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SKIN MANIFESTATIONS IN CHILDREN WITH COVID 19

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Abstract

Children are a unique subgroup of patients in relation to the COVID-19 pandemic, often presenting asymptomatically, mildly or atypically. Initial reports did not include skin manifestations as a feature of COVID-19, however, there is a growing repertoire of reports showing a range of dermatologic skin manifestations in children. Six clinical skin manifestations have been described: urticaria, maculo-papular rash, morbilliform eruption, vesicular rash, lividor-reticular and multiform rash.

Dermatological features occur before or simultaneously with other manifestations of COVID-19. Doctors play a key role in diagnosing patients with COVID-19 who may present for the first time unknowingly showing early signs of the disease. In this report are presented 4 patients with Covid 19 infection, where the skin is the target organ of the virus.

In all children, the skin manifestation is different, their markers of inflammation are different and the treatment is not the same. In patient number 1, we look at the benefit of immunoglobulins in viral infections and consider their use in COVID-19 infection.

Skin changes should never be ignored. The rash can spread and lead to a severe form of the disease. Skin manifestations may be the primary [or only] manifestation of a sign. It is extremely important to recognize it in time and to treat it accordingly.

***Keywords*:** children, covid 19, immunoglobulins, skin changes.

Introduction

Since the emergence in December 2019 of the novel coronavirus that causes acute respiratory distress syndrome type 2 [SARS-CoV-2], numerous articles have described its clinical spectrum in children, including the appearance of skin lesions [1].

Studies conducted during the first wave of the pandemic showed that up to 20.4% of patients with confirmed SARS-CoV-2 infection had skin manifestations, of which 1/3 were most commonly described as an erythematous rash [2-4]. Subsequently, other studies classified the types of rash, attributed to the disease and related to the stages and severity of the infection [1].

Pediatric series consistently describe the appearance of acral erythematous-purple lesions, similar to Chilblain, especially in the late stages, in oligosymptomatic or subclinical patients, with spontaneous remission. [2, 5-7,].

In adults, necrotic/ischemic lesions are associated with prothrombotic conditions caused by the virus, and this phenomenon has not been studied in children. Initial reports did not include skin manifestations as a characteristic of COVID-19, however, there is a growing repertoire of reports showing a range of dermatological skin manifestations in children [8].

The analyzes identified six clinical manifestations: urticaria, maculo-papular rash, morbilliform eruption, vesicular rash, livido-reticular and multiform rash.

Their pathophysiological mechanism is still elusive and is probably the result of the complex involvement of one or more mechanisms, such as direct damage to skin caused by the virus, vasculitis-like reactions and/or indirect injury as a consequence of a systemic inflammatory reaction[9].

In children, dermatologic features appear to occur before or concurrently with other manifestations of COVID-19[8]. Doctors play a key role in diagnosing patients with COVID-19 who may present for the first time unknowingly showing early signs of the disease [8].

We are reviewing cases in the pediatric population with skin manifestations of Covid 19.

Case report one

Male child aged 9 years, was admitted to our ambulance because of temperature of 37.5-38.7 C, sore throat, cough and malaise and the appearance of a generalized rash all over the body. The disease started 4 days before. He was tested with a rapid antigen test for Covid 19, the same was positive and he wasa hospitalized for further treatment. Epidemiological survey: father positive for Covid 19 infection.

From the status: He was hospitalized in our Institute as afebrile 36.4 C on admission, eupnoic and tachycardic. The skin had a multiform rash confluent in the inguinal region [livid erythema]. Rhythmic heartbeat, tachycardic, with clearly audible heart sounds, without accompanying heart murmurs. Abdomen soft on palpation without organomegaly.

From the investigations: biochemical investigations high biomarkers of inflammation - SE 40/90, CRP: 83.2mg/l, blood count with Leucocytes 18.1, and the next days they were rising to 25.4 and 30.2x10^9, LDH was 876 u/L. The other biochemical investigations within reference values.

Therapy: After admission, the patient was placed on parenteral rehydration antibiotic, corticosteroid and antihistamine therapy. During the hospital stay in the first 5 days without response to the given therapy and with worsening of the general condition and progression of skin changes with a simultaneous increase in inflammatory values.

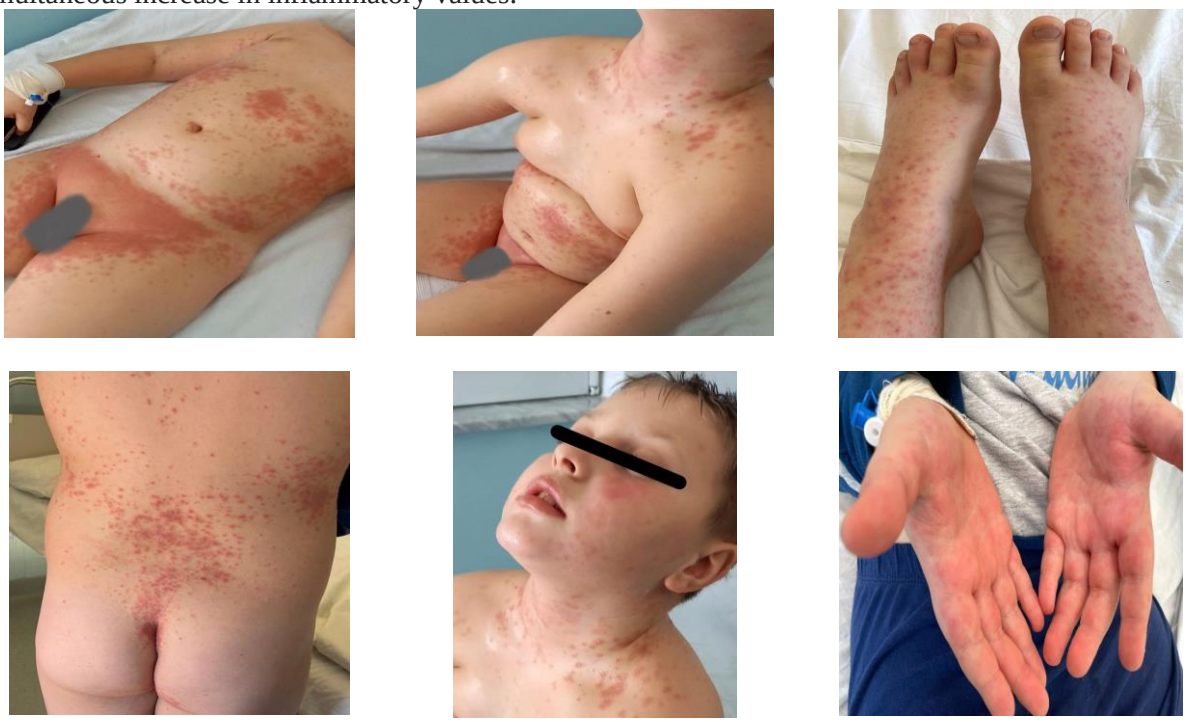

Figure1. Erythematous rash with pinhead-sized pustules with affection of the main folds axillary, inguinal and sub mammary area, the trunk and distal part of the limbs are also affected. Erythema /edematous rush is noticed in the palms and face area.

A dermatovenerologist has been consulted , and she described the patient's rash as Exanthema pustulosa. Intravenous immunoglobulins were included on the fifth day of therapy. After receiving the immunoglobulin therapy in just a few hours, the patient's general condition is improved, a significant and rapid regression of skin changes, as well as a decrease in inflammatory markers. [SE 10, CRP 2.5 mg/l., LDH 399 u/L, Leucocytes 9.4x10^9] (Figure 2).

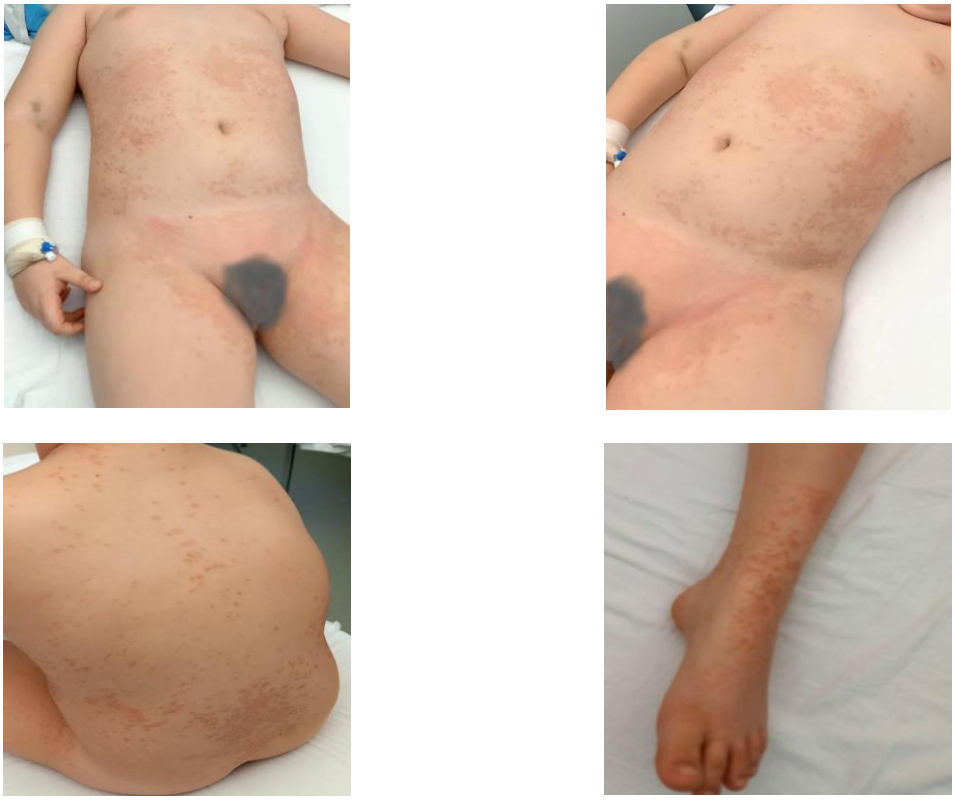

Figure 2. Improvement of skin changes after therapy with intravenous immunoglobulin

In the following, we present pictures of skin changes of several cases where the skin manifestation is the only clinical symptom in Covid 19 infection without other accompanying symptomatology. These patients had all normal biochemical analyzes and were in good general condition (Figure 3; Figure 4 and Figure 5).

They were placed on parenteral rehydration therapy with an oral antihistamine and short-term on low doses of corticosteroid. Spontaneous regression of skin changes has been noted.

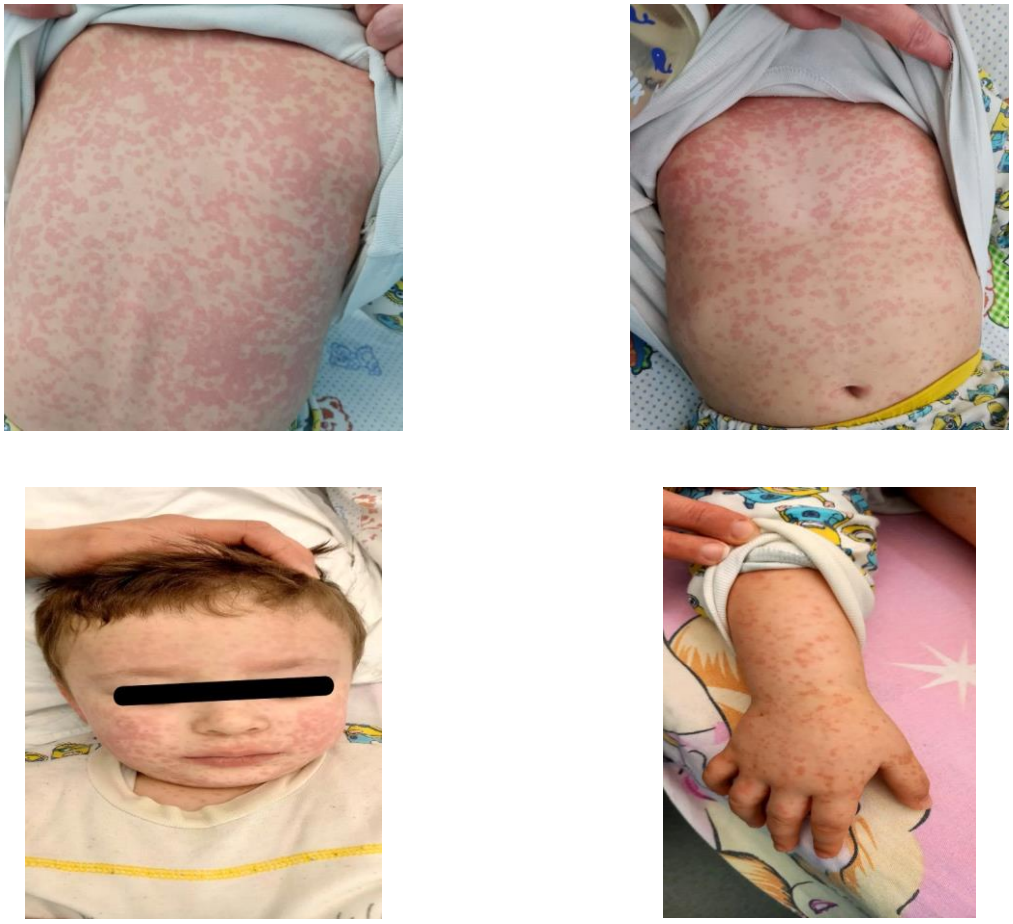

Figure 3. Generalized macular rush

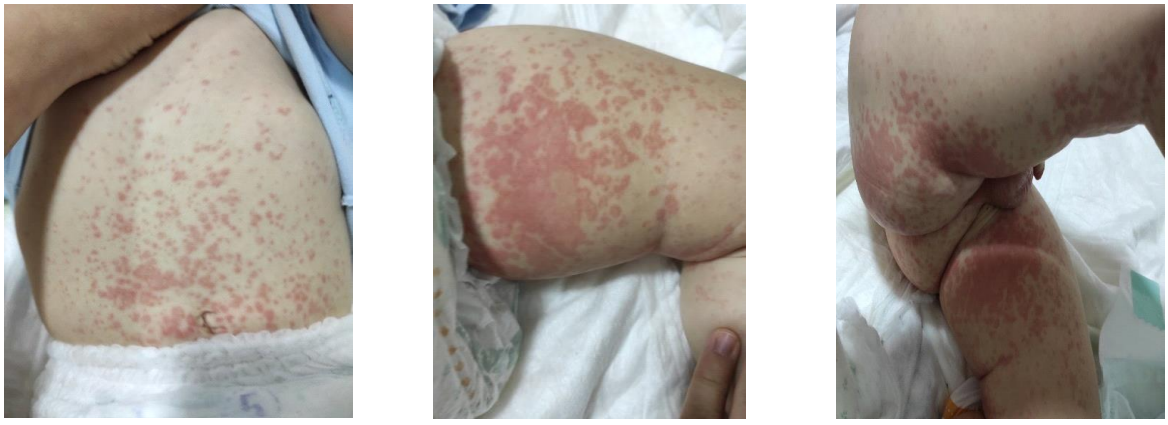

Figure 4. Generalized EEM-like rush with affection mainly of the inguinal, abdominal and napkin area.

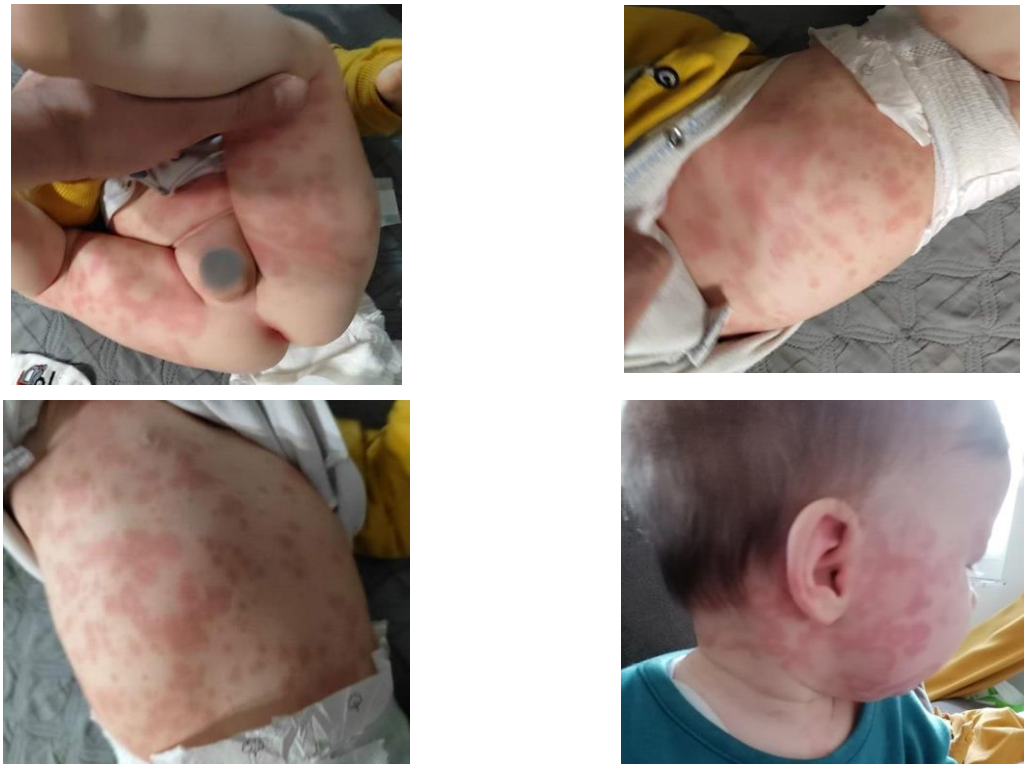

Figure 5. Generalized urticarial rush.

Discussion

Children are a unique subgroup of patients with respect to the COVID-19 pandemic, often presenting asymptomatically, mildly or atypically.

Skin manifestations may be the primary [or only] sign manifestation. Recognition of cutaneous manifestations of COVID-19 in the pediatric population is important for guiding precautions, testing, and management of patients and close contacts. While some dermatologic signs in children overlap with those in adults, other skin findings are reported with greater frequency in children and may be clues to multisystem sequelae [10].

There is no approved drug or consensus on the correct treatment algorithm for COVID-19[11].

There is increasing evidence for immune-based treatments that inhibit the infectious mechanism of the virus and improve the inappropriate immune response or regulate the hyperactive immune response in patients. [1] In the first case, we saw the benefit of intravenous immunoglobulin in viral infections and consider their use in COVID-19 infection [11]

Immune-based elimination of the virus with immunoglobulins is aimed at preventing infection. Entry of SARS-CoV-2 into host cells is mediated by the transmembrane glycoprotein [S] that binds to the angiotensin-converting enzyme 2 [ACE2] receptor, which is highly expressed on the apical surface of many cell types. The S protein forms a homotrimer that exits from the viral surface. Receptor binding is mediated by the S1 subunit through the receptor binding domain [RBD]. Upon binding to the ACE2 receptor, proteolytic activation of the S2 subunit mediates fusion between the viral and cell membranes [12].

Because of the essential role of S glycoprotein in cell infection, antibodies that bind to S1 and S2 can prevent infection. A neutralizing antibody can stop virus replication by blocking receptor binding, preventing cell wall fusion, or preventing virus uncoating in the cytoplasm [12].

Intravenous immunoglobulin is a product obtained from the plasma of thousands of donors used to treat primary and secondary immunodeficiency, autoimmune conditions, neuroimmunological disorders and inflammatory diseases where this immunotherapy has shown promise [11].

Intravenous immunoglobulin is a blood product containing polyclonal immunoglobulin G, isolated and pooled from healthy donors, and has been used for more than 30 years. As a complex preparation, it contains a large number of bioactive parts, and the totality of its effects is still not fully understood. INTRAVENOUS IMMUNOGLOBLOBULIN is the immunomodulatory therapy of choice for autoimmune or inflammatory disease and for the prophylaxis and treatment of severe infections, especially in immunocompromised patients [13, 14].

Several theories have been proposed to explain its potential immunomodulatory mechanisms, including Fc-mediated and Fab-mediated approaches [15, 16].

In previous studies on SARS and Middle East Respiratory Syndrome [MERS], intravenous immunoglobulin therapy has shown distinct clinical benefits with good tolerability [17-19]. Considering the efficacy in enhancing passive immunity and modulating immune inflammation and the overall safety profile, INTRAVENOUS IMMUNOGLOBLOBULIN may be considered a promising option in the early phase of clinical deterioration in patients with COVID-19 [20].

Conclusion

Skin changes should never be ignored. The rash can spread and lead to a severe form of the disease. Clinical practice shows that the rash in children can be the only symptom of Covid 19 infection, but the rash can also be preceded by a respiratory infection.symptoms such as cough, runny nose, headache and fever. It is extremely important to recognize it in time and treat it accordingly.

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