

COVID-19 ASSOCIATED SKIN MANIFESTATIONS: A CASE SERIES

OANA TIUCĂ *, **, ALEXANDRU OANȚĂ ***, MIRCEA AMBROS*, ROXANA ILCUȘ*,
ANCA GÎNȚ*, SMARANDA ȚĂREAN ***, ALEXANDRA PAȚA*, SIMONA SZASZ****,
HORAȚIU MOLDOVAN*, OVIDIU S. COTOI****, *****, SILVIU HORIA MORARIU *, **

Summary

Introduction: The clinical picture of SARS-CoV-2 virus infection is dominated by respiratory symptoms. Various skin manifestations have been described in association with SARS-CoV-2 infection. In this article, we try to provide an overview of some of the possible skin manifestations associated with COVID-19, starting from a series of cases encountered in clinical practice.

Clinical cases: We report several cases encountered in clinical practice regarding the skin picture of SARS-CoV-2 virus infection.

Conclusions: Epidemiological status' investigation should be an important step when approaching a dermatological patient in the current pandemic context.

Keywords: COVID-19, SARS-CoV-2, skin manifestations.

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Introduction

Since the first cases were reported in December 2019 in Wuhan, more than 300 million cases of infection with the new coronavirus SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus-2), COVID19 (Coronavirus Disease 19) have been reported worldwide. Although the clinical picture is dominated by respiratory symptoms, extrapulmonary damage has also been reported. Among these, various skin manifestations have been described. In this article we aim to present several skin conditions connected with COVID-19, starting from a series of cases encountered in clinical practice in patients consulted in the specialized dermatology services or online, between May and November 2021.

Clinical cases

Case no. 1. We present the case of a 28-year-old male BP patient, from the urban area, with RT-PCR (reverse transcription polymerase chain reaction) confirmed COVID-19 presenting with mild headache, rhinorrhea, and dry cough. 8 days after the confirmation of the infection, the patient developed a single erythematous round-oval plaque, of 5 x 4 centimeters (cm) in size, well defined, with fine scales more obvious on the periphery [Fig. 1]. 7 days after the initial lesion, the patient developed a slightly pruritic erythematous-squamous rash on the chest and abdomen, consisting of erythematous patches covered with fine scales, located at the periphery of the erythema as a scaly border [Fig. 2]. Based

* Dermatology Clinic, Mureș Clinical County Hospital.

** Department of Dermatology, UMFST "G.E.Palade" Târgu-Mureș.

*** SC Dermamed SRL Brașov.

**** County Emergency Clinical Hospital of Târgu-Mureș.

***** Department of Pathology, Mureș Clinical County Hospital.

***** Department of Pathophysiology, UMFST "G.E.Palade" Târgu-Mureș.



Figures 1 and 2. Pityriasis rosea lesions. Ill-defined erythematous patches, with fine scales. Heraldic plaques.

on the clinical aspect and evolution of the lesions, it was established the diagnosis of pityriasis rosea Gibert associated with COVID-19. The patient was prescribed local treatment with methylprednisolone aceponate 1 mg/g emulsion (Advantan Milk) once daily. At the 21-day follow-up, a complete resolution of the lesions was noticed.

Case no. 2. Patient MV, a 64-year-old male patient from the urban area, required hospitalization in the specialized clinic for RT-PCR confirmed COVID-19 presenting with marked shortness of breath on exertion, bilateral posterior chest pain, mucopurulent cough, and fever (38.2°C). 12 days after confirmation, the patient developed an erythematous-papular rash. The lesions had an intricate aspect, presenting with bright red erythematous papules, resembling those encountered in Gianotti-Crosti syndrome, in extensor areas (elbows and knees) and on the extremities (dorsal faces of the hands and feet) [Fig. 3, Fig.4] and with ill-defined erythematous patches, with a tendency towards confluence, in the axillary and inguinal folds and on the abdominal flanks. Laboratory tests did not identify any infectious foci, but showed elevated levels of gamma-glutamyltransferase (GGT) (100 U/L; NV: 12-64 U/L), with normal levels of direct, indirect and

total bilirubin and negative serological reactions for hepatitis B and C. Based on the appearance and distribution of the lesions, it was established the diagnosis of maculopapular exanthema associated with COVID-19. The patient underwent treatment with methylprednisolone aceponate 1 mg/g emulsion (Advantan Milk) twice daily and levocetirizine 5 mg (Xyzal) 1 tablet/day, with the complete resolution of the lesions in a week.

Case no. 3. A 54-year-old female patient, DP, from the urban area is consulted for slightly pruritic erythematous macules and papules located on the posterior face of the forefeet. The patient was confirmed with COVID-19 by rapid antigenic test 4 days before the onset of skin lesions [Fig. 5]. Based on the clinical aspect, it was established the diagnosis of maculo-papular eruption, most likely induced by COVID-19. Treatment with mometasone furoate 1 mg/g cream (Elocom) twice a day was started, with favorable evolution and the disappearance of the lesions in 10 days.

Case no. 4. A 71-year-old male patient, VV, from urban area with RT-PCR confirmed COVID-19 presenting with dyspnea at exertion and at rest, fatigue, chest pain, rhinorrhea, dysphagia, vertigo, and fever (38.7°C) developed during hospitalization for SARS-CoV-2 infection tense



Figures 3 and 4. Erythematous macules and papules located on the upper and lower limbs.



Figure 5. Acral erythematous macules and papules.



Figure 6. Hemorrhagic bullae, located on the internal part of left calf.

hemorrhagic vesicles and bullae, located on the inner part of the left leg, accompanied by multiple linear excoriations [Fig. 6, Fig. 7] and hematic crusts, as well as an abdominal giant purplish suffusion (measuring approximately 30 cm in the long axis) [Fig. 8]. Laboratory examinations revealed a gradually decrease in platelets number (from 143300/mm³ at admission to 73260/mm³ at discharge). Based on clinical and laboratory data, the diagnosis of immune thrombocytopenic purpura associated with SARS-CoV-2 infection is established. Systemic treatment with prednisone

0.5 mg/kg/day is initiated, with a favorable evolution and an increase in platelets' number after 14 days of treatment.

Case No. 5 A 20-year-old female patient, CL, from the urban area presented to our clinic 2 months after SARS-CoV-2 infection, manifested by rhinorrhea, cough, and generalized fatigue. Local dermatological examination



Figure 7. Linear excoriations, hematic crusts.



Figure 8. Giant abdominal suffusion. Post-bullous erosions.

revealed ill-defined erythematous plaques and plaquards, located on the flexural areas, erosions with linear distribution, crusts located predominantly at the anterior face of the forearms, areas of lichenification and marked skin xerosis [Fig. 9, Fig. 10]. The patient mentioned a personal history of asthma, autoimmune thyroiditis, allergic rhinitis, and documented dust allergy and denies previous existence of any similar lesions to those present at the time of the

consultation. Laboratory tests revealed peripheral eosinophilia (8.2%), with no other infectious foci identified. Based on personal history, clinical appearance and laboratory investigations, the diagnosis of COVID-19-triggered atopic dermatitis is established. Treatment with methylprednisolone aceponate 1 mg/g cream (Advantan) once daily and rupatadine 10 mg (Tamalis) 1 tablet/day was started, with favorable evolution and partial persistence



Figures 9 and 10. Ill-defined erythematous plaques, located on the flexural areas, linear erosions, crusts.

of atopic dermatitis lesions at the follow-up performed one month after.

Case No. 6 A 51-year-old-female patient, MM, from the urban area, with RT-PCR confirmed COVID-19 manifested by cough, runny nose and headache was consulted by telemedicine. The patient developed four days after COVID-19 confirmation persistent erythematous-edematous plaques and plaquards, with associated itch, located mainly on the buttocks and flanks. Based on the clinical appearance, it was established the diagnosis of COVID-19 associated urticaria-like rash. Systemic treatment with prednisone 20 mg/day, with gradual tapering and mometasone furoate cream 1 mg/g (Elocom) once daily was started, with complete resolution of the lesions within 7 days.

Cases no. 7 and 8. A 55-year-old female patient, OP, from the urban area, was consulted for diffuse hair loss, more pronounced on the temples, which started 10 weeks after COVID-19 manifested by headache and rhinorrhea [Fig. 11]. The patient denies any major stress, except the one caused by SARS-CoV-2 infection. A 73-year-old female patient, A.M, from the urban area presented with marked hair loss 8 weeks post-

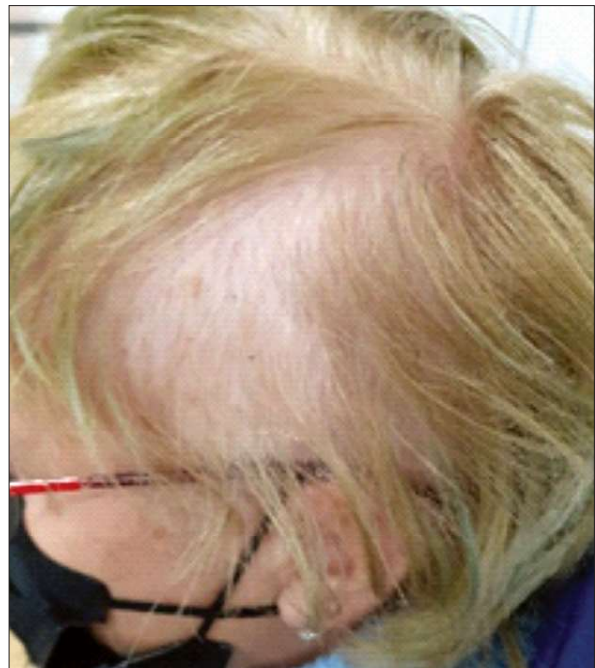
COVID-19 [Fig. 12]. Based on the clinical appearance and patients' history, the diagnosis of COVID-19 induced telogen effluvium was established.

Discussions

The cutaneous manifestations associated with COVID-19 take on various appearances. The first report of COVID-19 associated skin lesions belongs to Recalcati [1]. Although cutaneous manifestations in COVID-19 have been described in a variety of studies, the pathophysiological mechanisms are still incompletely understood [2]. In addition, it is difficult to differentiate between skin lesions induced by SARS-CoV-2 and the reactions resulting from the administration of different drugs used as part the treatment plan. Most reactions reported in the literature have a self-limiting evolution [3].

4 main types of COVID-19 associated skin reactions have been proposed: acro-papular rash, exantematous, vascular and urticaria-like pattern [4].

Morbilliform and papulo-vesicular rash varicella-like may be associated with COVID-



Figures 11 and 12. Effluvium telogen.

19. Maculo-papular rash accounted for 47% of skin manifestations in a study conducted by Galvan Casas et. al [5]. The lesions are located preferentially on the trunk and limbs, are generally associated with pruritus, and have clinical and histopathological similarities with the morbilliform rash found in other viral infections [4]. In addition, it appears that the onset of skin signs and symptoms is secondary to systemic ones [9]. Clinical pictures suggestive of pityriasis rosea Gibert [10, 11] and Gianotti-Crosti syndrome [12,13], like in the case of two of our patients, have been reported in association with SARS-CoV-2 infection. We consider that the rash presented by patient MV, would allow, based on its clinical aspect, evolution and laboratory data, the inclusion of SARS-CoV-2 among the potential etiological factors of Gianotti-Crosti syndrome. As such, testing for SARS-CoV-2 in patients with maculopapular rash should be considered. The link between the infection and the rash is probably due to the impact of the new viral agent on the immune system and the subsequent response. Papulo-vesicular eruptions in COVID-19 are different from chickenpox based on the predominant involvement of the trunk and the absence of pruritus [14].

Acro-papular eruptions are found in various viral diseases, the pathophysiological mechanisms implying the existence of circulating immune complexes or delayed hypersensitivity reactions. As in the case of one of our patients, this clinical aspect may be associated with COVID-19 [21], suggesting the possibility that the same mechanisms may be involved in SARS-CoV-2 infection.

Vascular damage in COVID-19 may present on the skin as chilblain-like lesions and vaso-occlusive lesions, such as livedoid, purpuric, and necrotic lesions. Unlike chilblain-like lesions, which occur predominantly in young people and are relatively common [5], vaso-occlusive lesions tend to occur more frequently in the elderly [15] and are associated with severe pneumonia and increased mortality [5].

COVID-19 is associated in some cases with the development of an immune or autoimmune response [16], most likely through molecular mimicry [17]. Molecular similarity between viral antigens and those produced by the patients'

platelets causes cross-immune reactions, leading to increased platelet clearance in these patients [18]. As such, thrombocytopenic immune purpura may be a key manifestation of thrombocytopenia found in patients with COVID-19. Small-vessel vasculitis is another possible manifestation of COVID-19, most often presenting with hemorrhagic bullae [19,20]. In this case, the skin lesions are the result of a microvascular thrombosis.

Urticarial reactions, first observed by Recalcati, tend to occur simultaneously with or immediately after systemic symptoms and are associated with moderate forms of the disease. Itching was present in most cases [5]. In addition, the association between urticaria and fever has been reported as an early sign of COVID-19, even without any respiratory symptoms, in 3 patients [6,7,8]. Isolation of patients with urticaria and fever may be warranted, especially if there is a positive epidemiological context, to prevent the transmission of SARS-CoV-2.

Effluvium telogen is found in patients usually 2 to 3 months after COVID-19. In the case of SARS-CoV-2, elevated cytokine levels appear to initiate telogen effluvium by destroying the cell matrix [22].

Currently, data on the association between COVID-19 and atopic dermatitis are limited. The common pathophysiological mechanisms that may explain a link between atopic eczema and COVID-19 are the following: identification of the same 14 up-regulated genes in atopic dermatitis and COVID-19; identification of a common locus on chromosome 14 for atopic dermatitis and COVID-19 and the fact that patients often have allergic rhinitis, which involves an aberrant response involving ACE2 receptors, the same receptors that are involved in COVID-19 [23]. In our case, we can consider SARS-CoV-2 infection a trigger for atopic dermatitis, either directly or, more likely, through immune-induced changes.

Conclusions

The spectrum of COVID-19 associated skin manifestations varies and is not completely known. Considering the existence of mild or even asymptomatic forms, the reluctance of some patients to declare specific symptoms of the

infection, we believe that the presence of certain skin lesions can and should raise the suspicion of SARS-CoV-2 infection and requires further investigation. A more accurate outline of these manifestations associated with SARS-CoV-2 infection would allow a better understanding of

the impact that this infection has on the human body. Investigating the epidemiological status of patients and corroborating it with cutaneous manifestations are essential steps in approaching the dermatological patient in a pandemic context.

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Conflict of interest
NONE DECLARED

Correspondance addresses: Alexandru Oanță
S.C Dermamed S.R.L Brașov,
e-mail: oanta_alexandru@yahoo.com