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Review Article

Pediatric Psoriasis: A Review

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Abstract

Psoriasis is a chronic inflammatory immune-mediated systemic skin disease with a significant genetic predisposition and associated with an important physical and psychological burden as well as multiple co-morbidities. While the majority of psoriasis patients are adults, it is not uncommon in children. Diagnosis is often made on clinical features alone with the distribution, morphology, and clinical presentation of psoriasis varying according to age group, encompassing a wide-ranged differential. As such, childhood psoriasis presents a special situation that is challenging for the treating dermatologist. Like many chronic skin conditions, psoriasis has profound physical and psychosocial effects on patients; therefore, it is essential for all dermatologists to recognize and appropriately manage psoriasis, both short-term and long-term, in the pediatric population. This review aims to outline the various clinical presentations of pediatric psoriasis, as well as to summarize updated information about the epidemiology, comorbidities, and management of psoriasis in children.

INTRODUCTION

Psoriasis is a chronic inflammatory immune-mediated systemic skin disease with a recognized genetic predisposition and associated with an important physical and psychological burden. Childhood psoriasis presents a special situation that is challenging for the treating dermatologist. As chronic skin conditions, such as psoriasis, are likely to have profound physical and psychosocial effects on patients, it is essential for all dermatologists to recognize and appropriately manage psoriasis in the pediatric population.

EPIDEMIOLOGY

The overall prevalence of psoriasis is roughly 2.20-3.15% worldwide [1]. However, psoriasis is far more prevalent in adults than in children [2]. Among pediatric patients, the prevalence of psoriasis is 0.5-1.2% [3,4]. As opposed to having a particular peak range, prevalence in children increases linearly with age, from 0.2% at 2 years to 1.2% at 18 years [4-7]. Additionally, approximately one-third of adults with psoriasis report an onset that began in childhood [8,9], and a fraction of patients with mild disease may not seek care or may be misdiagnosed; thus, prevalence rates may be underestimated [10]. Cradle cap and diaper dermatitis in new born children may be a fore-runner later psoriasis. Disease prevalence also varies geographically, ranging from 1.20% in the United States to 2.15% in Italy to 0.00% in Taiwan [2,3]. Variations in prevalence between these countries suggests the roles of genetics and environmental trigger factors [11].

In the United States, the incidence of psoriasis in children is estimated at 40.8 per 100,000 children per year [3]. Girls have a higher incidence than boys at 43.9 vs. 37.9 per 100,000 per year [3]. Interestingly, the reported incidence of psoriasis in children has doubled between 1970-1974 and 1995-1999 [3,12], It remains uncertain whether this increasing trend in incidence is due to a true rise in incidence or other factors such as improved diagnostic rates and awareness of disease or an increase in trigger factors.

Data is conflicting in regards to whether prevalence of psoriasis truly differs between genders [2]. Among pediatric patients with psoriasis, females appear to predominate, which is in contrast to the trend observed in adults [3,8,13]. However, studies data suggests that psoriasis tends to appear earlier in females compared to males [14].

A dual peak in the incidence of psoriasis has been described, with the first peak occurring in childhood or adolescence and the second peak occurring in adulthood [15,16]. Pediatric psoriasis may arise at any age, including infancy; however, the median age of onset during childhood is between 7 and 10 years [8,10,17]. Approximately 35% of psoriasis patients experience disease onset before the age of 20 years [8,9,15]. These patients are more likely to have a first-degree relative affected and to be positive for the HLA-Cw6 allele. HLA-Cw6 is the strongest HLA risk factor for early-onset disease. In contrast, late onset psoriasis is more likely to be sporadic with a less definitive genetic background [18-21].

Family history of psoriasis is positive in a first-degree relative in roughly 30-50% of pediatric psoriasis cases [3,11], which can predict early disease onset in these children [22]. If one or two parents have psoriasis, the lifetime risk of developing psoriasis is 28% and 65%, respectively, compared to 4% if no parent is affected [23]. In addition, monozygotic twins exhibit a two- to three-fold increase in risk compared to dizygotic twins [7].

Environmental risk factors for the development of psoriasis also exist. These include exposure to tobacco smoke, stressful life events, and being overweight or obese, as measured by body-mass-index (BMI) at or above 85th percentile or 95th percentile, respectively [24-26]. In addition, infection, such as streptococcal infections, and trauma (the Koebner phenomenon) can precede onset of psoriasis. Flares of psoriasis have also been associated with varicella zoster [27], Kawasaki disease [28], and staphylococcal infection [29] Certain medications, have also been associated with psoriasis flares, although this is less common in children. Dissecting out the influence of multiple genetic and environmental influences on the pathogenesis of psoriasis remains a challenge.

CLINICAL DISEASE

Diagnosis is often made on clinical features alone, which can pose a diagnostic challenge in the pediatric population. Although subtypes of psoriasis may be similar, the distribution, morphology, and clinical presentation may vary according to age group [30]. The differential diagnosis for pediatric psoriasis by sub-type and location is outlined in (Table 1) and (Table 2), respectively. Approximately 5% of children with psoriasis exhibit an overlap between psoriasis and atopic dermatitis, as lesions may be intermediate or characteristic of both entities [13]. Additionally, skin biopsy is not frequently performed in younger patients, thus making the diagnosis more difficult.

Erythematous plaques with overlying white scale are often thinner and smaller in young children compared to adults. They also tend to develop more often on the scalp, face, and flexural areas, as opposed to extensor surfaces; however, psoriatic papules and plaques can develop on any skin area despite predilection and are often symmetrically distributed. The scalp is most frequent and often the first site of involvement in young children [31-33]. Scalp involvement occurs in 40%-79% of pediatric cases [34], particularly in females [30].

Table 1: Differential diagnosis for pediatric psoriasis sub-types.

Type of Psoriasis	Differential Diagnosis
Plaque psoriasis	Seborrheic dermatitis Atopic or nummular dermatitis Pityriasisrubra pilaris Lichen simplex Tinea corporis
Guttate psoriasis	Tinea corporis Pityriasisrubra pilaris Pityriasisrosea Pityriasis lichenoides chronica Lichen planus Secondary syphilis
Inverse psoriasis	Intertrigo Candidiasis Erythrismal Contact dermatitis
Pustular psoriasis	Folliculitis Contact dermatitis Dyshidrotic eczema Acute febrile neutrophilic dermatosis (Sweet Syndrome) Acute generalized exanthematouspustulosis Dermatitis with secondary infection
Erythrodermic psoriasis	Staphylococcal scalded skin syndrome Atopic dermatitis Pityriasisrubra pilaris Langerhans cell histiocytosis Adverse drug reaction

Table 2: Differential diagnosis for pediatric psoriasis based on location.

Location	Differential Diagnosis
Scalp	Seborrheic dermatitis Tinea capitis Atopic dermatitis
Face	Seborrheic dermatitis Contact dermatitis
Palmoplantar	Contact dermatitis Tinea manuum/pedis Palmoplantar pustulosis
Genitals	Contact dermatitis Cadidiasis Tinea cruris Lichen planus Lichen simplex
Nails	Onychomycosis Alopecia areata Lichen planus

Psoriatic plaques on the face are more common in children than adults, occurring in 38-46% of children [13,35], and tend to be per orbital, less pruritic, and more clearly delineated than atopic dermatitis. Psoriasis may appear in school-aged children as erythema and fine white scale in the ear canals, often misdiagnosed as otitis externa, or the medial upper eyelids, often mistaken for contact dermatitis [30,36]. Nail disease is also common in this age group [30].

Psoriatic diaper rash is often the presenting manifestation in infants and is characterized by sharply demarcated, minimally elevated erythematous plaques involving the inguinal folds. Rash in this region must be differentiated from irritant or candidal diaper dermatitis and seborrheic dermatitis. Psoriatic lesions in the diaper region are often macerated, not scaly and unassociated with satellite pustules, differentiating them from candidiasis [13]. Psoriatic diaper rash often clears with toilet training; however genital psoriasis comprises 17% of genital complains in prepubescent females [37]. Diaper area involvement may also be accompanied by scalp involvement. Extension of patches with a greasy scale beyond the hairline and failure to respond to anti-seborrheic shampoos can distinguish psoriasis or sebopsoriasis from seborrheic dermatitis in infants and young children.

MORPHOLOGY

The most common subtype of psoriasis in the pediatric population is plaque psoriasis (73.7%). This is followed by guttate psoriasis (13.7%), scalp psoriasis (7.6%), and pustular psoriasis (1.1%) [3].

Plaque Psoriasis

The most common type of psoriasis is plaque psoriasis [5,7]. Approximately 75% of older children and adolescents

have chronic plaque psoriasis [31], with sharply defined symmetrically distributed erythematous plaques of various shapes and sizes with prominent adherent white-to-silvery scale (Figure 1). Psoriasis plaques can appear at any part of the body but are generally bilateral, with the most common sites of involvement being the elbows, knees, and scalp [33]. New lesions may appear following direct cutaneous trauma, which is known as the Koebner phenomenon and is described in 50% of pediatric patients, compared with 39% of adult patients [8]. Scratching the scalp is frequent and leads to asymmetrical plaque psoriasis on the scalp.

Guttate Psoriasis

The second most common type of psoriasis in children is Guttate psoriasis, which affects 14%-30% of patients [30,31], and is often the first clinical presentation of psoriasis [7]. Multiple small and circumscribed erythematous papules with silvery scale resembling "drops" (Figure 2) are symmetrically distributed and favor the trunk and proximal extremities. Guttate psoriasis is often self-limiting and resolves within 4 months of onset. However, up to 40% of patients with Guttate psoriasis progress to plaque-type psoriasis [38,39]. In fact, the risk of developing severe plaque psoriasis is much higher if Guttate psoriasis persisted [30,31]. Guttate psoriasis may be precipitated by Oropharyngeal or perianal streptococcal infection [17,40] or upper respiratory infection [9]. In such cases, treatment of infection may hasten resolution of psoriasis. When recalcitrant Guttate psoriasis is associated with multiple episodes of proven streptococcal tonsillitis, tonsillectomy is a potential option for patients [41].

Inverse Psoriasis

Intertriginous or inverse psoriasis is a relatively rare form of psoriasis affecting body folds, the genitals, and the per umbilical region. Although rare, inverse psoriasis is more common in children than adults [14]. It presents as shiny pink-red well-defined thin plaques (Figure 3), frequently associated with fissures and can be mistaken for intertrigo, candidiasis, erythrasma, or contact dermatitis.

Pustular Psoriasis

Pustular psoriasis is seen in only 1.0%-5.4% of pediatric psoriasis cases and is characterized by localized or diffuse superficial sterile pustules (Figure 4). Although pustular psoriasis is more common in adults, von Zumbusch pustular psoriasis and annular pustular psoriasis occur more frequently in childhood. Systemic symptoms such as fever, malaise, and arthralgia may also be present in the von Zumbusch type [31,33] . Additionally, early onset disease has been reported for pustular psoriasis, suggesting an association between age of onset and disease subtype [10,42].

Erythrodermic Psoriasis

Erythrodermic psoriasis is extremely rare in children and is characterized by diffuse erythema affecting over 90% of the total body surface area. It is most commonly triggered by poor management, such as abrupt withdrawal of systemic steroids. Erythrodermic psoriasis can lead to life-threatening hypothermia, hypoalbuminemia, and cardiac failure [33].

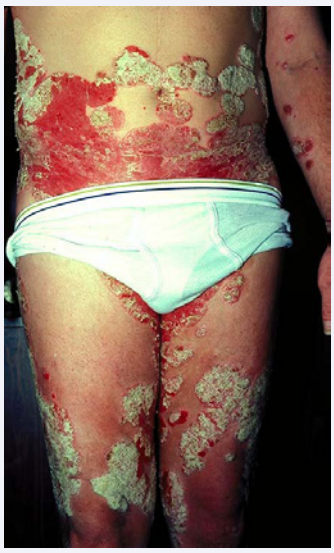

Figure 1 Thick erythematous plaques with prominent adherent white-to-silvery scale, often symmetrically distributed.

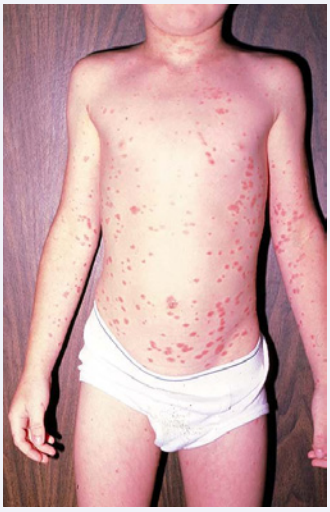

Figure 2 Numerous small, circumscribed erythematous or salmon-pink "drop-like" papules with scaling.

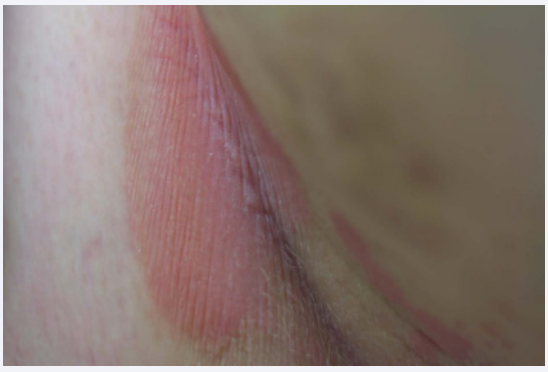

Figure 3 Smooth thin pink plaque without scaling in the axillary fold of a child.

NAILS

Nail manifestations of psoriasis occur in up to 40% of pediatric patients, are more common in boys, and may precede, coincide with, or develop after skin psoriasis [30,35,43]. Psoriatic nail changes (Figure 5) include pitting on the nail plate, onycholysis, subungual hyperkeratosis, onychodystrophy, oil spots, and splinter hemorrhages [31,33]. When skin manifestations are equivocal, nail pitting is a useful sign to aid in the diagnosis of psoriasis.

JUVENILE PSORIATIC ARTHRITIS

A common comorbidity of psoriasis in children is juvenile psoriatic arthritis. Due to difficulties in diagnosis and classification of psoriatic arthritis in children, prevalence data ranges from 1% to 10% of pediatric psoriasis patients [30]. The peak of onset of juvenile psoriatic arthritis in childhood is between 9 and 12 years of age. Diagnosis of psoriatic arthritis in children with the combination of psoriasis or arthritis, or when arthritis exists with either nail pitting or onycholysis, dactylitis, or a positive family history of psoriasis in a first-degree relative [44,45]. Presentation of joint disease varies with age, as dactylitis is more common in younger children while enthesitis is more common in older children [46] Approximately 30% of pediatric patients develop polyarthropathy, which can lead to severe bone destruction [44].

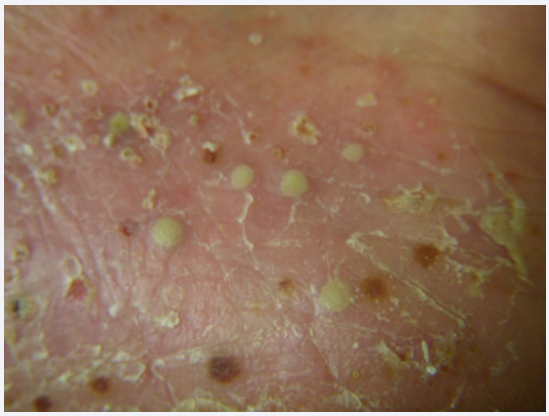

Figure 4 Superficial sterile pustules with surrounding erythema on the palm.

Figure 5 Onycholysis with erythema of the nail bed and splinter hemorrhages.

Frequently, skin manifestations of psoriasis precede psoriatic arthritis. As in adults, a relationship between nail involvement and psoriatic arthritis has also been suggested in children [45].

OBESITY AND METABOLIC SYNDROME

The most common co morbidity in pediatric patients with psoriasis is obesity, with over 90% of children exhibiting excess adiposity for at least two years prior to the onset of psoriasis [26,47,48]. Obesity, increased waist circumference percentile, and waist-to-height ratio are correlated with greater severity of disease. Weight and psoriasis reflect a dose-response effect, as mild-moderate psoriasis is associated with being overweight, and moderate-severe psoriasis is associated with central obesity [10]. It is suggested that the increase in severity and incidence of psoriasis beginning after 7 to 8 years of age could be related to the development of obesity [10]. It is also likely that the association between obesity and psoriasis is bidirectional; although it is unclear whether weight loss reduces psoriasis severity [49].

Additionally, approximately 30% of children with psoriasis meet the criteria for metabolic syndrome, compared with 7.4% of age-matched controls [50]. It is suggested that the relationship between psoriasis and metabolic comorbidities is linked to the underlying chronic nature of systemic inflammation in psoriasis [10].

Additional Comorbidities

Comorbidities in pediatric patients with psoriasis occur at a rate that is double that of peers without psoriasis, 14.4% vs 7.2% [51]. In addition to joint disease and obesity, children with psoriasis have an increased risk of developing inflammatory bowel disease such as Crohn's disease, type 2 diabetes, hyperlipidemia, and hypertension [4]. A higher prevalence of rheumatoid arthritis [4], uveitis [52,53], anxiety, and/or depression are also seen in pediatric patients with psoriasis [54,55].

PSYCHOLOGICAL BURDEN

Chronic dermatoses can profoundly affect quality of life, and children are uniquely sensitive to physical and psychosocial impact of chronic skin conditions. Psychological distress is known to be both a consequence and an aggravating factor for psoriasis onset and course [56,57]. Studies suggest that the prevalence of depression and anxiety among psoriasis patients may reach as high as 62% and 42%, respectively [58,59], Stress levels in children with psoriasis were found to be as high as in children with atopic dermatitis, asthma, arthritis, or diabetes [60]. The detrimental psychological effects of psoriasis are not just limited to the affected children. In fact, emotional well-being was found to be significantly affected in parents of children with psoriasis, as well, with nearly half of parents feeling sadness or frustration and 20% feeling depressed or anxious [61]. Dermatologists should be cognizant of the damaging effects of psoriasis on the quality of life of affected children and their parents, and support for families should be an important consideration of the treatment plan [61].

MANAGEMENT

Treatment of psoriasis in pediatric patients can often be a challenge due to the lack of clinical trials in the pediatric population. New guidelines for pediatric psoriasis will be

published by the American Academy of Dermatology early in 2019. It is crucial to have a positive and thorough approach in the treatment of this disease, and treatment success largely depends on the level of parental involvement and understanding. While the patient's age should be considered, psoriasis treatment depends largely on disease severity and should be tailored to the individual patient. Often times, combination and rotational therapy are helpful in both maximizing efficacy and reducing toxicity. Children with moderate to severe psoriasis are undertreated in the United States [62]; however, the landscape appears to be shifting with the advent of important safety data for biologic therapies.

Topical Therapy

Mild disease is being managed with topical therapies alone with immune modulators or a combination of corticosteroids and vitamin D analogues. Topical calcineurin inhibitors, tacrolimus and pimecrolimus, are effective in the treatment of mild facial and genital psoriasis [63], while mild to moderate psoriasis of the limbs and torso is intermittently treated with topical corticosteroids and vitamin D analogues such as calcipotriene. Low potency corticosteroids are recommended for the face, axillary areas, and groin, whereas moderate or high potency corticosteroids are recommended for thicker plaques on the trunk and limbs [64]. Although side effects from the sparing and intermittent use of topical steroids are not common, the risk of hypothalamic-pituitary-adrenal axis suppression is higher in children compared to adults due to the increased surface area to body mass ratio; thus, mandatory supervision during treatment is encouraged [65]. Tazarotene is a topical vitamin A derivative that can be used on palms, soles, and nails, as well as on thick plaques on the trunk and extremities. Its main side effect is skin irritation [10].

Phototherapy

In pediatric patients with moderate to severe psoriatic disease, phototherapy may be considered as a treatment option. The most frequently used form of phototherapy is narrow band UVB (311 nm), which is effective in the treatment of plaque or Guttate psoriasis. Long-term side effects, including increased risk of skin cancer and accelerated photo aging, depend on the cumulative dose of UV therapy [66]. Broadband UVB and psoralen plus UVA (PUVA) are also viable phototherapy options but are out of favor given the safety profile of narrow band UVB [10]. Phototherapy is often not the treatment of choice for pediatric patients as it is time consuming and interferes with attendance in school.

Systemic Agents

The use of systemic therapy in pediatric patients is often used for moderate to severe disease that is unresponsive to other treatment. Oral medications used for psoriasis treatment include retinoids, methotrexate, and cyclosporine.

Retinoids, such as a citretin, are effective in the treatment of pustular and erythrodermic forms of psoriasis. However, because retinoids bear a high teratogenic risk, they should be avoided in females of childbearing potential. If used, concomitant oral contraception during treatment and for a minimum of two years following treatment is recommended. Side effects of oral retinoids may include cheilitis, pruritus, conjunctivitis, epistaxis, or hair loss, and long-term use carries a low risk of growth retardation due to premature epiphyseal plate closure [67,68].

Methotrexate is safe and effective in approximately 40% of patients in the treatment of moderate to severe psoriasis as well as psoriatic arthritis in children. Regular screening of full blood count, liver function tests, and renal function are conducted throughout the duration of therapy, and folate supplements are recommended to reduce potential side effects such as headache, nausea, and gastrointestinal discomfort [69,70]. Cyclosporine, an oral calcineurin inhibitor and immunosuppressant, is highly effective in pediatric patients with severe plaque psoriasis. Because cyclosporine is fast-acting, it can also be used as a short-term therapy for psoriasis flares [71].The use of cyclosporine is limited, however, due to the potential side effects including nephrotoxicity, Immunosuppression, hypertension, hypertrichosis, and gingival hyperplasia [72].

Biologic Agents

Development of biologics is based on the understanding of the complex immuno pathogenesis of psoriasis, as biologic agents target specific parts of the immune system, inhibit T cell activation and migration, and block the inflammatory cytokines responsible for the development of psoriatic lesions. They represent newer therapeutic options for treating moderate-to-severe plaque psoriasis unresponsive to systemic therapy.

Tumor necrosis factor alpha inhibitors that have been used in the treatment of pediatric psoriasis include infliximab, etanercept, and adalimumab. Infliximab is a chimeric monoclonal antibody against TNF-alpha that has been FDA-approved for the treatment of pediatric patients ages 6 and older with Crohn's disease since 2006. Due to its rapid onset of action and its high efficacy, infliximab can also be used for generalized pustular or erythrodermic psoriasis [73,74]. Etanercept is a TNF-receptor fusion protein and was long considered the drug of choice for the treatment of juvenile psoriasis due to its efficacy, tolerability, and safety profile [75]. Etanercept is currently approved for the treatment of chronic severe plaque psoriasis in pediatric patients ages 4 and older who are poorly controlled by or are intolerant to other systemic therapies or phototherapy [76]. Adalimumab is a recombinant human monoclonal antibody specific to TNF-alpha and is approved in Europe for the treatment of chronic severe plaque psoriasis in children 4 years of age and older and adolescents with inadequate treatment response to other local therapies or phototherapy [77]. The most common side effect seen with anti-TNF agents are injection-site reactions; although, long- term use of anti-TNF agents may possibly increase the risk of malignancy, such as lymphoma [78]. TNF inhibitors are also associated with an overall increased risk of infection, including tuberculosis and invasive fungal or opportunistic infections [79]. Patients receiving TNF-alpha inhibitor treatment should be monitored for infections and be educated on early recognition of infection to avoid fatal complications.

Ustekinumab is a human monoclonal antibody targeting the p40 subunit of IL-12 and IL-23 and is approved for adolescents with psoriasis who have had an inadequate response to or are

inappropriate candidates for topical therapy or photo therapies [80]. The uses of the new IL-17 and IL-23 biologic agents currently approved in adults are currently in clinical trials for the pediatric psoriasis patient.

CONCLUSION

Psoriasis is a chronic immune-mediated inflammatory skin disease affecting the skin, nails, and joints and is not uncommon in children. Familial trends highlight the role of genetics and predisposition to psoriasis, and various environmental triggers are recognized in the development of psoriasis among the pediatric population. The distribution, morphology, and clinical presentation of psoriasis may vary according to age group. Specific guidelines for the diagnosis, management, and treatment of psoriasis are of extreme importance; with these guidelines for pediatric patients pending in 2019. Thus, childhood psoriasis may pose a management challenge for the treating dermatologist due to a lack of clinical trials and published data. Considering the impact of psoriasis on the quality of life of our population of young patients and their families, it is important for clinicians to understand the clinical profile of pediatric psoriasis patients and to remain cognizant of their common comorbidities. Treatment should be individualized, and patient education is an important part of treatment.

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