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Cutaneous autoimmune diseases during COVID-19 pandemic

Editor

The pandemic of infection with the severe acute respiratory syndrome coronavirus (SARS-CoV-2) causing the atypical pneumonia coronavirus disease 19 (COVID-2019) has become a global health emergency. In parallel with the spread of the infection, there is new information on cutaneous involvement reminiscent to autoimmune diseases and concerns about the risk of disease and management of patients with cutaneous autoimmunity under immunosuppression.

COVID-2019 mainly presents with fever, cough, loss of smell and taste, myalgia and fatigue.[1] Main complication of the infection is progression to acute respiratory distress syndrome (ARDS), coagulopathy, vasculopathy, cardiovascular failure and a cytokine storm syndrome requiring intensive care for days or even weeks.[1,2]

The risk factors for more severe COVID-19 infection are cardiovascular illnesses, diabetics, renal failure, respiratory failure, morbid obesity and older age (>65).[3,4]

Cutaneous symptoms of COVID-19 include petechial skin rash[5,6] or digitate scaly thin plaques[7] associated with severe respiratory disease (Table 1). A maculopapular urticarial rash may present as early sign of disease[8–10] or during disease[11] without a yet known association to severity.[12,13] There was also a case of pityriasis rosea like rash in one patient with mild febrile COVID-19.[14] In young children, infection with SARS-CoV-2 can be associated with Kawasaki syndrome including the maculopapular oedematous rash and conjunctival injection.[15,16]

Mild forms of disease in younger individuals seem to present with chilblain-like lesions on acral locations especially the toes[17] (Table 1). The skin appears shiny red and is painful (Fig. 1). The lesions resolve spontaneously after weeks and indicate a rather favourable outcome.[17] The symptoms may represent a form of inflammation induced by small vessel endotheliitis.[17] In histological section, these lesions may have a slight vacuolar

Table 1 Cutaneous lesions associated with COVID-19

Cutaneous findings	Histopathology	COVID-19	Reference
Acral chilblain lesions	Vacuolar interface dermatitis and superficial and deep perivascular and periadnexal lymphohistiocytic infiltrates	Mild or none, late symptom	17–19,21,27
Violaceous papules and digital swelling	Diffuse perivascular involvement of the dermis and hypodermis by a dense lymphoid infiltrate	Mild or none, late symptom	20
Symmetrical petechial skin rash on buttocks, thighs that might be similar to dengue virus exanthema	Superficial perivascular infiltrate with erythrocyte extravasation, dermal papillary oedema, and scattered dyskeratotic keratinocytes	Associated with severe acute respiratory syndrome	5,6
Digitate scaly thin plaques	Spongiosis in the epidermis and mild papillary oedema with lymphohistiocytic infiltrate in the dermis	Associated with severe acute respiratory syndrome	7
Erythematous and oedematous non-pruritic annular fixed plaques involving the upper limbs, chest, neck, abdomen and palms	Superficial perivascular lymphocytic infiltrate, papillary dermal oedema, mild spongiosis, lichenoid and vacuolar interface dermatitis, dyskeratotic basilar keratinocytes	Mild	9
Maculopapular and urticarial rash		Early symptom	8,10
Maculopapular symmetrical rash	Superficial perivascular lymphocytic infiltrate, papillary dermal oedema, ectatic vessels, vacuolar interface dermatitis[14]	Mild, associated mild lung disease	11,13
Maculopapular rash in young children		Kawasaki syndrome associated with COVID-19	15
Pityriasis rosea		Mild	14

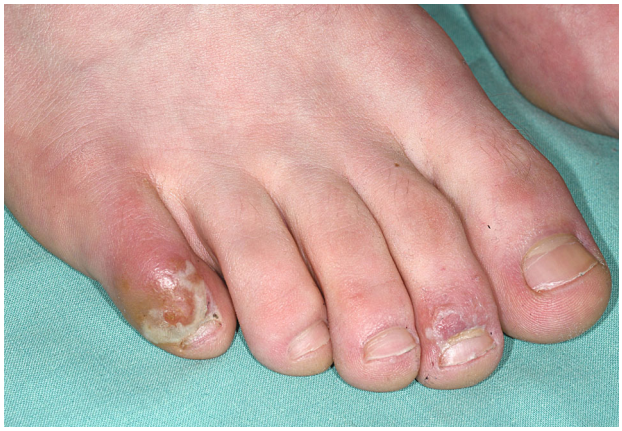

Figure 1 Chilblain lesions on acral locations occurring in a young man six weeks after visiting an area with high SARS-CoV-2 infection rate. He did not develop respiratory symptoms. Late swab testing at onset of chilblain lesions was negative. Lesions resolved with topical immunosuppressive treatment. There were no systemic or laboratory signs of autoimmunity.

interface dermatitis and a superficial and deep perivascular and periadnexal lymphohistiocytic infiltrate.[18] Reports from Italy and France documented an outbreak of chilblain-like lesions contemporarily to COVID-19 epidemic.[19–21] Despite the low rate of positive mRNA or antibody testing, the coincidence of both events is highly suggestive for direct correlation.

The induction of the lesions might be related to a direct viral effect, pathogenic priming[22] or mediated by upregulation of the antiviral cytokine type I interferon. Type I interferons cause a stimulation and activation of the immune response and a thrombotic microangiopathy by a dose-dependent toxic effect on the microvasculature.[23] Patients with high levels of type I interferon-mediated autoimmune diseases or type I interferonopathies frequently develop chilblain lesions.[21,24–26]

Chilblain or erythema multiforme like acral ischaemic lesions were also observed contemporarily to COVID-19 epidemic in Spain.[27] None of the 132 patients reported developed COVID-19 pneumonia or any other complication. The authors hypothesize that the latency time of up to 30 days between mild COVID-19 symptoms and skin manifestations, and the low positive rate for nasopharyngeal swabs (only 2 positive results) suggest that these chilblain-like ischaemic lesions represent a late manifestation of SARS-CoV-2 infection.[27]

There are no large reports on the frequency of infection or the risk of severe COVID-19 in patients with autoimmune diseases involving the skin such as lupus erythematosus, dermatomyositis, systemic sclerosis and autoimmune bullous diseases (Table 2). Currently, limited data suggest that patients with autoimmune disorders, especially rheumatoid arthritis, and immunosuppression do not appear to be more severely infected by COVID-19.[28–30]

However, immunosuppression and especially long-term hydroxychloroquine treatment did not prevent infection of lupus patients.[31] These patients may get infected and can also suffer from severe COVID-19 if they have concomitant risk factors such as obesity or chronic kidney disease[31,32] (Table 2).

Immunosuppressive treatment is necessary for the management of autoimmune diseases, and it is known from patients with rheumatoid arthritis that the risk for viral infection is increased if the disease is not controlled.[33]

Therefore, we should continue immunosuppressive treatment in patients with autoimmune diseases and not postpone diagnostic procedures if ever possible.[30] There are concerns especially regarding the long-term immunosuppressive effect of

Table 2 Outcome of patients with autoimmune diseases and COVID-19

Autoimmune disease (number of patients)	Relevant comorbidities[†]	Ongoing treatment	Outcome 19	Reference
Systemic sclerosis (1)	Yes	Tocilizumab	Mild	38
Granulomatosis with polyangiitis (1)	Yes	Rituximab	ARDS, survived	39
Systemic lupus erythematosus (17)	Yes	Hydroxychloroquine, other immunosuppressives interrupted	14 admitted to hospital 2 died	40
Rheumatoid arthritis, spondyloarthritis (4)	Yes	DMARDs, temporarily withdrawn	3 mild 1 hospitalized, survived	41
Systemic sclerosis (1 with positive swab of 123 total patients with connective tissue diseases),	Yes	Hydroxychloroquine, rituximab	severe pneumonia, died	42
Psoriasis, psoriatic arthritis, rheumatoid arthritis, ulcerative colitis, Crohn's disease and ankylosing spondylitis under (86)	Yes	Methotrexate, hydroxychloroquine, JAK inhibitors, TNF inhibitor or IL-17-, IL-23-, IL-12/23 blocker	mild 14 admitted to hospital, 1 died	43
Pemphigus vulgaris (1)	None	Mycophenolate mofetil	Nausea and fever, mild	44
Psoriasis (1)	None	IL-17 inhibitor	No symptoms	45
Psoriasis, arthritis, Crohn (1)	None	IL-23 inhibitor	Mild	46

DMARDs, methotrexate, etanercept, tofacitinib, leflunomide, abatacept; IL, interleukin.
[†]Older age > 65, obesity, cardiovascular disease, diabetes, kidney disease, lung disease, smoker

rituximab used for treatment of pemphigus.[34] The initiation of rituximab in patients with autoimmune bullous disease must be weighed against the risks of conventional immunomodulatory regimens on an individual basis.[35]

To reduce the risk of infection routine face-to-face appointments could be delayed if they are not urgently needed or substituted by teledermatology.[36] Patients should be encouraged to update appropriate flu and pneumococcal vaccination and maintain the hygiene and protection measures.

To improve current knowledge on the disease course of COVID-19 in patients with autoimmune disease, their risk of infection and potential treatment options, all cases should be reported to the COVID-19 registries set by organization such as the EULAR, EUSTAR, task force for autoimmune bullous diseases, the German network for systemic sclerosis and local epidemiology registries.[37]

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The patient in this manuscript has given written informed consent to the publication of his case details.

Conflicts of interest

The authors have declared no conflict of interest.

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Occupational skin disease during the COVID-19 pandemic, as captured in a Dermatology staff clinic in the United Kingdom

Editor,

A dermatology walk-in clinic available to all hospital staff (HS) was commenced to treat skin problems related to personal protective equipment (PPE) during the COVID-19 pandemic. An observational case series was conducted in a single district general hospital within Wales (United Kingdom) to record the dermatological diagnoses. Our participant sample is comprised of clinical and non-clinical staff working in COVID-19 and non-COVID-19 areas of the hospital. Over the data collection period (6 weeks), a total of 72 patients attended the clinic of whom 62 were females and 10 were males (mean age = 43 years). Data are comprised of demographic data, current occupation (shown in Table 1), duration of symptoms, past medical history, regular medication and treatment interventions. An analysis of the clinical diagnoses seen is reported in Table 2.

Irritant hand dermatitis caused by increased frequency in hand washing and use of alcohol-based hand sanitizers was the most common symptom, affecting 62.5% of patients in agreement with previous research.[1] Similar to Balato et al.,[1] our treatment regimen advised regular applications of fragrance-free emollients. To improve treatment acceptance and compliance, we offered a lighter emollient (cream or lotion) to be applied during the day and a lipid-rich emollient (ointment) to be applied at home. We recommended the use of a topical steroid preparation for patients with inflamed skin. Information leaflets were provided, and soap substitutes were suggested for home use. Soap substitutes have not been validated to eradicate SARS-CoV-2 and therefore were not proposed for use in the work environment, as supported by the British Society of Cutaneous Allergy guidance.[2]

Pressure-related facial symptoms, due to mask usage, were also seen in 3 patients (4%) but not observed in as high percentages as Jiang et al.[3] Our participant inclusion criteria included all staff rather than only staff caring for COVID-19 patients, and advice had been provided for the prevention of adverse effects, which could explain the difference. Skin protectant film was issued to staff for use prior to mask application and instructions about daily use of an emollient as a skin barrier and avoidance of mask overtightening was given. Facial cutaneous symptoms can lead to more frequent facial touching for relief of mechanical pressure, therefore increasing the risk of infection. We offered hydrocolloid dressings for use on pressure points on the face. To ensure an appropriate mask seal is not compromised by this intervention, a repeat 'fit mask testing' with the dressings already applied was recommended. Worsening of pre-existing skin conditions was managed following standard treatment of care.