Chapter

The Etiology, Pathophysiology, Differential Diagnosis, Clinical Findings, and Treatment of Nail Psoriasis

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Abstract

Psoriasis is an inflammatory and erythematous scaly disease that involves the skin, joints, and nails. Its prevalence is 1–3%. The incidence of nail involvement in psoriasis patient ranged between 15 and 69%. Nail psoriasis is an important problem affecting patients both functionally and psychologically. Patients with nail psoriasis can develop a wide variety of nail changes, such as pitting, onycholysis, subungual hyperkeratosis, nail discoloration, crumbling and leukonychia, oil spots, and splinter hemorrhages. Nail psoriasis is also strongly associated with psoriatic arthritis. It has been estimated that 80–90% of patients with psoriatic arthritis develop nail involvement. Dermoscopy can be useful in the evaluation of psoriatic nail when there are no typical clinical features. Dermoscopic findings vary depending on the affected area of the nail. Capillaroscopy and confocal microscopy help in the diagnosis. Treatment of the disease includes avoidance of trauma to the nails and different therapeutic approaches with topical, intralesional injections and systemic agents.

Keywords: nail psoriasis, etiology, diagnosis, treatment

1. Introduction

Psoriasis is a common skin disease characterized by inflammation and a chronic course with exacerbation and remission episodes. The worldwide prevalence is approximately 1–2% [1]. The most common involvement of the nail is encountered in psoriasis among all skin diseases. The nail changes may be accompanied by the skin lesions, but in some patients they occur alone. Regarding the literature, the prevalence of the nail involvement is between 10 and 83% [2]. Isolated nail involvement is observed only in 1–5% of all psoriatic patients [2, 3]. There is no difference between the genders considering the prevalence of the nail involvement. The incidence of the nail involvement in children is between 7 and 17%. The cutaneous psoriasis has usually a more severe course in patients with the nail involvement [1]. The changes affecting the nails are encountered in 90% of the psoriatic patients during their lifetime. The prevalence of the nail psoriasis is higher in patients with psoriatic arthritis. The nail involvement is between 75 and 86% in patients with arthropathic psoriasis [4]. It was reported that nail psoriasis is more common in hands compared to the feet. The nail involvement in psoriasis is concomitant with insertion points of

tendons and ligament inflammation. Several studies focused on the co-occurrence of nail involvement, and psoriatic arthritis confirmed the anatomical connection between the nail matrix and the enthesis of the distal interphalangeal (DIP) joint extensor. In the light of these observations, it is believed that the nail lesions are caused by a reaction, which is developing as a reaction to the abnormal tissue stress and inflammation in the nail-joint region, and not as an autoimmune response [5]. Gupta et al. investigated the toenails of 561 psoriatic patients and determined nail disorders in 47% of them [6]. Larsen et al. determined nail changes in 82.3% of 79 psoriatic patients and Salmon et al. in 78.3% of 106 psoriatic patients [7, 2]. The nail lesions emerge usually 10 years later than the skin lesions. This explains why nail psoriasis is less common in children.

2. Etiology and pathogenesis

The pathophysiology of nail psoriasis was first described by Nardo Zaias in 1969 [1]. The etiology of psoriasis is not fully elucidated yet. The genetic susceptibility may play a role, but also environmental factors, drugs, infections, trauma, and psychogenic factors may trigger the disease.

2.1 Genetic factors

The role of genetic factors has been a matter of research in the past decades. In his study, Lomholt demonstrated the presence of psoriasis at least in one of the first- and second-degree relatives of 91% of the psoriatic patients [4].

Genome-wide association studies have identified nine chromosomal loci (PSORS1 through PSORS9) that can be linked to psoriasis. Human leukocyte antigen (HLA)-Cw6, involved in antigen presentation, seems to be a susceptible allele located on PSORS1. HLA-CW6 allele is directly associated with the genetic base of the disease, and it is a major region leading the immunopathogenetic model. The HLA-CW 602 allele, which is localized in this locus, has a significant co-occurrence pattern with psoriasis. Other candidate genes, which may be related to psoriasis, are HLA-C, corneodesmosin, and HCR. Studies showed a co-occurrence with PSORS1 gene on the chromosome 6p12. However, HLA-C seems to be a gene marker rather than an etiological factor. In cases, in which there is a co-occurrence with HLA antigens, the rates of the nail involvement and arthritis are higher than the other types [8].

2.2 Immunologic factors

The tissue reaction seen in psoriasis involves a complex immunological reaction, which ends up with epidermal hyperproliferation along with severe inflammation and abnormal keratinocyte differentiation. The activation of the keratinocytes and dendritic cells follows particularly the activation of the T cells, which migrate to the skin. Certain functional T-cell subpopulations like Th1 and Th17 emerge under the influence of some cytokines like interleukin (IL)-12 and IL-23. These mediators stimulate the secretion of pro-inflammatory cytokines like the tumor necrosis factor-alpha (TNF-α), IL-17, IL-20, and IL-22. The secretion of the adhesion molecules and other mediators aggravates the inflammatory process in psoriasis. As a result of this cascade, neutrophil migration emerges, which ends up with the development of the epidermal microabscess. The increase of the proliferative activity and the abnormal maturation of the keratinocytes lead to hyperparakeratosis, which is characteristic for psoriasis. Studies showed that TNF-α, nuclear factor kappa B, IL-6, and IL-8 were increased in the affected nail tissue [8, 9].

It is believed that certain fungal infections like *Candida albicans* and some other bacterial infections play a role in the exacerbation of psoriasis. Thereby, the systemic inflammation is triggered by the extensive expression of the inflammatory cytokines. *Candida* stimulates the superantigen production and the cytokine secretion, which initiates the psoriatic process as a result of the non-specific T-cell activation [10].

2.2.1 Predisposition factors

The factors affecting the onset and the exacerbations of the disease vary from person to person. Trauma is among the factors, which trigger psoriasis. These factors are radiation (UV, X-ray), dermabrasion, burns, tattoos, vaccines, and inflammatory skin diseases [11]. It is well-known for a long time that infections may trigger and exacerbate psoriasis. Particularly, group A beta-hemolytic streptococci, *Staphylococcus aureus*, and *Candida albicans* are the most common microorganisms [12, 13]. Pregnancy may decrease the activity of the disease. Chronic plaque psoriasis is the most commonly worsening form of psoriasis during the pregnancy. It was also reported that psoriatic arthritis is aggravated during pregnancy [14]. Regarding the environmental factors, emotional disturbances are the most commonly blamed factor. Stress, anxiety, and depression may be the triggering factor for psoriasis. Stress can play a role not only at the onset of the disease but also in exacerbations [15].

Drugs currently known for affecting psoriasis are the following: beta-adrenergic receptor blockers, non-steroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors, tetracyclines, lithium, and interferons. Certain topical antipsoriatic agents like tar and anthralin may sometimes cause exacerbations in patients, who are in the active stage of the disease [16]. The relationship between the climatic features and psoriasis is well-known. In some patients, the lesions may be aggravated by the sunlight [17, 18]. The relationship between psoriasis and obesity was first reported by Lindegard [19]. Several studies showed that obesity is a risk factor for psoriasis. The demonstration of the pro-inflammatory character of obesity and the action of the adipose tissue like an endocrine and immune organ explained its role in psoriasis. Weight loss and diet restriction decrease TNF-α and IL-6 concentrations and consequently decrease the oxidative stress. It was reported that high-calorie diets and some foods that contain PUFA, such as nuts and fish, increase the severity and incidence of psoriasis. Therefore, it is believed that low-calorie diets may contribute to the remission of the disease [19]. Some studies reported that particularly smoking and alcohol had a correlation with psoriasis [12].

2.3 The components of the nail unity

The nail folds are soft tissue structures that protect the lateral and proximal edges of the nail plate. The nail originates from the matrix and is attached to the nail bed and ends up with a free margin at the distal side. The term "nail units" comprises all nail structures and involves nail fold, eponychium, paronychium, hyponychium, nail bed, and nail plate with proximal and lateral nail folds and soft tissue structures [20–23].

3. Pathophysiology

The main findings of the nail psoriasis are pitting, onycholysis, thickening of the nail plate, oil-drop discoloration on the nail bed, transverse ridges, Beau's lines, splinter hemorrhages, subungual hyperkeratosis, and psoriatic paronychia [24].

The histopathological features of the nail psoriasis are neutrophilic inflammation, psoriasiform hyperplasia, and dilated and inflamed capillaries. The granular layer of the hyponychium disappears in the psoriatic nail, and a granular layer emerges in the nail matrix and nail bed. The hyperkeratosis is usually mild or moderate. Spongiosis is common. Parakeratosis foci may emerge on the dorsal, medial, or ventral segments of the nail plate and may cause pitting, leukonychia, and onycholysis. Before the histopathological diagnosis of the nail psoriasis, a differential diagnosis regarding onychomycosis with the help of the Periodic acid Schiff stain is recommended [25].

In the finger nail psoriasis, the findings by order of frequency are pitting, red-oily spots, onycholysis, subungual hyperkeratosis, and splinter hemorrhage. In the toenail psoriasis, the common findings are subungual hyperkeratosis and diffuse yellow-brown discoloration in the nail plate, onycholysis, and splinter hemorrhage [26, 27].

3.1 The characteristics of the nail psoriasis

Matrix: Punctate depressions on the nail surface due to abnormal keratinization of the nail plate. Pitting occurs as a result of the parakeratosis in the superficial matrix. It is encountered also in other diseases affecting the matrix keratinization of the proximal nail (e.g., alopecia areata, eczema). The white-opaque appearance of the parakeratotic cells in the distal and medial segment of the matrix in the shape of a transverse band is called leukonychia. Red spots in the lunula a sign of the active distal matrix psoriasis and emerge a result of the vasodilatation and thinning of the suprapapillary plate. The involvement of the proximal nail matrix causes lesions such as transverse striations on the surface of the nail plate, longitudinal grooves, and superficial pitting. Beau's lines are common in the acute erythrodermic psoriasis [1, 28].

Nail Bed: The psoriatic plaques in the distal matrix and nail bed are called oil-drop spots (salmon spots). It emerges with the serum and debris migration to this region as a result of the local detachment of the nail plate from the nail bed. This finding is rare in other diseases except for psoriasis, and it is useful in the diagnosis of the psoriatic nail. Following the extension of the salmon spot to the hyponychium, parakeratosis resolves, and psoriatic onycholysis develops [28].

Splinter hemorrhages develop as a result of the erythrocyte extravasation from the dermal ridges located between the epidermis and the nail plate. This finding is similar to the Auspitz phenomenon in the skin. The "Auspitz sign" refers to the bleeding that can occur when the surface of a scaling rash has been removed. Onycholysis is defined as the detachment of the nail plate from the nail bed. The detachment area has a whitish appearance due to the air accumulation. The onycholytic area can be distinguished from the normal nail with its erythematous appearance. Onycholysis and subungual hyperkeratosis are predictors of the hyponychium psoriasis [26]. Pustular psoriasis in the nail bed and nail folds, nail loss (anonychia), onychomadesis, and absence of the nail growth are other findings in the psoriatic nail [20].

Psoriasis in the proximal nail fold: The cuticle is damaged, and there is a typical appearance of the chronic paronychia along with the erythema, squam, and edema in the proximal nail fold. Hyponychium involvement causes subungual hyperkeratosis and onycholysis [29].

4. Grading and scoring of psoriatic nail

Several numeric scales were developed to determine the numeric equivalent of the response to the treatment of psoriasis. These numeric scales enable an easier follow-up of the disease and of the response to the treatment. The Nail Psoriasis Severity Index

(NAPSI) is a scoring system developed by Riche and Scher in 2003 [30]. According to this system, the nail matrix findings (pitting, leukonychia, red spots in lunula, increased friability of the nail plate) and the nail bed findings (onycholysis, splinter hemorrhage, oil drop, and nail bed hyperkeratosis) are scored as follows: If any of these signs is present in all four quadrants, a score of 4 is given. A score of 0 represents no signs in any quadrant. Each nail is evaluated for a matrix and a nail bed score of 0–4. They are combined to yield a maximal score of 0–8 for each nail. [26] After the scoring is completed, the sum of the scores is recorded as the NAPSI score. The NAPSI scores calculated for each nail are summed up to find the total NAPSI score. The single nail score can be between 0 and 8 and the total score between 0 and 160. Regarding the Cannavo's scoring system, the nail findings are scored between 0 and 3, and the scoring is done according to the presence or absence of the findings [31].

The modified NAPSI, which is described by Parrish et al., is based on the scoring of the common findings [32]. The scoring is done between 0 and 3 according to the number of pitting. The modified NAPSI score for 1 finger can be between 0 and 14 and for 10 fingers between 0 and 140 [33].

5. Diagnosis

As the nail involvement pursues skin psoriasis, its diagnosis is rather easy. However, 5% of the cases are isolated nail psoriasis, and the diagnosis may become difficult. Like in the skin, biopsy has a diagnostic value. Biopsy sampling should be taken from the proximal segment, and it should enclose partly the subungual soft tissue to detect the matrix involvement [34].

Except for biopsy, dermoscopy, and videodermoscopy may support the clinical findings and thus the diagnosis. Videodermoscopy provides a 1000x higher magnification compared to the dermoscopy, and the images can be examined on a monitor. It is beneficial particularly for the observation of the capillaries in the hyponychium. The capillaroscopy is used to determine the dilated capillaries in the proximal nail fold. The vascular structures may be better visualized with the confocal microscopy. High-frequency ultrasonography (USG) can be useful only if performed by experienced hands. The increase in the blood flow and the thickening of the nail bed can be determined with the Doppler USG. The optical coherence tomography is a noninvasive imaging method and has a relatively higher resolution and thus is effective in the detection of the changes in the nail plate and vessels [35].

6. Differential diagnosis

The nail psoriasis is usually diagnosed with the help of the clinical findings. The differential diagnosis between nail psoriasis and other diseases, which causes nail dystrophy (e.g., onychomycosis), can be done with biopsy and histopathological examination. Klaassen et al. reported that the prevalence of onychomycosis is higher in psoriatic patients compared to the patients without psoriasis [36].

Several diseases affecting nails can be confused with the psoriatic nail. Following conditions should be considered during the differential diagnosis: trauma, onychomycosis, pityriasis rubra pilaris, palmoplantar keratoderma, chronic venous stasis, many drugs, alopecia areata, eczema, lichen planus, Darier disease, pachyonychia congenita, and Hailey-Hailey disease [37].

Besides, toenail dystrophy is particularly more common in elderly people. Peripheral artery disease, chronic venous stasis, peripheral neuropathy, and certain

drugs (beta-blockers, lithium, interferon-α) should also be considered during the differential diagnosis [38].

Pitting, which can be encountered in alopecia areata, lichen planus, and eczema, is one of the most common nail findings in psoriasis, and it is relatively more deep-seated in psoriasis compared to other diseases. The dorsal pterygium and longitudinal fissures are rather typical findings in lichen planus [38].

Onycholysis, which is another typical finding in the nail psoriasis, emerges first in the distal segment of the nail and extends in time to the proximal segment. This finding can be encountered also in nail traumas, fungal infections, and thyroid disorders [39].

Beau's lines characterized by the transverse lines on the nail can emerge in Raynaud's disease as a result of the exposure to the cold [40].

As the splinter hemorrhages, which progress with linear spotlike bleedings, can also emerge in vasculitis, bacterial endocarditis, and traumas. Therefore, they should be considered during the differential diagnosis [1].

7. Treatment

Regarding the treatment of nail psoriasis, the protection of the nail from the external physical and chemical factors is critical. Manicure and pedicure should be avoided due to the risk of the Köbner reaction. *Candida* infections are more common compared to the dermatophyte infections in the psoriatic nails. Onychomycosis, which may accompany nail psoriasis, should be diagnosed and treated before starting the psoriasis treatment [41].

As nail is a slow-growing cutaneous appendage, a long-term treatment should be considered in the nail psoriasis. The outcome of any treatment cannot be evaluated before 3–6 months, and the achievement of a maximum therapeutic success can be evaluated only after 1 year or longer [42]. There are various alternatives for the treatment. The decision on a treatment method depends on several factors such as the severity of the nail involvement and its effects on the quality of life, presence of other skin lesions, presence of psoriatic arthritis, comorbidities, occupation, age, patient's preferences, potential risks, and cost.

7.1 Topical treatments

Although the nail psoriasis is usually resistant to the topical treatments, it should be the first choice if the skin is also involved. As the applied drug can hardly penetrate into the matrix in the presence of subungual hyperkeratosis and pitting, resistance to the treatment is the rule. Nevertheless, at least a 3-month application is needed to observe the effect of the topical antipsoriatic agent [43].

7.1.1 Corticosteroids

The most common treatment agents in the nail psoriasis are the topical corticosteroids. If the matrix and nail bed are involved, high-potency topical steroids are applied once or twice a day to the nail plate and proximal nail fold. All high-potency steroids may cause atrophy and hyperpigmentation if they come into contact with the skin during the treatment [44]. In the recent years, studies showed that topical opaque nail polish formulations, which contain 8% clobetasol propionate, were more effective than the steroids. It was reported that this product, which was safe, effective, and easily applicable due to the cosmetic formulation, did not cause periungual skin atrophy like topical cream forms [45, 46].

7.1.2 Calcipotriol

Topical calcipotriol is used in the treatment of the chronic plaque psoriasis. It is effective on the thickening of the nail plate and subungual hyperkeratosis. Main side effects are local skin irritations. Vitamin D3 and its analogs are well established in the therapy of psoriasis vulgaris [47].

7.1.3 5-Fluorouracil (5-FU)

One study conducted on subject groups showed that topical 5-FU solutions with 20% urea were effective on pitting, subungual hyperkeratosis, and oil-drop appearance [48].

7.1.4 Cyclosporine

It is a calcineurin inhibitor, and cyclosporine is good effect on psoriasis. Although topical use of cyclosporine in nail psoriasis has been discussed, only limited success could be achieved with 10% oily preparations [49].

7.1.5 Anthralin

Anthralin is an effective treatment of skin lesions in psoriasis. In one uncontrolled study, anthralin in a Vaseline-containing ointment was applied to 20 psoriasis patients with nail involvement. Therapy was applied to the affected nail bed once daily, and 60% of the patients showed good improvement of onycholysis. The most important complication of this treatment is pigmentation [50].

7.1.6 Tazarotene

Tazarotene is a synthetic retinoid with anti-inflammatory and antiproliferative actions on keratinocytes. Gel formulations of 0.1% tazarotene were used in the topical treatment of the nail psoriasis, and varying results were achieved. It may cause certain side effects like erythema and burning sensation in the periungual region [51].

7.2 Intralesional treatments

The perilesional injections constitute another form of the local treatment (**Figure 1**). During this treatment, a maximum efficacy is obtained with a minimum dose of the drug, which is applied into the lesion. Intralesional injections of corticosteroids are the most common method. As injections into the matrix and under the nail bed are painful, local anesthesia is necessary. A proximal finger block or hand and wrist block can be preferred. Cold application to the proximal nail fold before the injection may reduce the pain. The injection is usually done with a 30G needle. 0.05–0.1 triamcinolone acetonide suspension is injected into both sides of the proximal nail fold monthly for 6 months. This treatment is most effective on salmon spots and subungual hyperkeratosis [52]. Possible complications of this treatment are subungual hematoma, transient nail dystrophy, atrophy of the terminal phalanx bone, extensor tendon rupture, and epidermoid inclusion cysts [53].

In nail psoriasis, methotrexate (MTX) and cyclosporine may be applied to the proximal fold with an intralesional injection technique. In patients with nail psoriasis, who had pitting and subungual hyperkeratosis on a single nail, Sarıcaoğlu et al. applied 2.5 mg MTX to two lateral points of the proximal fold once weekly for 6 weeks and observed no recurrence during the 2-year follow-up period [54].

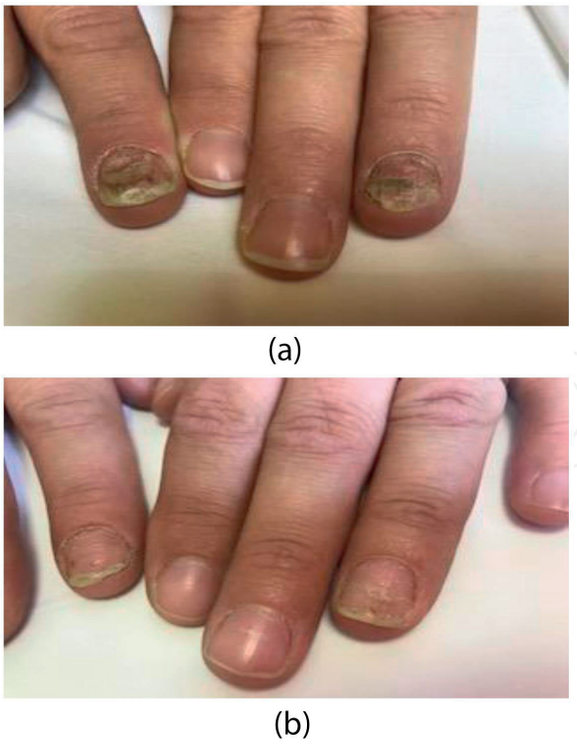

Figure 1.
(a) Subungual hyperkeratosis with pitting in fingernails before the MTX intramatricial injection. (b) Improvement of nail dystrophy was observed after 6 months of follow-up.

Mittal et al. conducted a study on 20 patients with nail psoriasis and compared the efficacy of intramatricial triamcinolone acetonide, methotrexate, and cyclosporine injections and found out that methotrexate and corticosteroid had comparable efficacies. They also reported that the side effects of MTX were less frequently and cyclosporine was less effective and caused pain, which lasted a couple of days [55].

7.3 Phototherapy and photochemotherapy

The combination of oral psoralen and UVA, which is also called PUVA is a photochemotherapy method. It was reported that it provided successful results in patients with nail bed involvement, which ended up with onycholysis and salmon patches. However, it was also stated that it was not effective on pitting, which is an indicator of matrix involvement. Marx and Scher conducted a study on ten patients and showed that PUVA improved all nail lesions except pitting in 95% of the patients [56]. Except for oral psoralen, local PUVA treatment with the topical 1% 8-methoxypsoralen is an alternative for the treatment of the psoriatic nail [57]. As the penetration of the narrow band UVB is rather superficial, it is not an effective option for the palmoplantar psoriasis lesions and nail involvement [58].

7.4 Ionizing radiations

Superficial radiotherapy is the application of the electromagnetic radiation on the skin surface. It is rarely used in the treatment of psoriatic nail. It was reported in one study that it decreased the nail thickness in the patients with subungual hyperkeratosis [59]. Grenz rays and electron beam therapy are low-voltage radiation treatments, which do not penetrate the subdermal structures. In patients older than 30 years, Grenz rays [maximum 10Gy (1000 rad)] to each area can be applied. If it is applied to healthy areas and surrounding skin, it may cause hyperpigmentation and malignant skin tumors in the late stage [60].

7.5 Laser therapy

As angiogenesis is considered as a pathogenetic factor for psoriasis, pulsed-dye laser (PDL) was used in several studies to treat nail psoriasis. The target of the laser therapy is the matrix and the dilated capillaries in the nail bed. A PDL laser at wavelength 595 nm and with a spot size of 7 mm was usually preferred. It was observed that the pain increased along with the pulse duration [61].

7.6 Systemic therapies

Several systemic agents are used for the treatment of the nail psoriasis. The most commonly used drugs are MTX, retinoids, and cyclosporine. However, they are usually preferred in patients with severe dermal and articular involvement. They are not the first choice for psoriasis, which affects only nails.

7.6.1 Retinoids

Acitretin is effective on the thickening of the nail plate, subungual hyperkeratosis, Hallopeau acrodermatitis, and the nail involvement in pustular psoriasis. Its usual dose is 0.5–1 mg/kg/day. Although etretinate decreases significantly the thickening of the nails, it was reported that it increased pitting and onycholysis [43, 62].

7.6.2 Methotrexate

Methotrexate (MTX), which is an antimetabolite agent, slows down the nail growth and therefore delays the healing process in the nail lesions. Intralesional MTX injections are preferred to the oral administration due to the side effects like hepatotoxicity and pancytopenia, and studies reported improvement in the affected nail with intralesional injections [54, 55]. MTX is used in the Hallopeau acrodermatitis and the affected nails in pustular psoriasis, which is resistant to the topical treatments [49].

7.6.3 Cyclosporine

The calcineurin inhibitor cyclosporine A is another systemic antipsoriatic agent and has powerful immunosuppressive activity. Its positive effect on cutaneous psoriasis and nail psoriasis was clearly demonstrated in both uncontrolled and comparative studies [63]. Its recommended dose is 3–5 mg/kg. Cyclosporine A treatment is limited to 6–12 months due to the potential of serious side effects such as kidney function disorder and arterial hypertension.

Fumaric acid esters can also be used in the treatment of psoriasis. Its efficacy on the affected nails was demonstrated in a case report [64].

Leflunomide is an antirheumatic agent effective in psoriatic arthritis. It was also reported that it is effective in nail psoriasis [65].

Apremilast is an oral phosphodiesterase-4 inhibitor, which decreases the expression of various pro-inflammatory mediators. Its mechanism of action is related rather to anti-inflammatory activity than the immunosuppressive activity. It has a preferable side effect profile [66]. Studies reported that it provided improvement in the skin and nail psoriasis after a 32-month treatment [67].

Tofacitinib is an oral Janus kinase inhibitor, which exhibits its effects through the JAK–STAT pathway. It was demonstrated that it was effective on the nail lesions of psoriasis and alopecia areata [68].

7.7 Biologic therapy

As there are only a limited number of studies focused on the use of biologic agents in the nail psoriasis, experience about their efficacy is limited. The number of the studies focused on the use of the biologic agents in the treatment of psoriatic nails will increase depending on their increasing use in psoriasis and psoriatic arthritis. In the studies, which compared the biologic agents with the conventional systemic drugs, it was shown that the efficacy of the biologic agents was lower and the improvement in the NAPSI score started approximately after 47 months [69]. Their high cost is another factor, which limits their usage.

Infliximab is a mouse-derived chimeric monoclonal antibody, which antagonizes membrane-bound and soluble TNF-α, and it is the most fast-acting TNF-α inhibitor. The recommended dose is 5 mg/kg IV at 0, 2, and 6 weeks and thereafter once every 8 weeks. In a study conducted on 38 patients, who had nail psoriasis, an almost complete improvement was achieved after 38 weeks [70].

Adalimumab is a human monoclonal IgG1 antibody against TNF-α. It has a similar mechanism of action to infliximab, but it does not increase the incidence of onychomycosis like infliximab. Van den Bosch et al. reported a 20% improvement in the NAPSI score with a dose of 40 mg/week after 20 weeks [71].

Etanercept blocks TNF-α depending on the fusion between the Fc portion of the IgG1 antibody and TNF receptor. In a randomized study, 564 patients with moderate psoriasis and nail involvement were treated with etanercept, and the NAPSI score decreased about 51% after 54 weeks [72].

The new-generation biologic agents inhibit interleukins, which affect the psoriatic process. However, their immunosuppressive efficacy is weaker than the TNF- α inhibitors. The IL-17 inhibitors secukinumab, ixekizumab, and brodalumab were recently introduced in the therapy. Ustekinumab is a monoclonal antibody targeting the p40 subunit of IL-12/23. Patsatsi et al. administered 45 mg ustekinumab at the baseline, in the fourth week and afterwards in every 12 weeks, and reported that the NAPSI scored was declined from 73 to 0 after 40 weeks [73].

Biologic agents and interleukin inhibitors are not the first choices in the treatment of the nail psoriasis due to their side effect potential. The treatment should be started with topical agents. The conventional systemic antipsoriatic agents should be administered if there is no improvement after 4–6 months with topical agents. The biologic agents should remain as the last choice.

The nail psoriasis is considered as the precursor of severe inflammatory joint disorders, and it has a positive correlation with the joint involvement [30]. The presence of the joint and nail symptoms may indicate the severity of psoriasis and affect the management of the disease. Therefore, in order to prevent the progressive joint damage, the nail findings should be considered as the early symptoms of psoriatic arthritis especially in patients with skin psoriasis.

8. Conclusion

Psoriasis vulgaris is an inflammatory skin disease involving the skin, nails, and joints. Nail changes are frequent in psoriasis and being found in up to 60% of patients. Patients with nail psoriasis can develop a wide variety of nail changes, such as pitting, onycholysis, subungual hyperkeratosis, and splinter hemorrhages. Nail psoriasis is also strongly associated with psoriatic arthritis. Nail psoriasis results from psoriatic inflammation involving the nail matrix or nail bed. As the nail involvement pursues skin psoriasis, its diagnosis is rather easy. However, 5% of the cases are isolated nail psoriasis, and the diagnosis may become difficult.

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Onychomycosis should be distinguished from nail psoriasis in the differential diagnosis. The decision on a treatment method depends on several factors and the severity of nail psoriasis.

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References

[1] Zaias N. Psoriasis of the nail. A clinical-pathologic study. Archives of Dermatology. 1969;**99**(5):567-579

[2] Salomon J, Szepietowski JC, Proniewicz A. Psoriatic nails: A prospective clinical study. Journal of Cutaneous Medicine and Surgery. 2003 Jul-Aug;**7**(4):317-321

[3] Kerkhof PCM, Schalkwijk J. Psoriasis. In: Callen JP, Horn TD, Mancini AJ, Salasche SJ, Schaffer JV, Schwarz T, et al., editors. Dermatology. 2nd ed. New York: Mosby Elsevier; 2008. pp. 115-135

[4] Lomholt G. Environment and genetics in psoriasis. Annals of Clinical Research. 1976 Oct;**8**(5):290-297

[5] McGonagle D, Tan AL, Benjamin M. The nail as a musculoskeletal appendage-implications for an improved understanding of the link between psoriasis and arthritis. Dermatology. 2009;**218**:97-102

[6] Gupta AK, Lynde CW, Jain HC, Sibbald RG, Elewski BE, Daniel CR 3rd. et al, A higher prevalence of onychomycosis in psoriatics compared with non-psoriatics: A multicentre study. British Association of Dermatologists. 1997;**136**(5):786-789

[7] Larsen GK, Haedersdal M, Svejgaard EL. The prevalence of onychomycosis in patients with psoriasis and other skin diseases. Acta Dermato-Venereologica. 2003;**83**(3):206-209

[8] Rashmi R, Rao KS, Basavaraj KH. A comprehensive review of biomarkers in psoriasis. Clinical and Experimental Dermatology. 2009;**34**(6):658-663

[9] Nast A, Rosumeck S, Sammain A, Erdmann R, Sporbeck B, Rzany B. S3-guidelines for the treatment of psoriasis vulgaris methods report. Journal der Deutschen Dermatologischen Gesellschaft. 2011;**9**(Suppl 2):64-84

[10] Kisand K, Bøe Wolff AS, Podkrajsek KT, et al. Chronic mucocutaneous candidiasis in APECED or thymoma patients correlates with autoimmunity to Th17-associated cytokines. Journal of Experimental Medicine. 2010;**207**(2):299-308

[11] Jiaravuthisan MM, Sasseville D, Vender RB, Murphy F, Muhn CY. Psoriasis of the nail: Anatomy, pathology, clinical presentation, and a review of the literature on therapy. Journal of the American Academy of Dermatology. 2007;**57**(1):1-27

[12] Fry L, Baker BS. Triggering psoriasis: The role of infections and medications. Clinics in Dermatology. 2007;**25**:606-615

[13] Tagami H. Triggering factors. Clinics in Dermatology. 1997;**15**:677-685

[14] Horn EJ, Chambers CD, Menter A, Kimball AB. Pregnancy outcomes in psoriasis: Why do we know so little? Dermatology. 2010;**220**:71-76

[15] O'Leary CJ, Creamer D, Higgins E, Weinman J. Perceived stress, stress attributions and psychological distress in psoriasis. Journal of Psychosomatic Research. 2004;**57**:465-471

[16] Tsankov N, Kazandjieva J, Drenovska K. Drugs in exacerbation and provocation of psoriasis. Clinics in Dermatology. 1998;**16**:333-351

[17] Chandran V, Raychaudhuri SP. Geoepidemiology and environmental factors of psoriasis and psoriatic arthritis. Journal of Autoimmunity. 2010;**34**:314-321

[18] Lindegard B. Diseases associated with psoriasis in a general population

of 159,200 middle-aged, urban, native swedes. Dermatologica. 1986;**172**(6):298-304

[19] Bremmer S, Van Voorhees AS, Hsu S, Korman NJ, Lebwohl MG, Young M, et al. Obesity and psoriasis: From the medical Board of the National Psoriasis Foundation. Journal of the American Academy of Dermatology. 2010;**6**:1-12

[20] de Berker D, André J, Baran R. Nail biology and nail science. International Journal of Cosmetic Science. 2007;**29**:241-275

[21] Achten G, Parent D. The normal and pathologic nail. International Journal of Dermatology. 1983;**22**:556-565

[22] Zook EG. Anatomy and physiology of the Perionychium. Clinical Anatomy. 2003;**16**:1-8

[23] Rich P, Scher RK. Nail anatomy and basic science. In: Rich P, Scher RK, editors. An Atlas of Diseases of the Nail. 1st ed. USA: The Parthenon Publishing Group; 2003. pp. 7-9

[24] Lawry M. Biological therapy and nail psoriasis. Dermatologic Therapy. 2007;**20**:60-67

[25] Sánchez-Regaña M, Umbert P. Diagnosis and management of nail psoriasis. Actas Dermo-Sifiliográficas. 2008;**99**:34-43

[26] Haneke E. Nail psoriasis: Clinical features, pathogenesis, differential diagnoses, and management. Psoriasis. 2017;**7**:51-63

[27] Koo J, Lee E, Lee CS, Lebwohl M. Psoriasis. Journal of the American Academy of Dermatology. 2004;**50**:613-622

[28] Haneke E. Non-infectious inflammatory disorders of the nail apparatus. Journal der Deutschen Dermatologischen Gesellschaft. 2009;**7**:787-797

[29] Tendais-Almeida J, Fátima Aguiar F, Torres T. Nail pitting and onycholysis. Australian Family Physician. 2016 Mar;**45**(3):120-121

[30] Rich P, Scher RK. Nail psoriasis severity index: A useful tool for evaluation of nail psoriasis. Journal of the American Academy of Dermatology. 2003 Aug;**49**(2):206-212

[31] Cannova SP, Guarneri F, Vaccaro M, Borgia F, Guarneri B. Treatment of psoriatic nails with topical cyclosporin: A prospective, randomized placebo controlled study. Dermatology. 2003;**206**:153-156

[32] Parrish CA. Modification of the nail psoriasis severity indeks. Journal of the American Academy of Dermatology. 2005;**53**:745-746

[33] Cassel SE, Bieber JD, Rich P, Tutuncu ZN, Lee SJ, Kalunian KC, et al. The modified nail psoriasis severity index: Validation of an instrument to ases psoriatic nail involvement in patients with psoriatic arthritis. The Journal of Rheumatology. 2007;**34**: 123-129

[34] Haneke E. Histopathology of the Nail – Onychopathology. Boca Raton: CRC Press; 2017

[35] Dogra S, Yadav S. What's new in nail disorders? Indian Journal of Dermatology, Venereology and Leprology. 2011;**77**:631-639

[36] Klaassen KM, van de Kerkhof PC, Pasch MC. Nail psoriasis: A questionnaire-based survey. The British Journal of Dermatology. 2013;**169**(2):314-319

[37] Schons KR, Knob CF, Murussi N, Beber AA, Naumaier W, Monticielo OA. Nail psoriasis: A review of the literature. Anais Brasileiros de Dermatologia. 2014;**89**:312-317

[38] Fawcett RS, Linford S, Stulberg DL. Nail abnormalities: Clues to systemic disease. American Family Physician. 2004;**69**:1417-1424

[39] Wolska H. Nail psoriasis. Przegląd Dermatologiczny. 2010;**97**:243-253

[40] Scher RK, Daniel CR. Nails: Therapy, Diagnosis, Surgery. Philadelphia: W.B. Saunders Company; 2003

[41] Brem J. Effective topical method of therapy for onychomycosis. Cutis. 1981;**27**(1):69-76

[42] de Vries AC, Bogaards NA, Hooft L, Velema M, Pasch M, Lebwohl M, et al. Interventions for nail psoriasis. Cochrane Database of Systematic Reviews. 2013;**1**:CD007633

[43] de Berker D. Diagnosis and management of nail psoriasis. Dermatologic Therapy. 2002;**15**:165-172

[44] Rigopoulos D, Gregoriou S, Katsambas A. Treatment of psoriatic nails with tazarotene cream 0.1% vs. clobetasol propionate 0.05% cream: A double-blind study. Acta Dermato-Venereologica. 2007;**87**(2):167-168

[45] Baran R, Tosti A. Topical treatment of nail psoriasis with a new corticoid-containing nail lacquer formulation. Journal of Dermatological Treatment. 1999;**10**:201-204

[46] Tosti A, Piraccini BM, Cameli N, Kokely F, Plozzer C, Cannata GE, et al. Calcipotriol ointment in nail psoriasis: A controlled double-blind comparison with betamethasone dipropionate and salicylic acid. The British Journal of Dermatology. 1998;**139**(4):655-659

[47] Lamba S, Lebwohl M. Combination therapy with vitamin D analogues. The British Journal of Dermatology. 2001;**58**:27-32

[48] Fritz K. Successful local treatment of nail psoriasis with 5-fluorouracil. Zeitschrift für Hautkrankheiten. 1989;**64**:1083-1088

[49] de Berker D. Management of nail psoriasis. Clinical and Experimental Dermatology. 2000;**25**:357-362

[50] Yamamoto T, Katayama I, Nishioka K. Topical anthralin therapy for refractory nail psoriasis. The Journal of Dermatology. 1998;**25**:231-233

[51] Bianchi L, Soda R, Diluvio L, Chimenti S. Tazarotene 0.1% gel for psoriasis of the fingernails and toenails:An open, prospective study. The British Journal of Dermatology. 2003;**149**:207-209

[52] Saleem K, Azim W. Treatment of nail psoriasis with a modified regimen of steroid injections. Journal of the College of Physicians and Surgeons–Pakistan. 2008;**18**(2):78-81

[53] Bjorkman A, Jorgsholm P. Rupture of the extensor pollicis longus tendon: A study of aetiological factors. Scandinavian Journal of Plastic and Reconstructive Surgery and Hand Surgery. 2004;**38**(1):32-35

[54] Sarıcaoglu H, Oz A, Turan H. Nail psoriasis successfully treated with intralesional methotrexate: Case report. Dermatology. 2011;**222**:5-7

[55] Mittal J, Mahajan BB. Intramatricial injections for nail psoriasis: An open-label comperative study of triamcinolone, methotrexate, and cyclosporine. Indian Journal of Dermatology, Venereology and Leprology. 2018;**84**(4):419-423

[56] Marx JL, Scher RK. Response of psoriatic nails to oral photochemotherapy. Archives of Dermatology. 1980;**116**:1023-1024

[57] Zhang P, Wu MX. A clinical review of phototherapy for psoriasis. Lasers in Medical Science. 2018 Jan;**33**(1):173-180

[58] Dogra S, De D. Narrowband ultraviolet B in the treatment of psoriasis: The journey so far. Indian Journal of Dermatology, Venereology and Leprology. 2010;**76**:652-661

[59] Finnerty EF. Successful treatment of psoriasis of the nails. Cutis. 1979;**23**:43-44

[60] Baran R, Dawber RPR, editors. Diseases of the Nail and their Management. 3. baskı. Oxford: Blackwell Scientific Publications; 2001. pp. 172-189

[61] Treewittayapoom C, Singvahanont P, Chanprapaph K, Haneke E. The effect of different pulse duration in the treatment of nail psoriasis with 595-nm pulsed dye laser: A randomized, double-blind, intrapatient left-to-right study. Journal of the American Academy of Dermatology. 2012;**66**:807-812

[62] Baran R. Etretinate and the nails (study of 130 cases) possible mechanisms of some side-effects. Clinical and Experimental Dermatology. 1986;**11**:148-152

[63] Syuto T, Abe M, Ishibuchi H, Ishikawa O. Successful treatment of psoriatic nails with low-dose cyclosporine administration. European Journal of Dermatology. 2007;**17**(3):248-249

[64] Vlachou C, Berth-Jones J. Nail psoriasis improvement in a patient treated with fumaric acid esters. The Journal of Dermatological Treatment. 2007;**18**(3):175-177

[65] Behrens F, Finkenwirth C, Pavelka K, Stolfa J, Sipek-Dolnicar A, Thaci D, et al. Leflunomide in psoriatic arthritis: Results from a large European prospective observational study. Arthritis Care & Research (Hoboken). 2013;**65**(3):464-470

[66] Torres T, Puig L. Apremilast: A novel oral treatment for psoriasis and psoriatic arthritis. American Journal of Clinical Dermatology. 2017;**19**:23-32. DOI: 10.1007/s40257-017-0302-0

[67] Papp K, Reich K, Leonardi CL, Kircik L, Chimenti S, Langley RG, et al. Apremilast, an oral phosphodiesterase 4 (PDE4) inhibitor, in patients with moderate to severe plaque psoriasis: Results of a phase III, randomized, controlled trial (efficacy and safety trial evaluating the effects of apremilast in psoriasis [ESTEEM] 1). Journal of the American Academy of Dermatology. 2015;**73**(1):37-49

[68] Di Lernia V, Bardazzi F. Profile of tofacitinib citrate and its potential in the treatment of moderate-to-severe chronic plaque psoriasis. Drug Design, Development and Therapy. 2016;**10**:533-539

[69] Gniadecki R, Bang B, Bryld LE, Iversen L, Lasthein S, Skov L. Comparison of long-term drug survival and safety of biologic agents in patients with psoriasis vulgaris. The British Journal of Dermatology. 2015;**172**(1):244-252

[70] Rigopoulos D, Gregoriou S, Stratigos A, Larios G, Korfitis C, Papaioannou D, et al. Evaluation of the efficacy and safety of infliximab on psoriatic nails: An unblinded, nonrandomized, open-label study. The British Journal of Dermatology. 2008;**159**:453-456

[71] van den Bosch F, Reece R, Behrens F, Wendling D, Mikkelsen K, Frank M, et al. Clinically important nail psoriasis improvements are achieved with adalimumab (Humira): Results from a large open-label prospective study (STEREO). Annals of the Rheumatic Diseases. 2007;**66**(Suppl. 2):421

[72] Luger TA, Barker J, Lambert J, Yang S, Robertson D, Foehl J, et al. Sustained improvement in joint pain and nail symptoms with etanercept

therapy in patients with moderate-to-severe psoriasis. Journal of the European Academy of Dermatology and Venereology. 2009;**23**:896-904

[73] Patsatsi A, Kyriakou A, Sotiriadis D. Ustekinumab in nail psoriasis: An open-label, uncontrolled, nonrandomized study. The Journal of Dermatological Treatment. 2013;**24**:96-100