

Management of psoriasis in children (Review)

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Abstract. Psoriasis is a common long-lasting, inflammatory disease that mainly affects the skin. The incidence of this condition has increased significantly over time and at this point, it affects approximately 1% of children. Psoriasis can appear at any age, including childhood and adolescence, with a higher frequency in girls, an earlier onset being associated with severe psoriasis. The pathology is the result of the interaction between genetics and trigger factors such as infections, stress, diet, obesity, and chemical irritants. Paradoxically, tumor necrosis factor (TNF)- α inhibitors (infliximab, adalimumab) may induce psoriasis in children. Psoriasis is a long-term condition with periods of exacerbation; thus, the quality of life can be affected and patients should receive psychosocial support. Although most children have mild disease and topical treatment is efficient, some cases are challenging to treat. The aim of this review was to provide an overview of the current knowledge concerning the epidemiology, etiology, pathogenesis, clinical features, comorbidities, and treatment of psoriasis in children and also to emphasize the need for a multidisciplinary approach to this complex pathology.

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1. Introduction

Psoriasis is a chronic, systemic, inflammatory, immune-mediated disease that primarily affects the skin, characterized by abnormal hyperproliferation of the epidermis (1-3). There are many trigger factors involved (stress, infections, medications, trauma) that can induce the disease in a predisposed population (3).

To collect reports of psoriasis etiopathogeny, a literature search was conducted using electronic databases Google Scholar, PubMed, Key Elsevier, UpToDate and Medscape for the terms 'psoriasis' in combination with 'psoriasis in children', 'management of psoriasis', 'napkin psoriasis', 'biologic therapies', 'pathogenesis', 'treatment'. Our study includes case reports, case series, and literature review-type papers. Based on 63 publications found in the literature, we compiled a concised report, illustrated with images from individual patients. A parental written informed consent before the publication of de-identified patient photographs was obtained.

2. Epidemiology

Psoriasis is the second most frequent disorder after atopic dermatitis in childhood and affects approximately 1% of children (4,5). The incidence of childhood psoriasis has increased dramatically over time from 29.6 per 100,000 individuals in 1970-1974 to 62.7 per 100,000 in 1995-1999 (6). The disease can appear at

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any age, more commonly at 9-10 years, and has a durable course with exacerbation periods that can last between a few weeks and 1.5 years (7). The incidence of pediatric psoriasis increases with age. In the UK, the prevalence was found to increase from 0.55% in children between 0-9 years of age to 1.37% in children between 10-19 years (8,9). In Italy, the prevalence of psoriasis in children is estimated at 2.1% (10). The exacerbations are more likely to appear in the autumn and winter seasons (7). Psoriasis appears earlier and more frequently in girls. Earlier onset is also associated with severe forms of psoriasis (11,12).

3. Pathogenesis

Psoriasis is the result of polygenic predisposition and environmental triggers. Genetic predisposition is easier to detect in children than in adults. Family history is present in 35 to 90% of patients with psoriasis, of which 30% are first-degree relatives and the pathology is more common in monozygotic twins compared to dizygotic twins (3,13). Family history has been associated with earlier onset of psoriasis and the presence of enthesitis (14). There are over 1,300 susceptibility genes identified in psoriatic skin which are differently expressed compared to normal skin (15). The most important psoriasis-susceptibility gene (*PSORS1*) is human leukocyte antigen HLA Cw6 (16). The presence of this gene is associated with a relative risk of developing psoriasis of 13% for Caucasians and 25% for the Japanese population. Based on this, some clinicians consider that there are two types of psoriasis, type I with early-onset, positive family history, and the presence of HLA Cw6 and type II with late-onset, without family history and no expression of HLA Cw6 (3). The corneodesmosin (*CDSN*) gene has been associated with psoriasis in the Caucasian population. Other genes involved are the MHC class I polypeptide-related sequence A (*MICA*) gene, according to a study of psoriasis in the Chinese population, and the angiotensin I converting enzyme (*ACE*) gene in some patients (1). Promoter region polymorphisms in the tumor necrosis factor (*TNF*) α gene are associated with psoriasis in the Polish population and interleukin 12B (*IL12B*) gene polymorphisms are found in different patients (1). In addition, protein tyrosine phosphatase, non-receptor type 22 (*PTPN22*) region polymorphisms are related to early-onset psoriasis (1).

The pathogenesis of psoriasis is based on chronic inflammation, increased keratinocyte proliferation, and dysfunctional differentiation. Although the main changes in psoriasis are found in the most superficial layer of the skin, formed by keratinocytes, the psoriatic plaque is not limited to inflammation of the epidermis. It is characterized by the interaction between keratinocytes and many different cells, extending to the dermal layer of the skin (17-19). The factors that have a key role in the pathogenesis of psoriasis are T cells, keratinocytes, Langerhans' cells, macrophages, and some types of cytokines. Self-antigens activate dendritic cells and release cytokines including TNF, γ -interferon, interleukin (IL)-12, and IL-23 that recruit T cells, Th-1, Th-17 and Th-22 (2). T cells release cytokines and maintain the abnormal differentiation of keratinocytes and cell cycle turnover (16,20). Keratinocytes from psoriatic plaque express signal transducer and activator of transcription 3 (STAT3), a transcription factor that was found to produce psoriasis-like injuries in mice. The fact that STAT3 is activated by cytokines (IL-6, IL-20, IL-22)

could explain the connection between keratinocyte proliferation and the immune system in the pathogenesis of psoriasis (3). There are several vascular changes such as angiogenesis [stimulated by IL-8 and transforming growth factor (TGF)- α], dilated sinuous vessels in the papillary dermis, and the formation of high endothelial venules. Therefore, the size of the microcirculation expands and facilitates the passage of T lymphocytes (T helper 1 subclass), maintaining psoriatic plaque. Severe psoriasis is accompanied by microvascular hyperpermeability mediated by vascular endothelial growth factor (VEGF) (1).

The pathogenesis of psoriasis can be structured in an initiation phase possibly caused by trauma, infections, or drugs, and a chronic phase with long-term clinical progression. The main trigger factors in children include stress and infections, especially streptococcal infections (3,5,21). Some possible causes of psoriasis morbidity in children are social and home problems, emotional issues, pollution, and a decrease in immune reactivity (5). In addition, overweight and obesity have been recently discovered as risk factors for psoriasis in children (2). Paradoxically, TNF inhibitors such as infliximab and adalimumab may induce psoriasis (4).

4. Clinical features

The history and symptoms of psoriasis can be different according to the age of children and the type of psoriasis. Most common psoriasis lesions are found in the extremities (60%) and the scalp (47%) (6). The most common clinical manifestation is pruritus (22). In many cases, infants have persistent diaper rash that remains despite many treatments. Older children may have an asymptomatic scaly rash or severe dandruff (2). Adolescents have the same clinical features as adults. Some children may present the Koebner phenomenon that consists in the appearance of new skin lesions on previously unaffected skin secondary to trauma, lesions that are pronounced and long-lasting (2,5).

Psoriasis is characterized by erythematous papules that merge to create well-demarcated plaques with irregular borders, covered by a silvery-white scale. If the scale is removed, pinpoint bleeding will result, known as the Auspitz sign. Children with psoriasis have more facial and flexural lesions and the plaques are smaller and thinner compared to adults (2,23) (Figs. 1 and 2). The differential diagnosis is often difficult to make with seborrheic dermatitis (2,16).

There are several types of psoriasis: vulgaris: chronic plaque (Fig. 3), guttate (Fig. 4), and inverse psoriasis (Fig. 5), pustular and erythrodermic.

The most common type of psoriasis in children is chronic plaque psoriasis (75% of children with psoriasis) followed by guttate psoriasis (15-30% of children with psoriasis) (2,24). In addition, diaper psoriasis is a common variant exclusively seen in infants (Figs. 6-8). Chronic plaque psoriasis is most common on the extensor extremities, trunk, flexures, and face. Guttate psoriasis is characterized by the sudden onset of droplet papules with symmetrical disposal over the trunk, limbs, and face (Fig. 9). These lesions may be preceded by streptococcal infection and resorb within 3 to 4 weeks or they can persist and transform into severe psoriasis (2). The development of lesions in flexural areas and the face is more common in children and is known as inverse psoriasis. The psoriasis of the scalp



Figure 1. Facial lesions in napkin psoriasis.

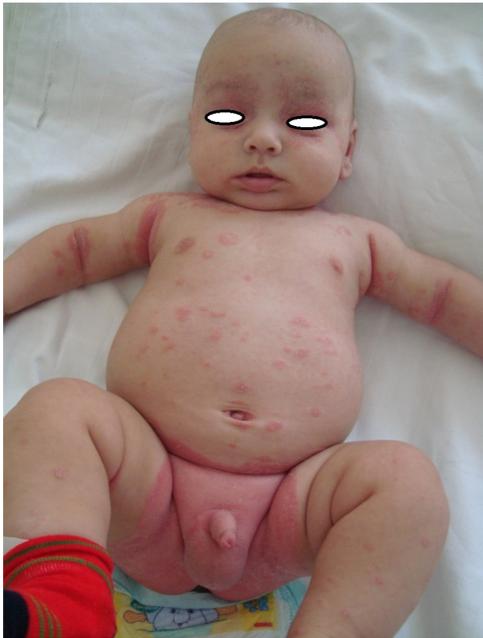


Figure 2. Facial and flexural lesions in napkin psoriasis.



Figure 3. Chronic plaque psoriasis.



Figure 4. Guttate psoriasis.

has well-defined, scaly, erythematous, and pruritic lesions. In children with alopecia, the hair grows back when the disease is under control (2). Nail psoriasis is less frequent in children compared to adults but can be observed in approximately 40% of the children. The most common changes are pitting, leukonychia, and longitudinal ridges that are very difficult to treat (2,25,26) (Fig. 10). Pustular psoriasis is rare and consists of sterile superficial pustules with annular disposition (Fig. 11). If pustules are generalized, children may develop a fever and they may be often mistaken for an infection. Another variant of this disease is erythrodermic psoriasis (Fig. 12) that affects more than 90% of the body surface and is extremely rare (2,16).

The severity of skin disease is classified based on the affected body surface area (BSA) According to this, the

disease is mild if lesions cover less than 5% of BSA, moderate if it affects between 5 and 10% of BSA and severe if the BSA involved is greater than 10% (16). Fortunately, most children with psoriasis have mild disease (2,22).

5. Comorbidities

Some recent studies have discovered that children with psoriasis are twice as likely to have comorbidities as those without psoriasis (2). Psoriasis has been associated with type 1 diabetes, rheumatoid arthritis, Crohn's disease, systemic lupus erythematosus, vitiligo (Fig. 13), alopecia areata, eczema, and



Figure 5. Inverse psoriasis.



Figure 7. Napkin psoriasis.



Figure 6. Napkin psoriasis.



Figure 8. Napkin psoriasis.

lichen planus (2,27,28). Psoriasis can be mistaken with seborrheic dermatitis and avitaminosis, but they can also coexist. Just like in adults, the association with atopic dermatitis is frequently seen in children. In terms of association with systemic diseases, children with psoriasis have a higher rate of obesity, especially boys. Patients with this comorbidity are more likely to have a severe form of psoriasis compared to normal-weight psoriatic children (29). The major comorbidity is psoriatic arthritis. Prevalence in the children population is still unknown. Psoriatic arthritis can occur at any age, but the onset is more common between 2 and 3 years and 9 to 12 years of age. This condition causes joint pain and mostly affects finger and toe joints (30,31). Younger children with psoriasis, especially girls, present an onset with an oligoarticular disease

or dactylitis while older children, especially boys, present an onset with enthesitis and axial joint involvement.

Pediatric patients with concomitant arthritis can develop uveitis (4). Children and adolescents with this condition are reported to have an increased risk of hypertension, hyperlipidemia, and diabetes, probably due to the high rate of metabolic syndrome. Low levels of HDL cholesterol and high concentrations of fasting glucose appear in the early stages of metabolic syndrome in psoriatic children (32).

The presence of skin lesions harms the children. Many patients are stigmatized by other children and recreational activity is highly affected. This stigmatization can induce changes in behavior, depression, and anxiety. More than that, the association between psoriasis and obesity increases the risk of social isolation, withdrawal, depression, and anxiety (4,33). Psoriasis affects the quality of life of children and their parents and they should receive psychosocial support (34).

As in most systemic, inflammatory, chronic diseases, ocular manifestations can occur (35). The incidence of ocular involvement in psoriasis largely varies in the literature



Figure 9. Guttate psoriasis.



Figure 11. Pustular psoriasis.



Figure 10. Nail psoriasis.



Figure 12. Erythrodermic psoriasis. Iatrogenic Cushing syndrome.

between 12 and 58% (36,37) and even up to 81.4% in more recent studies (38). The eyelid manifestations include blepharitis, which is the most frequent one, together with erythema, psoriatic plaques, and edema leading to eyelid abnormalities such as ectropion, trichiasis, and madarosis. In moderate and severe forms of the disease, chronic conjunctivitis can lead to limbal lesions and keratoconjunctivitis sicca further responsible for corneal lesions such as punctate keratitis, recurrent erosions, opacities, and vascularization (39). The anterior uveitis associated with childhood psoriatic arthritis and onset before the age of 6 years has been described as bilateral, long-lasting, and severe requiring biologic therapy (40).

6. Treatment

Psoriasis therapy varies according to patient age, type of psoriasis, affected sites, and extension of the disease (16). This condition requires the involvement of several specialists such as dermatologists, pediatricians, and rheumatologist. There are 4 types of treatment as described.

Topical agents. Topical agents such as emollients, vitamin D analogs, and corticosteroids should be the first choice of treatment for children with mild to moderate psoriasis (41).

Vitamin D analogs, calcipotriene, and calcitriol inhibit the proliferation of keratinocytes and are safe to use.

Corticosteroids reduce inflammation and proliferation of keratinocytes, scaling, and erythema. Side effects of topical steroids are divided into local and systemic. Local side effects occur with prolonged treatment and are related to the corticosteroid potency and site of application (42). The most frequent side effects are atrophy, striae (Figs. 14 and 15) acne, rosacea, perioral dermatitis, and purpura. Patients can also experience less common side effects such as hypertrichosis, delayed wound healing, pigment alteration, and aggravation of skin infections (42). Systemic side effects are more common in long-term topical treatment with highly potent corticosteroids on large areas, thin skin, or inflamed surfaces. Children have a large body surface area as related to the body volume so they have



Figure 13. Psoriasis guttate and vitiligo.



Figure 15. Post-dermocorticoid striae in psoriasis.



Figure 14. Post-dermocorticoid striae in psoriasis.

a higher risk of developing hypothalamic-pituitary-adrenal axis suppression due to systemic absorption. Some systemic adverse effects are iatrogenic Cushing syndrome (moon face, centripetal obesity, striae) (Fig. 12), corticosteroid-related Addison crises, growth retardation (reduced bone mineral density, osteopathy), hyperglycemia and diabetes mellitus, edema, hypocalcemia, hypertension. During continued treatment, psoriatic patients may develop tachyphylaxis. Rebound phenomena may occur upon withdrawal of topic steroids applied on large areas of psoriasis for a long time. They are characterized by relapse or a papulopustular flare and may precipitate severe generalized pustular psoriasis (42).

Second-line topical treatments include retinoids, tars, anthralin, and keratolytics. Tazarotene decreases inflammation and helps to restore normal epidermal proliferation and differentiation (43). It is effective in the treatment of nail psoriasis. Tars have antipruritic and antiproliferative effect. Anthralin is especially used on thick plaques or large involved areas. Phenol and saline solution can be used for scalp lesions (2,16).

Phototherapy. Phototherapy [narrow-band ultraviolet B (NB-UVB); psoralen plus ultraviolet A (PUVA)] is an alternative therapy for children with chronic plaque or guttate psoriasis that have an unsatisfactory result to topical treatment. Side effects of phototherapy in children include erythema, burning, hyperpigmentation, viral reactivation, and risk of cutaneous

carcinogenesis in long-term treatment with PUVA. Psoralen is avoided in children under 12 years of age. Phototherapy is contraindicated in children with cutaneous cancer syndromes or generalized erythroderma (4,16).

Systemic therapy. Systemic therapy is required in moderate to severe disease. Methotrexate is the most common systemic medication used for psoriasis in children and it requires folic acid supplementation. The most serious side effects of methotrexate are bone marrow suppression, hepatic and pulmonary toxicity. Other options may include cyclosporine and systemic retinoids. Cyclosporin is well tolerated in pediatric patients and has a quick effect on severe, pustular, and erythrodermic psoriasis (4,16,44-46).

Biologic therapy. Biologic therapy is becoming much more commonly used in pediatric patients. FDA has approved etanercept (TNF inhibitor) for patients 4 years and older, ustekinumab (IL-12 and IL-23 antagonist) for patients 12 years and older, and adalimumab (TNF inhibitor) was approved in Europe for patients 4 years and older (4). Etanercept is the favorite biologic therapy for pediatric patients and it was proved to be effective for moderate to severe psoriasis (15). It is a TNF inhibitor, which prevents activation of the inflammatory cascade. Studies have revealed that etanercept is more efficient and safe in long-term usage compared to other systemic treatments such as methotrexate, cyclosporine, and PUVA. Side effects include mild injection site reaction, increased risk of infections and cold-like illnesses, hepatitis B virus reactivation, and the possibility of weight gain (47,48). Studies have shown that adalimumab is more efficient than methotrexate and has a similar safety profile (49). The advantage of adalimumab over other biologics consists in the efficacy in the treatment of psoriatic arthritis. Just like other TNF- α inhibitors, adalimumab has absolute contraindications to treatments such as tuberculosis and other severe infections (50). The precautions for the use of TNF- α inhibitors are hepatitis B infection, allergy, history of malignancy, and demyelinating conditions (51). Ustekinumab

targets the IL-12 and IL-23 axis and it is efficient for psoriasis and psoriatic arthritis. A statistically significant increased response to ustekinumab in HLA-Cw6-positive patients has been noted. The different action mechanism of this drug provides an alternative treatment to TNF inhibitor failure, but there can be a certain problem for some patients regarding the slow onset of action (52). Some biological therapies are off-label (53). Infliximab has been approved for children with Crohn's disease, and several cases of induced psoriasis have been reported after a few weeks of therapy (54). Infliximab is used in limited cases such as for children with severe pustular psoriasis (55,56). Certolizumab pegol is approved for psoriasis only in adults and it is currently being investigated in childhood arthritis and Crohn's disease (57,58). Secukinumab is not FDA-approved for any medical condition in children, but clinical trials are ongoing to evaluate the efficacy of this therapy in pediatric psoriasis (59,60). Other biologics such as ixekizumab, guselkumab, and brodalumab, currently approved for adults with psoriasis, have been included in clinical trials for children with psoriasis (61-63).

7. Conclusions

Pediatric psoriasis is an increasing chronic skin disease, with exacerbations and remissions. The complexity of the pathology requires the involvement of a multidisciplinary team. Psychosocial support is an important part of psoriasis treatment due to the significant impact of the disease on the quality of life of the patients. Unfortunately, the lack of standardized treatment guidelines and the limited number of randomized clinical trials concerning biologic therapy make systemic treatment challenging in children with severe psoriasis.

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Availability of data and materials

All information provided in this review is documented by relevant references.

Authors' contributions

DEB and DCB contributed to the study design, participated in the entire review process, and prepared the manuscript. SG, DB, ACN and CIB contributed to collecting the relevant literature, data analysis, and critical interpretation. RB, MAM, MG, ACP, AD and ILS conceived the concept of the review and modified the manuscript. All authors read and approved the final version of the manuscript for publication.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

A parental written informed consent before the publication of de-identified patient photographs was obtained.

Competing interests

All the authors declare that they have no competing interests.

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