International Journal of Community Medicine and Public Health
Alyamani NR et al. Int J Community Med Public Health. 2021 Nov;8(11):5557-5561
http://www.ijcmph.com
pISSN 2394-6032 | eISSN 2394-6040

DOI: https://dx.doi.org/10.18203/2394-6040.ijcmph20214053

Review Article

Skin manifestations of autoimmune diseases in the pediatrics

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Received: 22 September 2021
Accepted: 29 September 2021

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ABSTRACT

Autoimmune diseases during childhood are common and are usually observed to affect multiple systems. Among many pediatric autoimmune diseases, several cutaneous manifestations were reported in the literature, and the adequate examination and detection of these manifestations might significantly enhance the chances of establishing an adequate diagnosis of the underlying diseases and conditions because the affected patients usually present with typical symptoms. Establishing a proper diagnosis can enhance the prognosis of the affected patients and might prevent the development of serious complications and other adverse events. Besides, it was also previously indicated that establishing an early diagnosis will furtherly help with deciding the most appropriate interventions, which will also enhance the prognosis of the pediatric population. In this literature review, we have discussed the cutaneous manifestations of several autoimmune diseases that might affect the pediatric population. We have majorly discussed the conditions that are associated with systemic lupus, juvenile idiopathic arthritis, dermatomyositis, juvenile-onset systemic sclerosis and morphea. The cutaneous manifestations of these conditions are hugely variable and usually need careful examination and adequate differential diagnosis to establish the best management modality. Besides, some manifestations might gradually develop which might even make the diagnostic approaches even more difficult. Accordingly, clinicians should provide full and thorough examination and diagnosis of the suspected patients because detecting such cases might significantly enhance the prognosis and lead to adequate treatment.

Keywords: Autoimmune disease, Pediatric, Systemic lupus erythematosis, Dermatomyositis

INTRODUCTION

Autoimmune diseases during childhood are common and are usually observed to affect multiple systems. There is no doubt that the skin is a vital organ in these diseases, and evidence shows that it is commonly reported together with the different manifestations of autoimmune diseases.[1-3] Furthermore, environmental and genetic factors are usually associated with the disease and are found to be significant in the pathology of these diseases. Such factors usually trigger the development of several inflammatory conditions within the affected bodies, leading to significant cellular response and increased release of inflammatory mediators, which will finally be characterized by the presence of significant clinical manifestations.[4,5]

Among many pediatric autoimmune diseases, several cutaneous manifestations were reported in the literature, and the adequate examination and detection of these manifestations might significantly enhance the chances of establishing an adequate diagnosis of the underlying diseases and conditions because the affected patients usually present with typical symptoms.

In a previous investigation by López-Quintero et al, the authors reported that the prevalence of cutaneous manifestations among patients with autoimmune diseases is 27.1%.[6] Atopic dermatitis and skin infections are commonly reported among these patients, in addition to other various symptoms and manifestations.

Establishing a proper diagnosis can enhance the prognosis of the affected patients and might prevent the development of serious complications and other adverse events. Besides, it was also previously indicated that establishing an early diagnosis will furtherly help with deciding the most appropriate interventions, which will also enhance the prognosis of the pediatric population.

Accordingly, the current literature review aims at providing a thorough discussion about the cutaneous manifestations of the most commonly reported autoimmune diseases within the pediatric population. This can significantly aid the diagnostic value of these diseases and will help clinicians provide better care and management for the affected patients.

METHODS

This literature review is based on an extensive literature search in Medline, Cochrane, and EMBASE databases which was performed on 14 August 2021 using the medical subject headings (MeSH) or a combination of all possible related terms. This was followed by the manual search for papers in Google Scholar while the reference lists of the initially included papers. Papers discussing the skin manifestations of autoimmune diseases in the pediatrics were screened for relevant information, with no limitation on date, language, age of participants, or publication type.

DISCUSSION

Juvenile-onset systemic sclerosis and morphea

Many pediatric autoimmune diseases can significantly cause skin manifestations. In the present section, we will discuss the potential cutaneous manifestations among children with the most common autoimmune diseases. We have aimed to discuss the manifestation of the following diseases: juvenile-onset systemic sclerosis, morphea, systemic lupus erythematosis, juvenile idiopathic arthritis and dermatomyositis.

The cutaneous manifestations in juvenile-onset systemic sclerosis (JSSc) are mainly attributable to the surrounding vascular dysfunctions of the affected tissues. Additionally, it has been previously reported that Reynaud's phenomenon is the mosts common cutaneous manifestation in the affected children, with estimates showing that it can affect up to 75% of the cases, while digital tip ulcers, sclerodactyly, and proximal skin induration can affect up to 35%, 55%, and 66% of the affected patients, respectively.[7] Cyanosis, pallor, numbness, pain, hyperhidrosis, swelling, and tingling of the acral surfaces are the main manifestations of Reynaud's phenomenon and are mainly attributable to vasospasms. The most commonly affected parts include the feet and hands, while it was also reported that the lips, ears, nose, and cheeks might also be affected.[8] Emotional distress and episodes can significantly predispose to the development of these manifestations. Sclerodactyly is usually edematous in the first presentation. However, it was also reported that it usually develops to shiny skin of the finger types, and the range of movement of the affected parts usually reduces. Together with these sclerotic manifestations, matted telangiectasis, calcifications, and ulcerations might also be associated.[7,9] Furthermore, dyspigmentation might also be a characteristic of salt and paper appearance [1]. Ichthyotic skin might also appear in the prodromal stage of the disease.[10] Thinning of the epidermis, in addition to atrophic adnexal structures dermal hyalinized or compact collagen is the main finding that can be found under microscopic examination. The management of the disease is critical to enhancing the outcomes. However, there is not enough evidence regarding the management of these manifestations in the pediatric population. It must be suggested that these patients should avoid triggers that might cause vasospasm.

A differential diagnosis should be considered to differentiate morphea from JSSc, and the histological hallmark of morphea has been observed to be the presence of dense bundles of thickened collagen fibers within the dermis. In children, it has been estimated that linear morphea is the commonest type, and the regional distribution usually includes the head, and trunks or limbs.[11] The lesion is usually observed as an erythematous linear strip that is observed in a longitudianl pattern of indurated plaques, finally leading to a scar-like appearance. There also might be significant involvement

of the underlying structures, and the joints are affected. Deep manifestations and stiffness of the skin might also be associated, which can significantly impact the mobility of the affected joints. Significant discrepancies to the size of the affected limb might also be observed secondary to the circumferential distribution of the affected lesions.[1] Besides, it was also reported that Parry-Romberg syndrome and en coup de sabre might clinically manifest when the head is involved.[11,12] Ipsilateral cerebral atrophy and calcifications might also present, in addition to some neurological manifestations in up to 68% of the cases.[13] In another context, circumscribed morphea is usually characterized by the presence of erythematous, or flesh-colored, edematous plaques. The lesion is usually observed as scar-like tissue, and other manifestations as loss of sweat glands and hair were also reported. It has been reported that the lesion is usually asymptomatic that some patients might not even observe it. Moreover, it has been reported that dyspigmentation and residual atrophic changes can also be observed in such cases. Pansclerotic morphea might be associated with disabling manifestations that usually affect the face, trunk, limbs, and scalp. In addition, it has been reported that the fingers and toes are usually spared in this disease, unlike systemic sclerosis. Sclerosis can lead to significant fixation of the affected joints with permanent disabilities. However, it was also reported that internal organs are usually spared.[14-16]

Dermatomyositis

Many cutaneous manifestations have been reported with dermatomyositis. However, the most common findings usually include heliotrope rash around the eyes and Gottron's disease. The latter manifestations are usually defined as tiny pink or purple lichenoid disease that usually appears on the dorsum of the hands of the affected patients. The most commonly affected parts might include the distal interphalangeal, the proximal interphalangeal, and the metacarpophalangeal joints. Dyspigmentation and atrophy telangiectasia are the prominent manifestations that appear when these lesions resolve. Besides, it was also reported that over the bony prominences of the elbows, knees, and ankles, other manifestations are similar to the Gottorn's manifestations but are usually psoriasiform, and are purple or pink. The eyelids might also be involved by the heliotrope rash that usually appears as a purplish red discoloration. Associated edema might also be observed in such cases. Forehead, temples, ears, and cheeks might be involved. Besides, the scalp was also reported to be involved by scaling or erythema.[17-20] Dermal mucin accumulation, basal keratinocytes-related vacuolar changes, and dermal lymphatic infiltration that is usually mild to moderate are the main histological manifestations of the disease, in addition to some dermal sclerosis.[21] In another context, poikiloderma (telangiectasias, and dyspigmentations, together with epidermal atrophic changes to the same affected regions) is usually the manifestation of chronic dermatomyositis. The distribution of the lesion usually appears as the "shawl sign", which can be identified as a photodistribution of the aforementioned manifestations, usually affecting the anterior chest and the upper back. Telangiectasia of the nail folds and ragged cuticles are also commonly reported, with an estimated prevalence rate of 68% of the affected patients. Fissuring and hyperkeratosis of the hand, together with palmar erythema might also be observed, leading to the appearance of the mechanic's hand. Gingival bleeding, telangiectasia, and ulcers might be observed as mucosal affection. It has also been reported among studies that calcinosis cutis can affect 18-25% of the affected children, and is usually associated with significant morbidities, and other complications (including ulceration and cellulitis), and is usually an indicator of disease chronicity. The lesion is usually observed as hard nodules within the parts of the body that are prone to trauma, including the knees, elbows, buttocks, shoulders, and fingers. Besides, it was also observed that the lesions are located deep within the fascia, and it has been reported that it may connect to the skin surface, with chalky drainage. However, recent evidence shows that the prognosis is good among patients receiving aggressive therapy.[22-24]

Lupus erythematosus, and juvenile idiopathic arthritis

There are three main types of cutaneous lupus erythematosus, including, acute, subacute, and chronic lupus.[25] Several subclassifications were also reported for chronic cutaneous lupus, including lupus erythematosus tumidus, discoid lupus erythematosus, chilblain lupus erythematosus, and lupus panniculitis. Furthermore, it has been previously indicated that more than a type of cutaneous lupus can affect a single patient, and not one type can be found exclusive without the others.[26] Generalized and localized cutaneous manifestations of acute lupus were reported in the literature, and the conditions usually affect patients with active lupus.[27] Malar rash is the main significant presentation of the localized form, and the nasolabial folds are usually impaired. Scaling, intense edema, or mild erythema can also be observed among these patients and can even last for up to several weeks. Although the malar rash can affect up to 61% of the case, estimates show that generalized forms of cutaneous manifestations are rare.[28] Such lesions might include the presence of symmetric macules and papules on the extremities and torso, and pruritis was also previously reported to be associated.[27] Besides, erythematous plaques were found to affect the skin between the joints more than other skin. Mucosal involvement was also observed among several patients in the form of gingivitis, ulcerations, or silver-white changes to the gingiva, vermilion border, nasal, and buccal mucosa. It has been estimated that these manifestations usually affect up to 30% of the cases of pediatric lupus.[8] Bullous lupus erythematosus was also reported in the literature as a rare form, where generalized or localized tense subepidermal bullae and vesicles might be found on top of erythematous or normal skin. These lesions have been observed to affect more the areas with the most exposure to the sun.[29,30] Exposure to the sun is also associated with the development of manifestations of subacute cutaneous

lupus. Besides, it has been reported that the condition is usually associated with systemic affection, however, it was also reported that it is not a very common disease.[26,31] Annular configurations are the main presentations that might even lead to the development of psoriasiform or eczematous epidermal characteristics. In another context, the lesions of chronic cutaneous lupus are the most common forms in the pediatric population and are usually found as slightly indurated, round to annular, erythematous to violaceous plaques. Dyspigmentation and atrophy might also be associated in such cases, with associated alopecia and scarring. In Figure 1, we have furtherly listed other unusual cutaneous manifestations that might be associated with cutaneous lupus.

Diffuse non-scarring alopecia
Raynaud's phenomenon
Nailfold telangiectasia and erythema
Vasculitis
Urticarial vasculitis
Small vessel vasculitis (*e.g.*, palpable purpura)
Polyarteritis nodosa-like lesions
Ulcerations
Cutaneous signs of antiphospholipid syndrome
Livedo reticularis
Ulcerations
Acrocyanosis
Atrophie blanche-like lesions
Degos'-like lesions
Livedoid vasculopathy
Palmar erythema
Papular and nodular mucinosis

Figure 1: Unusual cutaneous manifestations that might be associated with cutaneous lupus.

Furthermore, cutaneous findings in patients suffering from juvenile idiopathic arthritis are typically observed in 25-50% of the cases affected cases and usually present before other lesions are several years. The characteristic lesions are mainly formed of edematous papules, salmon-pink macules (Figure 2), that is usually associated with fever, often resolve within hours, and are typically 2-5 mm. No pruritic observations were noticed among these patients when an eruption occurs, and are usually observed within the pressure areas, extremities, and chest.[32]

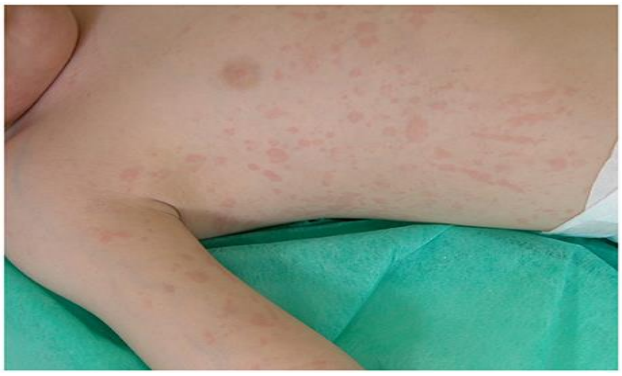

Figure 2: Salmon-pink macular rash in a patient with juvenile idiopathic arthritis.[33]

CONCLUSION

The cutaneous manifestations of these conditions are hugely variable and usually need careful examination and adequate differential diagnosis to establish the best management modality. Besides, some manifestations might gradually develop which might even make the diagnostic approaches even more difficult. Accordingly, clinicians should provide full and thorough examination and diagnosis of the suspected patients because detecting such cases might significantly enhance the prognosis and lead to adequate treatment.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Alyamani NR, Alsuwayq RM, Bahatheq NM, Alkhatir ZA, Alhawdar AW, Alharthi YH, et al. Skin manifestations of autoimmune diseases in the pediatrics. Int J Community Med Public Health 2021;8:5557-61.