

Psoriasis in children: a comprehensive review article

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Abstract: Psoriasis is a chronic inflammatory disease that is very common in childhood. In a significant percentage of patients, the disease develops in ages less than 18 years. Psoriasis in children present with a variety of manifestations. The diagnosis of the disease at early ages is difficult, because of atypical lesions. The plaque type is the most common form of the disease in children. Different treatments such as phototherapy and systemic therapies have been proposed, but using any of them leads to serious complications in children. Therefore, early diagnosis and proper management are the main part of the treatment in these cases.

Here in this article we aimed to provide a general overview on the pediatric psoriasis, its epidemiology, pathogenesis, clinical manifestations and the treatment and discuss the latest information and data existed in this context.

Key words: *Clinical manifestations; Pediatrics; Psoriasis; Systemic treatment*

1. Introduction

Psoriasis is a common chronic papulosquamous skin disease. Approximately 4 percent of all skin diseases which are diagnosed in children less than 16 years are attributed to psoriasis (1). The peak incidence occurs in two ranges of age. One of them is the child under 18 and the other on is adults over 18 years of old. Psoriasis is a chronic inflammatory disease that is dependent on skin T cells characterized by excessive proliferation of keratinocytes and finally desquamative red plaques (2). Onset is somewhat different in children and adults, and is associated with factors such as pharyngitis, stress and trauma. Pediatric Psoriasis is often occurring as an infant's psoriasis in the first year of life and is self-limiting, as well as may manifest as psoriatic arthritis (3-5). Although there are some differences between pediatric and adult psoriasis, the treatment is the same in these two ranges of ages. Except that, pediatrics should be given more attentions for age, weight and available formulations. Congenital psoriasis is commonly represented as scaling erythematous pustular eruptions at birth (7, 8).

Epidemiology

Incidence and prevalence of psoriasis in children is not yet entirely clear. However, various reports have been reported 10% of cases before age ten, and 2% occur before the age of two years (9). In a study conducted in 2011 in Southern California over 710,000 children, the results showed that the prevalence of psoriasis in children was 30 per 10,000 people, while the rate in adults was 78.9 per 100,000 persons (10-12). The incidence is varying in men and women according to geographic region. Peak age of disease onset among boys is between 6 and 10 years and 10 to 14 years in girls. The annual incidence of the disease is 40.8 per 100,000. Some studies have noted that the incidence has doubled from 1970 to 2000 (13). Psoriasis in children is associated with hyperlipidemia, obesity, hypertension, diabetes mellitus, and Crohn's disease. Some studies indicated that 4.5% of patients had a family history of the disease. The most common site of involvement in patients is extensor areas of the leg and scalp (14). Classic Plaque type psoriasis is the most common

form of the disease with a prevalence of 60.6 %, and plantar psoriasis in 12.8 % cases is the next prevalent type (15).

2.Pathogenesis

The exact pathogenesis of the disease is not identified. But it is believed that genetics play an effective role in the pathogenesis of disease. So that 23.4 % to 71 % of patients have a positive family history of disease. It seems that HLA-Cw6 is a predisposing gene in developing of the disease (16-21).

Childhood obesity (overweight) has been proposed as a risk factor for the disease. The results of a study conducted in Turkey showed that most patients with psoriasis have had respiratory tract infections history (14.8 %) and positive throat cultures for Streptococci Group A bacteria (21.3%) (22, 23). Staphylococcal super-antigens and DNA HPV are other causing factors. Other factors that are responsible for causing generalized pustular psoriasis including: drugs, bacterial infections, sunburn, pregnancy, the use of coal tar, emotional stress, vaccination, hypocalcaemia and stop taking corticosteroids (24).

The disease is not dependent to a single gene, however, series of changes in genes such as: IL12-B9 (1p31.3), IL-13 (5q31.1), IL-23R (1p31.3), HLABW6 PSORS6 STAT2/IL-23A (12q13.2), TNFAIP3 (6q23.3), and TNIP1 (5q33.1), have been linked to causing psoriasis. These genes play an important role in Th2 and Th17 cell activity and are responsible for NF- κ B signaling (25). Patients with Crohn's disease are prone to psoriasis five times more than normal people (26). History of psoriasis and autoimmune conditions are associated with disease. People with simultaneous autoimmune diseases such as multiple sclerosis are more prone to develop psoriasis. Simultaneous occurrence of autoimmune thyroiditis and psoriasis has been reported in some studies in adults (27-29).

3.Clinical manifestations

The disease clinical manifestations are relevant to: age of onset, family history and genetic factors, and is divided into two types totally. Type I, has early onset, and the patients have positive family history. This type of disease is related to HLA-Cw6, HLA-B57 and HLA-DR7. Type II diseases of late onset (after age 40) and is associated with HLA-Cw2 (30, 31).

Psoriasis may rarely be present during infancy. At this age, the disease appears in two forms of psoriatic, psoriatic Diaper rash and erythroderma. Moreover, differential diagnoses such as seborrhea dermatitis, irritant contact dermatitis, Candida albicans infection, Nonbullous congenital ichthyosiform erythroderma, atopic dermatitis and immune deficiencies are also considered. All of should be ruled-out by an exact physical examination and through a complete history taking (32-35, 6). Pediatric Psoriasis is similar to the disease in adults in many ways. As adults, the most common form pediatric psoriatic is classic plaques type form (36). Various forms of psoriasis that affects the skin and other body areas are described to in **Table 1**.

Diagnosis:

Some clinical points in patient's examination include:

1. Isomorphic response or Koebner phenomenon,
2. Altered pigmentation with lesional clearance,
3. Auspitz's sign - the appearance of punctate bleeding spots when psoriasis scales are scraped (40),
4. Nails Pitting

Grading of the disease severity is based on the area surface and the presence of psoriatic arthritis. Psoriasis Area and Severity Index (PASI) can be used to assess disease severity (41, 42). Other ways of classification are: mild (surface involvement of less than 3 %), moderate (3 to 10%) and severe cases for more than ten percent (45) .

Abnormalities associated with the disease

Recent studies have shown that psoriasis is associated with chronic diseases and even life-threatening conditions in children. Increased rates of diabetes, arthritis, Crohn's disease, obesity, hypertension and high cholesterol levels have been linked with juvenile psoriasis. 32 % of children with moderate to severe forms of psoriasis are overweight (46). Obesity in early adulthood can lead to an increased risk of developing psoriatic arthritis (47)

Psychological effects of the disease can be especially harmful for children. Children suffering from this skin disease are often ostracized from society. These people are often discriminated against in educational institutions and being teased in public places such as swimming pools. The big concern is that; studies show that these negative experiences in adolescence may have long-term negative effects on self-esteem in adulthood and leads to anxiety (43, 44).

Table 1. Mean± SD level of the patients

Types of involvement	Description
Plaque psoriasis (psoriasis vulgaris)	This type may present like typical psoriatic lesions in adult, but the lesions are often more little in childhood and crusts are softer. The distributions of lesions resemble to adults, in extensor areas, knees, buttocks, elbows and the scalp. The prevalence of this type is between 34 and 84 percent (37).
Guttate psoriasis	Small papules in a wide surface of body which is often begins with weakness, pharyngitis or group A beta-hemolytic tonsillitis in children. This type of psoriasis is seen in 6.4 to 44% of patients. This form may be converted or plaque-like forms or fully heal within three to four months.
Follicular psoriasis	Small follicular papules on the extensor surfaces of the limbs, especially is more common black children. This form very common it should be differentiated from atypical Pityriasis Rubra Pilaris (PRP).
Facial involvement	Facial involvement is more common in children rather than adults. The lesions are often erythematous and with distinct boarder. Infra-ocular lesions are common and often circular.
Scalp psoriasis	Presentation of scalp involvement in the disease varies from mild forms to severe. Scalp psoriasis is present as thick white silvery scales on patches of erythema and may be beyond the hairline. Form of the disease that is confined to the scalp, is most common in children. Complications such as secondary bacterial infections and hair loss may occur. Tinea capitis is an important differential diagnosis which is considered in children (38).
Inverse psoriasis	This type is seen genital, perianal, axillary, inguinal and periumbilical area.
Palmoplantar psoriasis	This form included four percent of all cases of pediatric psoriasis and seen in the children often walking with bare feet.
Psoriasiform Acral Dermatitis	This type was reported for the first time in 1980. It is determined as involvement of the nail without typical atrophy of psoriatic nail.
Nail psoriasis	Nail changes is seen in 7 to 40 percent of patients that include pitting in 87% of cases, onycholysis at ten percent, subungual hyperkeratosis in 8%, and discolored nails is observed in five percent of cases.
Pustular psoriasis	This type is rare in children and is often seen in adults. Pustular psoriasis includes 4 types: generalized pustular psoriasis, Subacute annular pustular psoriasis, palmoplantar postular psoriasis, and pustular acrodermatitis. Subacute annular pustular psoriasis is the most common form in children (39).
Mucosal involvement	This type exists in 5.6% of cases. Mucosal patches in oral and genital mucosa, oral erosions and geographic tongue are reported.
Psoriatic arthropathy	This type of psoriasis is uncommon among children. The time of disease onset is between 9 to 12 years of old, and females are more prone to develop the disease. A diagnostic criteria is existed for pediatric psoriatic arthropathy that is mentioned below: <ol style="list-style-type: none"> 1. Arteritis and psoriasis or 2. arthritis and (positive family history for psoriasis, dactylitis or nail disorders) 3. ruling out of other etiologic factors such as positive rheumatoid test and existence of systemic arteritis

Differential Diagnosis

Psoriasis differential diagnosis (DDX) includes other papulosquamous diseases in children that include: Lichen planopilaris, Psoriasiform id reaction, nummular dermatitis, pityriasis rosea, and pityriasis rubra pilaris (3, 18). Biopsy can help distinguish psoriasis from other diseases. However, differential diagnoses are varying based on the various forms of psoriasis.

For instance, the differential diagnosis which proposed for plaque type psoriasis include: nummular dermatitis, tinea capitis, id reaction, pityriasis rubra pilaris, lichen planopilaris and atopic dermatitis. But these cases can also propose simultaneously in rare cases (52). the differential diagnosis of Guttate type are: nummular dermatitis, pityriasis rosea , ID Reaction, pityriasis rubra pilaris and tinea corporis . In terms of Inverse psoriasis, Intertrigo, Erythrasma and tinea corporis are noted.

The differential diagnosis of nail psoriasis can be onychomycosis, lichen plan and pityriasis rubra pilaris (39). Diaper dermatitis, candidiasis dermatitis of diaper and allergic contact dermatitis noted are mentioned to be as a DDX of Napkin or diaper form. Another type of psoriasis is erythrodermic psoriasis which its differential diagnosis includes atopic dermatitis, pityriasis rubra pilaris, mycosis fungoides and Staph scalded skin syndrome (SSSS) is (53, 54). Pustular psoriasis should be differentiated from dactylitis with Blister follow Tinea mentagrophytes infection and herpetic whitlow. And eventually the differential diagnosis of oral psoriasis can be geographic tongue; lichen planus and white sponge nevus (55, 56).

4.Treatment

much progress has been made in treatment of Psoriasis during recent years. However, the skin limited cases the topical treatment in combination with oral antibiotics is considered as first-line treatment in children. In cases of chronic or severe diseases, the systemic therapy and phototherapy may help in reducing symptoms and to mitigate the severity of the disease (1). Multiple psychiatric disorders are seen as significant in children with Psoriasis. The disease should be treated promptly Even if the skin is the only part of involvement, to prevent psychological problems and enhance the quality of life (57).

Topical treatment

Topical treatments include agents like tar, salicylic acid and the hyperkeratosis removing factors. The using of tar in pediatric psoriasis especially during the combination with UV ray is controversial, due to the genotoxic risk, chromosomal damages in

peripheral lymphocytes and releasing of hot shock protein (22, 58).

Anthralin, topical corticosteroids and topical calcineurin inhibitors are used for psoriasis vulgaris, but there are no drugs approved by the FDA for ages under 12 years. Anthralin 1% or Dithranol can be used rarely in limited local areas and may cause irritation. Topical clobetasol is approve for the patients less than 12 years or more, but increases the risk of atrophy (59). Corticosteroids are prescribed in children with psoriasis as atopic dermatitis. Agents with low to medium power are used for facial lesions and intertrigo, while the limbs and scalp lesions usually treated with greater power agents. Topical corticosteroids increase the risk of atrophy and systemic absorption. Calcipotriol (INN) or calcipotriene (USAN) are used in pediatric psoriasis, that the second agent is well-tolerated by sensitive skins (60, 61). Side effects are generally limited to local intolerance. Calcineurin inhibitors, tacrolimus ointment 0.03 % and pimecrolimus cream 1% are beneficent in areas such as the face, groin and intertrigo area. However, it is not recommended for use in children under 12 years (62).

Phototherapy

Phototherapy is a safe and effective treatment for children and adolescents, especially in the severe extensive diseases. psoralens with UV light in a narrow range (NBUVB) or psoralens and UVA (PUVA) can be used for the generalized or limb limited treatments. Although the use of PUVA is associated with cancer risk, but NBUVB is more reliable treatment (63, 64).

Systemic Treatment

Systemic medications must be used in cases of severe diseases and psoriatic arthritis. Systemic medications such as cyclosporine, acitretin or methotrexate usually prescribe for less than 6 months longer usage is seen in patients with rheumatoid arthritis receiving etanercept. An appropriate response is observed for a longer period of treatment (65).

Oral antibiotics

Oral antibiotics are useful in the treatment of psoriasis vulgaris, especially in cases of positive throat culture, perianal bacterial dermatitis, pustular psoriasis, or Guttate type of children (but not effective in adult's Guttate type) (18). Oral antibiotics therapy showed various results in studies. In addition, the ideal antibiotic regimen has not been reported (66).

Methotrexate

Systemic treatment is effective in chronic and severe cases of disease and improves the quality of life. The

main systemic treatment for widespread psoriasis is methotrexate that was used over the past three decades for children with psoriasis and psoriatic arthritis. A recent cohort studies have evaluated the therapeutic effects of methotrexate. Treatment response followed by 0.2 - 0.7 mg/kg/week was significant. Although controlling of blood indexes and liver tests are necessary, but changes in liver function are rarely seen, and most of them led to fatty liver or weight gain (67). Methotrexate is also better compared with cyclosporine in improving psoriatic arthritis.. The treatment starts with low-dose 7.5 mg and increases forasmuch as laboratory control. Adding folic acid supplements prevent macrocytic anemia and pancytopenia (10, 51).

Cyclosporine A

Cyclosporine A is a systemic immune suppressor drug which is used to prevent transplant rejection and can be prescribed orally with the doses of 3-5 mg/kg for pediatric psoriasis. Changes in liver function and urea and creatinine levels besides rise of blood pressure may be happen (68). Therefore, control and close monitoring of patients is recommended. It seems that, the risk of cancer and lymphoproliferative disorders would be minimal in children affected with skin psoriatic receiving less than 5 mg per kg per day of this therapeutic agent (69).

Retinoid

Oral acitretin 0.5-1 mg/kg per day is associated with a good response in the treatment of psoriasis. Because of teratogenicity; OCP in pregnant women should be used simultaneously and 3 years after cessation of drug. Short-term side effects such as increased levels of lipids or blood cell changes require regular monitoring. Long-term changes such as bone disorders can occur. In these cases the treatment should be limited and the periodic approach should be used in the treatment. Bone assessment may also be required (70, 71).

Biologic Drugs

Etanercept and Infliximab are TNF- α inhibitors that are used for treatment of autoimmune diseases in children like rheumatoid arthritis, (TRAPS), juvenile idiopathic arthritis and Crohn's disease for nearly a decade. Long-term improvement of bone disease in children with arthritis with etanercept has been approved (56). In cases resistant to etanercept, infliximab can be an alternative choice (32, 69, 72).

Supplements

Although various supplements and diet cannot cure psoriasis, but it is effective in reducing the severity (13). The best supplement is omega-3 fatty acids rich

fish oil. Supplements rich in omega-3 and omega-6 to a lesser extent has been effective in adults psoriasis and may be caused by changes in the production of arachidonic acid and the dose of pentanoic acid .

6-4 servings of fish a week could be as effective enough as the consumption of omega-3 supplements. Indigo naturalis, as a traditional Chinese drug, could be formulated in a form of pomade. Eight week use of this natural agent had effective clinical results in studies.

5.Conclusions

The incidence of psoriasis in children is unclear. There is no difference in the sexes and individuals may be affected at any age before age of 18. Plaque-type psoriasis is most common form in children. The exact pathogenesis is unknown. However, the disease has a genetic component, and several factors including weight gain, respiratory infections, positive throat cultures for group A streptococci, the frequency of psychological stress and etc, play important role in the induction and exacerbation of disease. Recent advances in genetics and solving processes involved in psoriasis have made response to treatment and better outcomes possible, although each of these therapeutical approaches have its own limitations.

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