinocytes were bound to each other by regular desmosomal intercellular junctions (Fig. 2).

Significant degenerative changes were found in the epidermis and dermis of skin with tinea pedis. The most affected layer was the stratum spinosum, which lacked regular cellular organization (Figs. 3, 4). The keratinocytes had large nuclei with diffuse euchromatin and relatively inconspicuous nucleoli (Figs. 3, 5). Tonofilament bundles were of varying thickness and lengths and irregularly distributed along the cytoplasm. Round granules with 250-400 nm diameter and electron-dense cores containing fine granular material were seen in the keratinocytes of stratum spinosum (Fig. 5). Beside significant expansion in intercellular spaces with respect to controls, keratinocytes of varying cell shapes were observed to lose their intercellular junctions by disrupted desmosomes (Figs. 3-5). An amorphous and dense material was accumulated in the expanded intercellular spaces (Fig. 4). Also, lymphocytes and polymorphonuclear leucocytes (PNL) were seen between the keratinocytes (Figs. 3, 5).

Significant degenerative ultrastructural defects were seen in the stratum basale of epidermis with tinea pedis. Basal cells were observed to have flattened cell shapes along the disrupted epidermodermal junction which was observed to loose interdigitations with papillary dermis. In these areas basal lamina was not observed (Figs. 6,8). Tonofilaments were arranged in small bundles and irregularly dispersed in the cytoplasm of basal cells. Round granules with comparable ultrastructure to

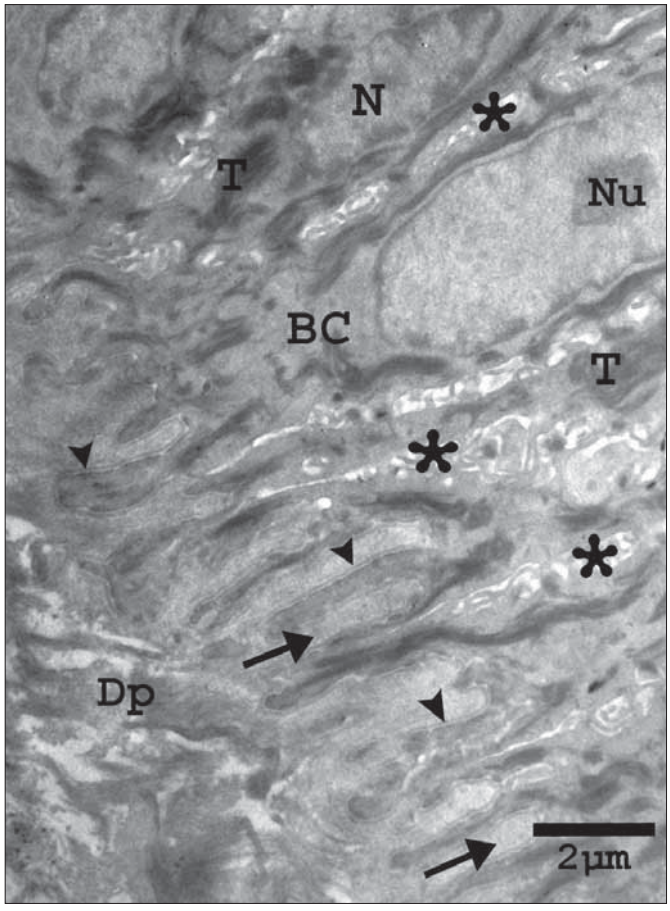

Figure 1. Stratum basale of normal skin. Note the interdigitations (arrows) between the basal cells (BC) and papillary dermis (Dp). N: nucleus, Nu: nucleolus, T: tonofilament bundles, asterisks: intercellular space, arrowheads: basal lamina

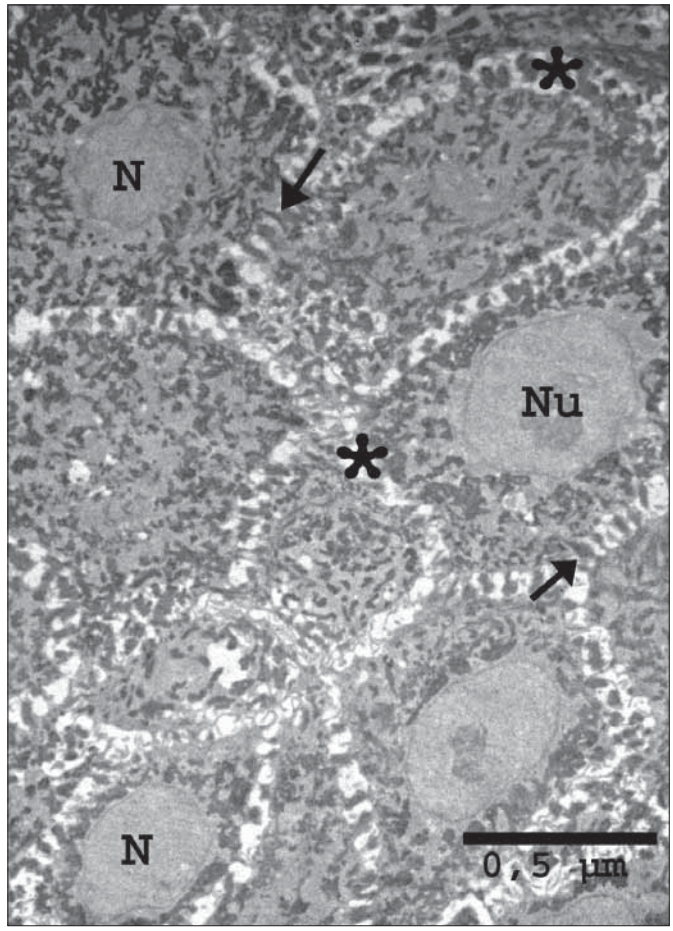

Figure 2. Keratinocytes in the stratum spinosum of normal skin. N: nucleus, Nu: nucleolus, T: tonofilament bundles, arrows: desmosomes, asterisks: intercellular space

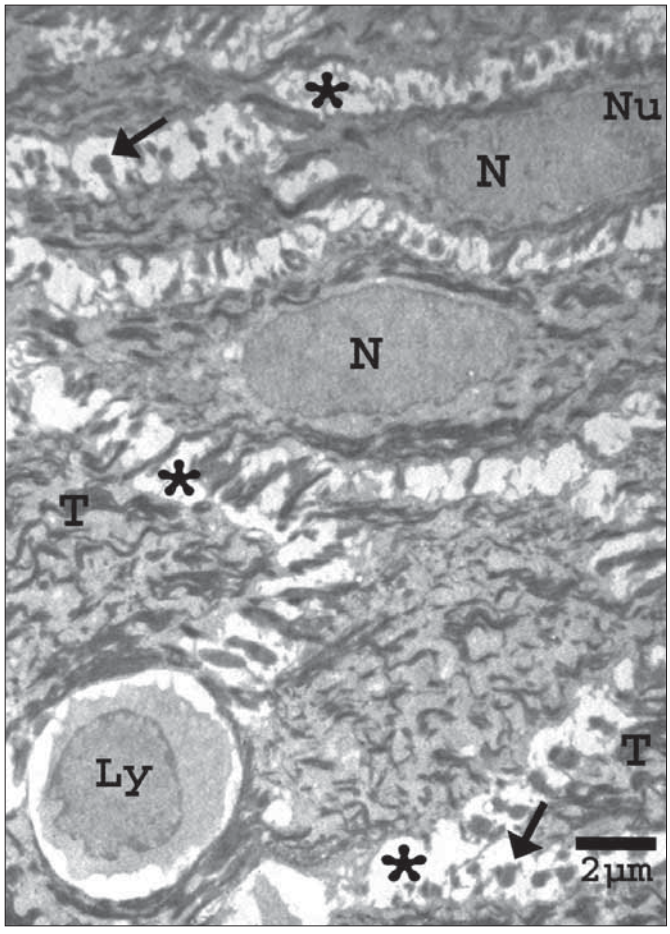

Figure 3. Stratum spinosum from a patient with tinea pedis. Note the widened intercellular spaces (asterisks) and disrupted desmosomes (arrows) between adjacent keratinocytes. N: nucleus, T: tonofilament bundles, Ly: lymphocyte

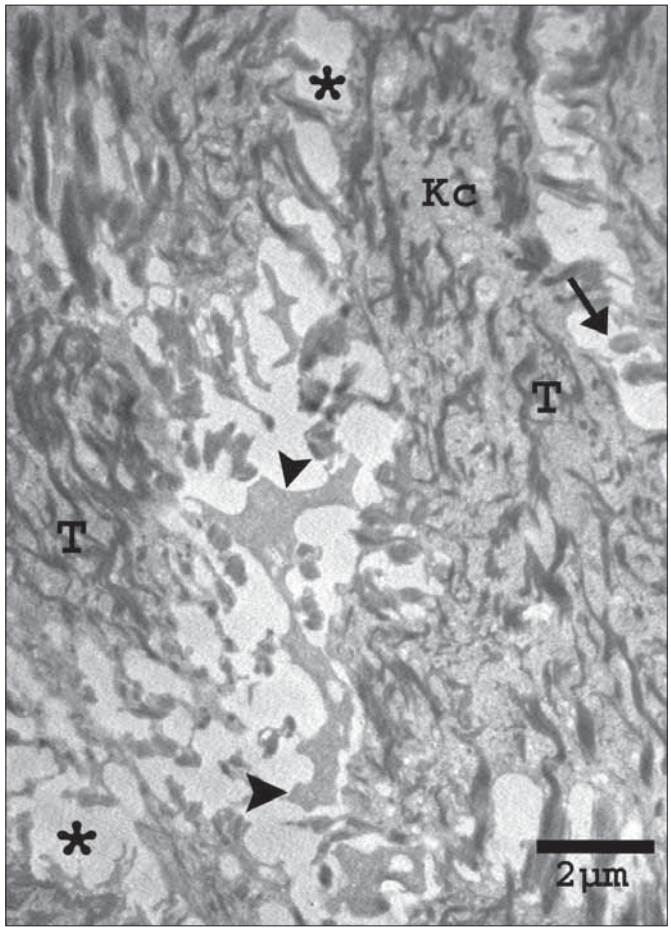

Figure 4. In the stratum spinosum of skin with tinea pedis, the tonofilament bundles (T) in the keratinocytes (Kc) are irregularly distributed. The widened intercellular spaces (asterisks) contain dense material (arrowheads) and desmosomes (arrow) are disrupted

those observed in keratinocytes of the stratum spinosum were noted in the cytoplasm basal cells (Fig. 7). Intercellular spaces were found to preserve their normal ultrastructure only in rare areas, presenting widening in most basal regions (Figs. 6-8). Melanocytes showing a moderate number of melanosomes were found among basal cells in the stratum basale (Fig. 8).

Blood capillaries with distended lumens were noted in the dermal layer of the skin with tinea pedis. Expansions between the collagen fibers of connective tissue probably representing edematous areas and accumulation of a homogenous material were significant (Fig. 6).

Discussion

Dermatophytosis is a very common superficial fungal infection. As known, dermatophyte infections can be spread by three main sources; humans, animals and soil (1, 5-7, 11, 16). Dermatophytes inhabit keratinized structures by digesting them with the keratinases they produce (6, 16). Cellular immunity and antimicrobial activity of PNL restrict the pathogenity of dermatophytes (7, 17). Factors such as atopy, usage of corticosteroids, ichthyosis, collagen vascular disease, infections by dermatophytes promoted by high humidity (7, 10, 12).

The clinical appearance of dermatophytes depends on the location of the infection, immunological response of the host and the type of fungus. Dermatophyte infections of the feet are called tinea pedis (athlete's foot). Tinea infections are contagious and can be spread easily. As well as animals such as cats and dogs or soil, it is generally contracted through direct contact with people or sharing of personal items in public facilities, such as schools, swimming pools, dormitories, and manicure/pedicure centers or military establishments (2, 3, 15, 18-22). Infection frequently presents with itching and maceration between the fourth and fifth toes and expands to the other interdigital spaces. This type of manifestation is called the intertriginous form. In addition, a dishydrotic form characterized by vesicles and a hyperkeratotic form characterized by erythema and squama constitute the other variants of the clinical syndrome (8, 9, 11).

In our study, electron microscopic evaluation revealed significant disturbances in the form and organization of keratinocytes of the stratum spinosum and basale, with irregularly dis-

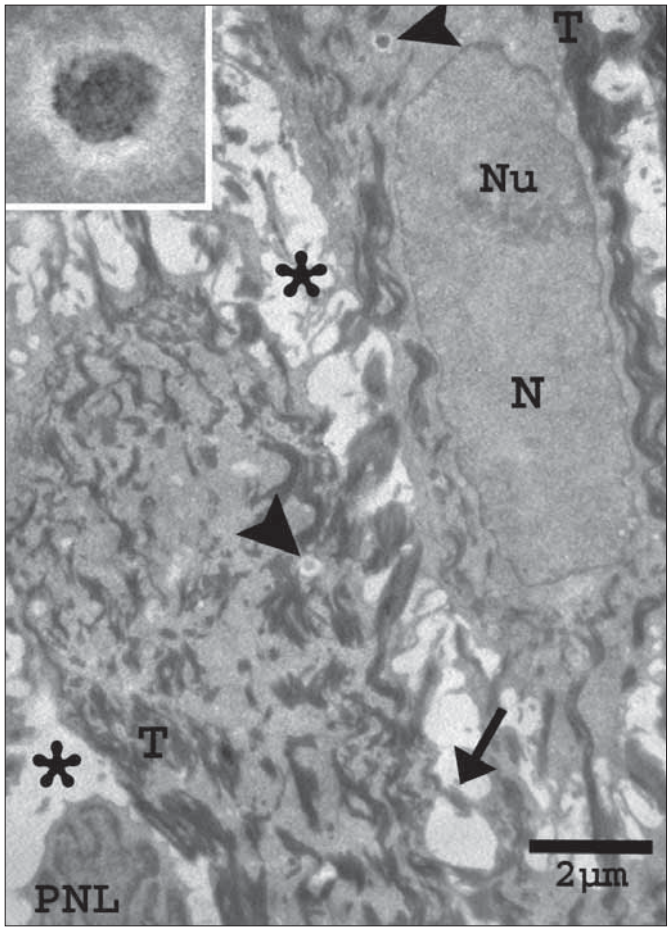

Figure 5. Keratinocytes of stratum spinosum with tinea pedis. Round granules with electron-dense cores (arrowheads) are seen in the keratinocytes. N: nucleus, Nu: nucleolus, T: tonofilament bundles, arrow: desmosome, asterisks: intercellular spaces, PNL: leukocyte. Inset shows higher magnification of a round granule containing fine granular material within electron dense core

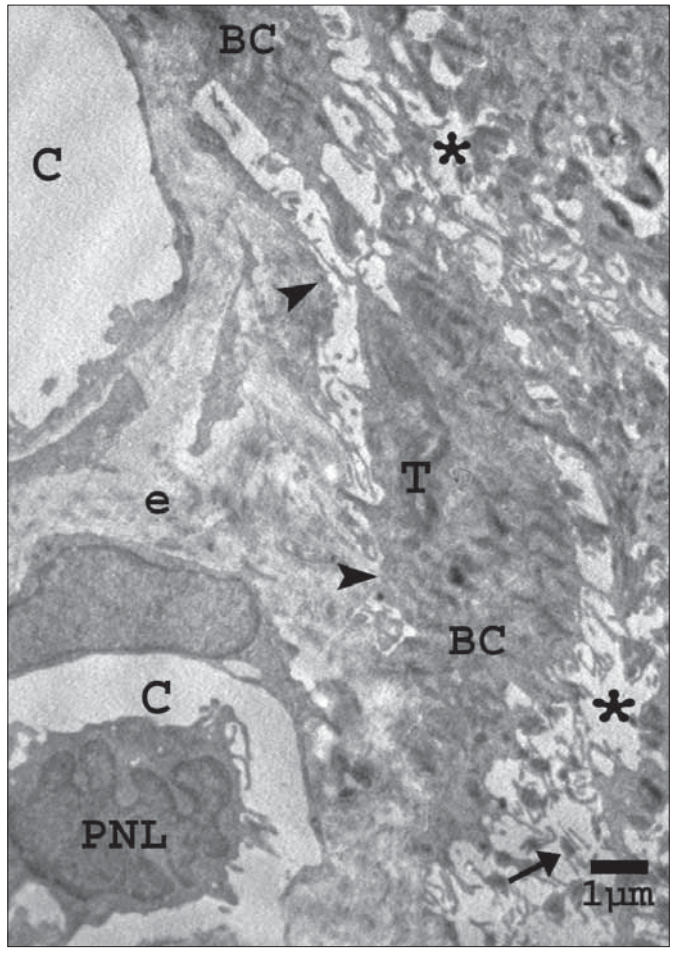

Figure 6. Stratum basale and papillary dermis from a tinea pedis lesion. Basal cells (BC) show deterioration of cellular attachments with disrupted desmosomes (arrow) and papillary dermis exhibits pericapillary edema (e). T: tonofilament bundles, asterisks: intercellular space, arrowhead: gaps in basal lamina, PNL: leucocyte, C: capillaries

tributed short tonofilament bundles. In addition, disruption of desmosomes leading to detachment of adjoining keratinocytes and excessive widening of intercellular spaces was prominent. These findings correlate well with the well-known light microscopic characteristics of tinea pedis which shows the histologic features of spongiotic dermatitis. Spongiotic dermatitis is characterized by increased intercellular space with stretching of desmosomes and accumulation of edema fluid between epidermal cells leading to stellate shaped keratinocytes (8). Furthermore, we observed migration of lymphocytes and PNL's between keratinocytes in stratum spinosum. A variety of mechanisms, such as complement activation by the alternative pathway and low-molecular-weight chemotactic factor production, have been described to elucidate the mechanisms by which inflammatory cells are attracted to the sites of cutaneous fungal infection (7, 8, 11, 17, 23, 24). Our ultrastructural observation of migration of leucocytes is also consistent with the light microscopic findings of epidermal lymphohistiocytic infiltration frequently encountered in spongiotic dermatitis (8).

In this study, we demonstrated disrupted epidermodermal junction with diminished interdigitations between the stratum basale and papillary dermis in patients with tinea pedis. In these areas the basal lamina was observed to degrade and lose its continuity. We consider that deterioration in the basal lamina in tinea pedis is important in terms of evaluating the severity of the pathology. These gaps in the basal lamina may provide routes for PNL's and lymphocytes to migrate towards the upper layers of epidermis. Deterioration of this barrier between dermis and epidermis may lead to pathologic conditions that can affect all layers of the skin (25, 26).

Through the studies conducted, it is known that feedback mechanisms between keratinocytes and melanocytes are known to have an important role in pigmentation of the skin. Although hypopigmentation is not a feature of tinea pedis, we found that melanocytes in the basal layers of epidermis with tinea pedis contained few granules. Also we found round granules of 250-400 nm diameter and electron-dense cores containing fine granular material in the keratinocytes of stratum spinosum. These structures resembled lamellar bodies which contribute to the formation of intercellular epidermal water barrier (27-29).

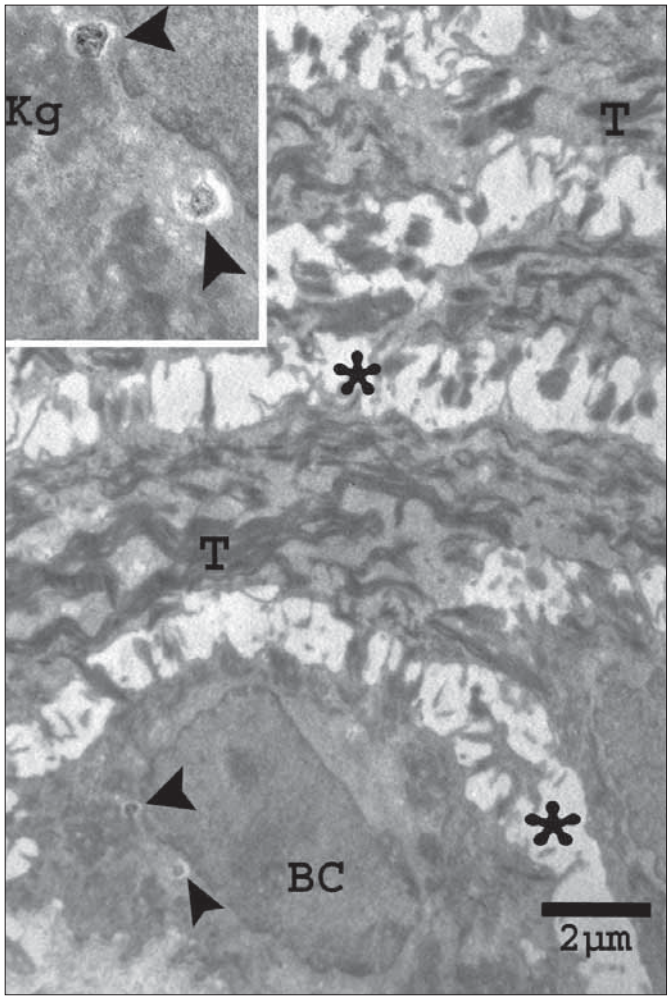

Figure 7. Epidermal basal layer of a tinea pedis lesion. BC: basal cell, T: tonofilament bundles, asterisks: intercellular spaces. Inset shows a portion of a basal cell containing round granules containing granular cores and electron-lucent mantle (arrowheads) and keratohyalin granules (Kg)

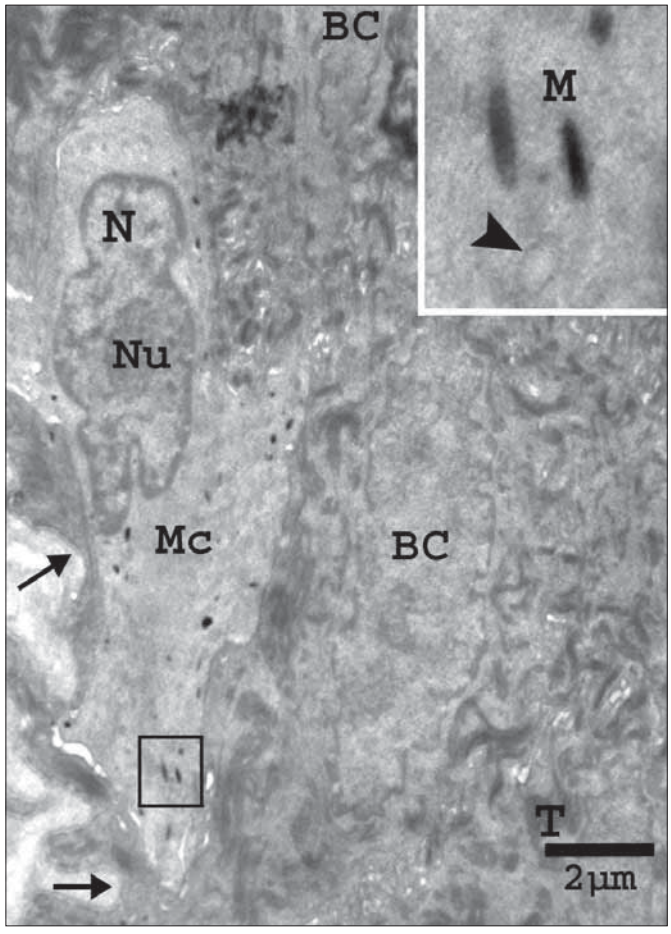

Figure 8. A melanocyte (Mc) from the stratum basale of a tinea pedis lesion showing moderate numbers of melanosomes. BC: basal cell, N: nucleus, Nu: nucleolus, T: tonofilament bundles, arrows: diminished interdigitations in epidermodermal junction. Inset shows higher magnification of the area in the square with melanosomes (M) and mitochondria (arrowhead)

In this study, we observed blood capillaries with distended lumens, expansions between the collagen fibers of connective tissue and accumulation of a homogenous material in the dermal layer of the skin with tinea pedis. These findings provide evidence of papillary dermal edema which is one of the diagnostic features of spongiotic dermatitis and correlates with the degree of spongiosis (8).

In conclusion, although light microscopic characteristics of the lesions of tinea pedis are already described and well known, electron microscopic data is still lacking. This is the first study which outlines the ultrastructural features of epidermis in patients with tinea pedis

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Conflict of Interest

No conflict of interest was declared by the authors.

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