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CLINICAL CASE

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CUTANEOUS FINDINGS IN COVID-19 INFECTION – ADULT VERSUS CHILD

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**ABSTRACT**

*COVID-19 is causing a rapidly expanding pandemic, representing global concern. In the current COVID-19 outbreak that is affecting all countries, research did not focus on the cutaneous manifestations of the new coronavirus infection. However, over the past few weeks, some case reports have been published in the literature describing cutaneous manifestations in COVID-19 positive patients. Skin manifestations suggestive for coronavirus infection have been described: morbilliform rash, erythematous-purpuric coalescing macules, varicella-like vesicles, petechial rash, widespread urticaria, transient unilateral livedo reticularis, chilblains-like papules located at the acral level and peripheral cyanosis which can evolve with bullae up to dry gangrene. The timing of these varied eruptions in the disease course remains unclear, as do any potential associations between morphological subtypes with different COVID-19 associated syndromes, disease courses and/or outcomes. In addition to those described, there is an increased risk of developing adverse reactions to drugs recently introduced in patients treated for COVID-19, with the appearance of cutaneous manifestations in any stage of the disease. We report one case of coronavirus disease that had as primary symptoms erythematous rash associated with pyrexia.*

**KEYWORDS:** *COVID-19, pandemic, viral exanthem, skin manifestations, erythematous rash*

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**INTRODUCTION**

The first group of pneumonia cases associated with the novel coronavirus was reported in China in 30 December 2019. COVID-19 is causing a rapidly expanding pandemic, representing global concern. As of April 30,

2020, a total of 2 995 758 accumulated cases and 204 978 deaths have been reported around the world [1]. SARS COV-2 is part of the coronavirus family, as is SARS CoV-1, which was responsible for the SARS epidemic in 2003 and MERS CoV, which was responsible for the 2013 MERS epidemic. A significant number of

articles presented the main manifestations of COVID-19 infection. Typically, because the initial infection of SARS COV-2 occurs in the ciliary epithelial cells of the bronchi, the primary symptoms of the disease are fever, dry cough, shortness of breath myalgia and diarrhea [2]. In the evolution of the disease, some patients may develop ARDS (acute respiratory distress syndrome) with a significant mortality rate [3]. Low levels of leukocytes and thrombocytes, along with elevated levels of D-dimers are associated with an increased risk of venous thromboembolism [4]. The average incubation period of the virus is 4.6 days, but the patient becomes symptomatic after 10 days in most cases. Severe cases recorded an average period of 11 days from the onset of the first symptoms until the need for mechanical ventilation and an average period of 23.7 days until death. Death can occur after the development of acute respiratory distress syndrome (ARDS), multiorgan failure or septic shock [5]. The discovery of a vaccine against the novel coronavirus is the key to resolving this global crisis, given that the pandemic cannot be entirely stopped by social distancing and good hygiene practices. The tactical therapies identified so far have not been entirely effective, especially for the most vulnerable individuals, being unable to prevent severe disability and ultimately death. While healthcare systems are still struggling not to crumble under pressure from coronavirus patients, research laboratories around the world are competing to produce an effective vaccine against SARS CoV-2 as soon as possible, in order to be able to stop the spread of the new coronavirus [6].

Around the world, important research efforts are made for a better understanding of the transmission patterns, clinical and paraclinical features, prevention and treatment options. However, there are very few data and images in the literature regarding the cutaneous manifestations associated with COVID-19 infection, due to the fact that there are just a small number of dermatological consultations in this category of patients. The frequency of cutaneous manifestations (ranging from 0.2 to 20.4 percent of cases) and the moment of appearance in the evolution of the disease are difficult to ascertain [7]. In a review of clinical manifestations of COVID-19 in China, erythematous rash was

recorded at a percentage of only 0,2% of total cases [8]. Despite this, from the perspective of dermatologists this percentage is certainly much higher.

Over the past few weeks, several case reports have been published in the literature describing cutaneous manifestations in COVID-19 positive patients. Thus, skin manifestations suggestive of viral exanthem have been described: morbilliform rash, erythematous-purpuric coalescing macules, varicella-like vesicles, petechial rash (associated with thrombocytopenia) and widespread urticaria [8,9]. Other skin manifestations are those caused by vasculitis or thrombotic vasculopathy: livedo reticularis (transient and unilateral-in the majority of cases), chilblains-like papules located at the acral level (toes and fingers) and peripheral cyanosis which can evolve with bullae up to dry gangrene [10,11]. Regarding the cutaneous manifestations in non-laboratory-confirmed cases of new coronavirus disease, they are represented by urticaria and painful erythematous-violaceous patches that evolved into vesicles [12,13].

## CASE PRESENTATION

We report one case of coronavirus disease that presented primary with cutaneous manifestations.

A 51-year-old woman was admitted to the hospital for pyrexia (38.2°C), myalgia and fixed erythematous rash on the back of both arms (Figure 1). She reported that the rash appeared three days before the rest of the symptoms. The patient denied any change of treatment or habits in the previous four weeks. She has no allergies. The medical history of the patient includes Celiac disease, dyslipidemia and high blood pressure. Given the high suspicion of coronavirus infection, due to her journey to Austria one week before the first symptom, a SARS-CoV-2 RT-PCR test of pharyngeal exudate was taken and the result was positive.

Physical examination revealed erythematous plaques located at the elbows, symmetrical and bilateral. The contours of the lesions are irregular and near the plaques erythematous papules are observed. According to the patient's reports, initially several papules appeared which later converged into large

lesions. No biopsy was taken. Increased levels of C reactive protein, lymphopenia, thrombocytopenia, and increased levels of lactate dehydrogenase have been observed in laboratory tests. The pulmonary CT was typical for COVID-19.



**Figure 1 – Erythematous plaques made up of converged tiny papules located at the elbows, symmetrical, bilateral; the contours of the lesions are irregular, and near the plaques, erythematous papules are observed**

Affected areas were mildly pruritic, expanding for five days and subsequently regressing completely in ten days. In terms of arising suspicion of COVID-19, we feel that erythematous rash may be useful as indicator of disease, in the current context of the global pandemic. Clinical differential diagnosis of an erythematous rash most commonly includes post-drug rash and viral infections. Positive SARS-CoV-2 RT-PCR in our patient strongly suggests an exanthem caused by a viral infection.

## DISCUSSIONS

In the current COVID-19 outbreak affecting all countries, research did not focus on the cutaneous manifestations of the new coronavirus infection. Due to the safety that must be maintained by medical staff when in contact with patients positive for the new virus, it is difficult to photograph skin lesions, if they exist; so, there are few image reports that can help dermatologists to determine the skin features of SARS-CoV-2 infection.

If skin lesions in patients COVID-19 positive are related with the infection remains unclear. After a detailed analysis of all clinical cases of skin lesions possible associated with COVID-19 published so far in PubMed, two major groups according to their pathophysiological mechanisms are described: skin manifestations that are similar to those of the viral exanthem, representing the consequence of the triggered immune response to viral nucleotides, and skin rash/eruption representing the consequence of systemic damage produced by SARS-CoV-2, the most common being vasculitis or thrombotic vasculopathy [4,14]. The timing of these varied eruptions in the disease course remains unclear, as do any potential associations between morphological subtypes with different COVID-19 associated syndromes, disease courses, and/or outcomes. In addition to those described, there is an increased risk of developing adverse reactions to drugs recently introduced in patients treated for COVID-19, with the appearance of cutaneous manifestations in any stage of the disease. We emphasize the need to seek evidence, in order to support the etiopathogenesis of skin lesions, in favor of a post-drug rash or associated with the viral infection, sometimes this being difficult due to the clinical and histopathological similarity [15,16,17]. However, it is necessary to note that many patients have been treated with lopinavir/ritonavir or/and hydroxychloroquine and skin reactions have been described in very few cases. HCQ was recently suggested for both chemoprophylaxis and treatment of SARS-CoV-2 infection. HCQ adverse effects include exanthema, stomatitis, itching, and hyperpigmentation, and even severe side effects like Stevens-Johnson syndrome, toxic epidermal necrolysis and AGEF [18,19].

Cases of skin manifestations associated with coronavirus disease are multiplying these days. Hunt and Koziatek reported a case with the association of fever and morbilliform rash as the first symptom of the disease [11]. Joob and Wiwanitkit reported a case which had as primary symptoms petechial rash, that was initially misdiagnosed as dengue fever, which delayed the correct diagnosis [8]. Recalcati showed that, among 88 patients COVID-19 positive, who had not used new drugs in the fifteen previous days, a total percentage of 20.4% (18 patients) developed cutaneous manifestations: majority of cases developed erythematous rash, 3 of them developed generalized urticaria and 1 patient developed varicelliform rash. All lesions were pruritic, with the resolution of the lesions in a few days. Until now, no correlation was established between the occurrence of the skin manifestations and the severity of the disease [12]. Clinicians caring for patients with COVID-19 should consider that the skin manifestations may be the result of viral infection, systemic damage produced by the new virus or newly introduced treatment. Precise etiology of the rash requires a detailed medical history. It is also important to determine if the skin lesions represent the aggravation of a pre-existing skin pathology or even the consequence of excessive use of disinfectants during this period. In our case, the patient had no new drugs introduced in recent months, nor did she have pre-existing dermatological pathology and she denied exposure to new disinfectants, which is why other differential diagnoses were excluded.

Recently, mainly due to new viral strains, multiple skin reactions have been reported in children. We would like to highlight the main types of skin manifestations in children with COVID-19 infection. It is known that skin manifestations are different between adults and children. In a systematic review with three parts, the authors summarize all important cutaneous eruptions/lesions, caused by COVID-19 infection and reported to date [20].

The first type of lesions reported in children with COVID-19 infection were chilblain-like lesions, which are inflammatory entity, located on acral regions, and persist more than one day. Clinically, they are erythematous-edematous macules/nodules or plaques, on dorsal surface of fingers or toes. The most frequent,

chilblain lesions are triggered by cold, but may also develop because a connective tissue disease or a malignancy [21]. Since March 2020, many studies reported pediatric chilblain-like lesions associated with SARS-COV-2 infection [22-25]. As for clinical aspect, they are usually multiple, round, different in size, and affect the entire toe, with demarcation at metatarsophalangeal level, located most frequent on feet [74-100% of cases], but also on hands or fingers [26-28]. As it is reported in the specialty literature, adults with COVID-19 infection develop symptoms. On the other hand, infected children are usually asymptomatic [29]. Also, dermoscopic characteristics were different from adults: reticular network, globules and a purple, grey, brown or red background area [20]. The evolution of these lesions is favorable, with spontaneous regression and no sequelae. Very rare, when itching or pain occurred, analgesics or antihistamines were administered. Just one case was reported with severe pain, so oral gabapentin was administered [20]. Usually, lesions resolved between 12 days and 8 weeks [30].

Another cutaneous manifestation of COVID-19 infection, in children, is erythema multiforme (EM), a condition of hypersensitivity [31]. Unlike adults, in pediatric patients, EM is sometimes associated with chilblain-like lesions, as many studies reported. Another notable difference would be that these children were most asymptomatic, or had mild gastrointestinal or respiratory symptoms [32-35].

As reported in the specialty literature, about 10-20% of pediatric patients with COVID-19 infection, experienced urticarial rash, and despite of this cutaneous manifestation, were asymptomatic. Affirmative, they had household contact with confirmed patients with SARS-COV-2 [36].

Vesicular exanthem is, most often, reported in middle-aged women, and rare, in children. It is a varicella-like papulovesicular rash, and it is characterized by disseminated vesicles, papules, crusted or hemorrhagic lesions, located on the trunk, and sometimes on the limbs. Patients associate itch. The eruption appears 3 days after respiratory symptoms [37-44].

Perhaps the most discussed pathology associated with pediatric COVID-19 infection is Kawasaki disease-like inflammatory syndrome (pediatric inflammatory multisystem

syndrome=KDSS) [31]. KDSS affects 1.5-7% of patients with KD. Laboratory findings reveal severe inflammatory syndrome with high levels of CRP, procalcitonin and IgE. Also, the heart is affected with myocardial dysfunction and decreased peripheral vascular resistance [45, 46]. As for skin manifestations in PIMS, they vary between nonexudative conjunctivitis, polymorphic rash, perineal or face desquamations or even hand and feet anomalies (erythema, firm induration) [47-49].

Also, there are many other nonspecific eruptions associated with SARS-COV-2 infection in pediatric patients, like: maculopapular exanthems, purpuric rashes, pityriasis rosea-like eruptions, or even oral findings [50].

## CONCLUSIONS

It is still unclear whether these injuries are caused by SARS-CoV-2 infection, new studies being needed to establish with more certainty the characteristics of skin lesions. That could help establish the need for testing, as these patients can inadvertently infect others, thus spreading the new disease. Based on our findings and the review of the literature, we want to warn physicians that erythematous rash (simultaneously or preceding pyrexia) in the actual crisis of COVID-19 pandemic can be the primary evidence of this infection, even without any respiratory symptoms. During this current context of COVID-19 pandemic, dermatologists around the world have the opportunity to analyze the skin manifestations of the new coronavirus infection, images helping other colleagues identify them in their patients. Another important challenge is represented by COVID-19 infected, pediatric patients with polymorphic eruptions. Unlike adults, children are most often asymptomatic. More than that, laboratory tests for SARS-COV-2 are negative, so it becomes very difficult to establish the association between them. Fortunately, children react well, and, most often, cutaneous manifestations remit spontaneously, without complications. A basic principle of medicine is becoming even more important in this period: "the more you see, the more you know, and the more you know is the more you see".

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