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Skin aspects of COVID-19

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ABSTRACT

Background. COVID-19 is a disease that has changed the realities of society, medical personnel, and patients worldwide. The long-term course of the COVID-19 pandemic has allowed us to observe the many changes occurring during this disease. Lesions resulting from SARS-CoV-2 infection manifest in the lungs and other systems, including the skin.
Methods. The paper presents a comprehensive description of skin lesions occurring. The course of COVID-19 was based on a literature review and my experience acquired in the intensive care unit.
Results. The mechanism of formation of the cutaneous manifestations in SARS-CoV-2 infected patients due to the course of the disease was discussed. Skin lesions from the treatment, hospitalisation and immobilisation of the patient were also considered. The causes of developing bedsores are also highlighted, with examples provided with photographs. In addition, the paper includes tables comparing the appearance of skin lesions with the severity of the course and caused by pharmacotherapy, which may be a practical instrument in clinical practice.

Conclusions. Cutaneous manifestations may be the single symptom of COVID-19, which may facilitate the diagnosis of this disease. It seems necessary to extend the diagnostics of skin lesions during COVID-19 to understand their pathogenesis. Inadequate care due to staff shortages or inadequate education may lead to the development of pressure sores. Implementing solutions that could protect patients and staff is imperative. In the event of future pandemics.

Introduction

COVID-19 is a disease that has changed the realities of society, medical personnel, and patients worldwide. The long-term course of the COVID-19 pandemic has allowed us to observe the many changes occurring during this disease. Patients with COVID-19 require specialised care from physicians of many specialities. Lesions resulting from SARS-CoV-2 infection manifest in the lungs and other systems, including the skin.

Vascular damage and hypercoagulability are characteristic manifestations [1] of COVID-19 disease. These results from the pathomechanisms discussed in detail in this article can cause vascular skin lesions. The clinical manifestation of skin lesions is also presented, and the different types of skin lesions are summarised along with the duration and severity of COVID-19.

This paper discusses the mechanisms of cutaneous manifestation of COVID-19, which results from hypercoagulability and endothelial dysfunction, prolonged patient stay and inadequate decubitus prophylaxis due to staff shortages, among other factors.

COVID-19 skin lesions may manifest in association with the patient's treatment.

The skin lesions observed in patients with COVID-19 were selected based on a literature review.

Methods and materials

A literature search was conducted, using electronic databases PubMed and The Lancet for the terms 'COVID-19' and 'SARS-CoV-2' in combination with 'skin manifestations', 'skin lesions', 'pharmacotherapy', 'cutaneous manifestations', 'pressure ulcers', 'pressure injuries', 'endotheliopathy'. The paper was based on 80 literature sources.

Endotheliopathy and coagulopathy in the course of COVID-19

Endotheliopathy and coagulopathy are becoming increasingly common in the course of COVID-19 disease [2]. For this reason, many scientific works focus on understanding these disorders' pathophysiology. This chapter discusses the main mechanisms of derangement of hemostasis during SARS-CoV-2 infection.

SARS-CoV-2 virus penetrates human cells through the angiotensin two converting enzyme (ACE2) receptor [3]. Consequently, ACE2 receptor activity is lost, causing a reduced ability to inactivate angiotensin two and reduced production of angiotensin 1–7 [4]. The angiotensin 2 vasoconstricts severely and causes vascular inflammation. The imbalance between angiotensin 1–7 deficiency and angiotensin two hyperactivity has caused thrombosis and inflammation in experimental models [4]. A specific marker of glycocalyx degradation is angiopoietin-2. Angiopoietin-2, a crucial mediator of glycocalyx damage, regulates endothelial homeostasis, including angiogenesis and inflammation [5]. Therefore, the study conducted by Smadja et al. presents the predictive significance of angiopoietin-2 in COVID-19 patients admitted to the intensive care unit. It was shown that angiopoietin-2 level above 5000 pg/ml is a potential criterion for admission of patients to the intensive care unit (Sensitivity = 80.1%, Specificity = 70%, Positive Predictive Value = 72.7%, Negative Predictive Value = 77%) [5]. So far, it has not been shown whether endothelial damage is caused directly by SARS-CoV-2 virus infection or by congenital, autoimmune processes based on the "cytokine storm" [6]. "Cytokine storm" during COVID-19 is characterised by increased expression of IL-6 and TNF-α. Most probably, many factors influence the degree of endothelial damage and, thus, the severity of symptoms during COVID-19.

Coagulopathy associated with COVID-19 (CAC) is most commonly manifested by elevated D-dimers, products of plasmin-mediated fibrin degradation, related to the severity of COVID-19 infection. They are an independent risk factor of mortality [7]. The analysis of 1099 patients with laboratory-confirmed COVID-19 infection showed that D-dimer ≥ 0.5 mg/dL was present in 46.4% and 60% of those with severe disease status [8]. In the analysis, including 191 patients, we observed that the odds ratio (OR) of mortality for D-dimer > 0.5 µg/ml was 2.14 (p = 0.52), and for D-dimer > 1 µg/ml was 18.42 (p = 0.0033). The ACTIV-4B clinical trial showed that about 10% of all patients infected with SARS-CoV-2 have elevated D-dimer levels, demonstrating the significant role of coagulopathy in COVID-19 [9]. Fibrinogen is a glycoprotein involved in blood clotting, of which an elevated blood concentration indicates coagulopathy [10]. A study conducted by Ranucci et al. showed that at the time of admission of COVID-19 patients, fibrinogen levels were four times higher than the upper limit of normal (ULN) for fibrinogen (ULN for fibrinogen-400 mg/dL; p = 0.001) [10]. Mean activated partial thromboplastin time (APTT) was slightly prolonged in severe COVID-19 patients compared to mild (29.7 seconds vs 26.9 seconds; p = 0.0003) [11]. Thrombocytopenia (<150 × 10^9/l thrombocytes in the blood) in sepsis correlates with severity and mortality, but no such correlation was demonstrated with COVID-19 [12]. The study presented by McConnell et al. has confirmed the significant impact of interleukin-6 (IL-6) in the process of coagulopathy and endotheliopathy [13]. The study by Ranucci et al. has shown a correlation between the presence of inflammation and coagulopathy by noting high fibrinogen and high IL-6 levels in patients with confirmed SARS-CoV-2 infection [10]. In addition, IL-6 trans-signalling leads to increased production of pro-coagulation factors such as factor VIII and vWF [13].

In summary, coagulopathy and endotheliopathy occur most frequently in critically ill, hospitalised patients with COVID-19. The markers used to assess endotheliopathy are angiopoietin-2, IL-6, factor VIII, vWF, and soluble thrombomodulin [14–17]. Soluble thrombomodulin, vWF, and angiopoietin-2 are predictive markers of severe COVID-19 infection, while soluble thrombomodulin, based on vWF, is a predictive factor of mortality in patients with COVID-19 [14,18]. On the other hand, we assess coagulopathy by D-dimer level, IL-6, fibrinogen, PT and APTT time, and platelet count [8,11,19]. Only D-dimer level is a predictive factor of mortality during COVID-19 [7]. The other markers need further studies to determine their usefulness in assessing the severity of COVID-19 infection.

Cutaneous manifestations of COVID-19

The incidence of skin lesions in COVID-19 ranges from 0.2% to up to 29% in patients infected by SARS-CoV-2 [20–23]. Vesicular eruptions, maculopapular exanthema, urticarial eruptions, livedo or necrosis, and chilblain lesions are the most common skin presentations during COVID-19 [23].

According to the pathomechanism, cutaneous manifestations due to the COVID-19 course may be divided into vascular-related and inflammation-related lesions [24].

Vesicular eruptions are lesions similar to those occurring in the course of chickenpox [21]. These lesions are most commonly located on the trunk and appear as monomorphic vesicles in contrast to the polymorphic vesicles seen in chickenpox [23]. These lesions occur in approximately 15% of patients before presenting other symptoms associated with COVID-19 [23]. Vesicular eruptions resolve in approximately 10–12 days and are associated with moderate to severe SARS-CoV-2 infection [25]. The lesions may be accompanied by pruritus [26].

Maculopapular exanthema occurs along with other COVID-19 symptoms, usually in patients with severe disease. The mortality rate for patients with this type of lesion is estimated to be 2% [27]. These lesions typically appear more than 20 days after the first symptoms of COVID-19, resolve in 7–11 days, and are accompanied by pruritus in 50% of cases [23,24]. This is the most common form of skin lesions during the COVID-19 [28]. These lesions may result from a direct reaction to a viral infection or an adverse drug reaction [24,25].

Urticarial eruptions are most common on the trunk [25]. They occur in moderate to severe cases of COVID-19 and resolve after about 6–8 days,

often parallel with systematic symptoms [23,24]. Vesicular, maculopapular and urticarial eruptions are classified as lesions caused by inflammation. Due to elevated amounts of inflammatory cytokines caused by SARS-CoV-2 infection, perivascular infiltration of inflammatory cells develops—consequently, a dilatation of vascular vessels and oedema result in inducing skin eruptions formation. ACE2-related mechanisms and the direct effect of the SARS-CoV-2 virus on the epidermis (basal layer and keratinocytes) also have additional influence, which is also responsible for this type of skin manifestation.

Livedo or necrosis and other symptoms of COVID-19 [23]. These lesions are secondary to COVID-19-induced thrombotic vasculopathy [25] occur. They have been observed to occur most frequently in elderly patients who undergo severe disease. They are characterised by a high mortality rate of approximately 10% [26]. Chilblain (COVID Toes) are macular lesions resembling frostbite, occurring in young patients with a mild to asymptomatic disease course (24,29,30). Skin symptoms resolve in about 12–14 days, and 1/3 of people with these lesions experience pain and itching [31].

The severity of infection is related to the type of skin lesions observed [32]. From the mildest course of COVID-19 in people with chilblain to those requiring hospitalisation and intensive care with livedo or necrosis lesions [23].

Skin lesions can be divided into early and late onset, depending on their onset. Early manifestations include urticaria eruptions and maculopapular exanthema, whereas late lesions include chilblain [33].

Depending on the time of appearance of the skin lesions, the nature of the lesions can be determined. Lesions that appear up to 7 days after the onset of the first symptoms of COVID-19 usually have the character of a viral rash (**Figure 1**), whereas lesions that appear seven days after the first symptoms of SARS-CoV-2 infection typically have a vascular origin [34]. Lesions of vascular origin include livedo or necrosis and chilblain lesions [34]. A summary of skin lesions during COVID-19 is shown in **Table 1**.

Among the lesions observed during COVID-19, noteworthy are those formed due to the so-called "skin failure." These lesions develop during the acute, critical period of hypoperfusion and multi-organ failure. They often assume a butter-

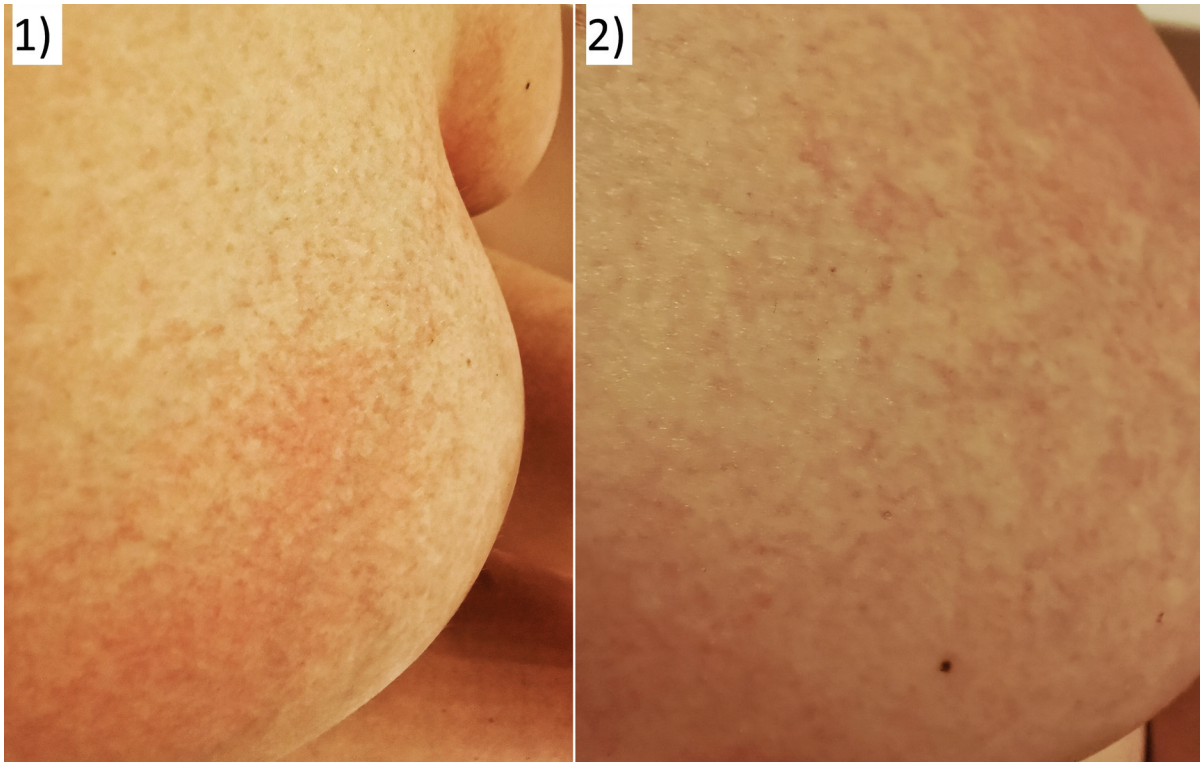

Figure 1. Viral exanthem during COVID-19 localised on the breasts.

Table 1. Summary of skin lesions in the course of COVID-19.

Cutaneous manifestation	Potential causes in COVID-19	Time to lesions resolve	Frequency	Course of COVID-19	Most common localization	Associated cutaneous symptoms	Association with other COVID-19 symptoms	Mortality	Differential diagnosis	References
Inflammatory and exanthematous rashes										
Vesicular eruptions (+ papulovesicular exanthem/varicella-like lesions)	direct viral damage to basal keratinocytes	8–12 days	9%	moderate to severe	trunk	pruritus	3 days after systemic symptoms	lack of data	Herpes infections and Grover's disease[2]	24–27
Maculopapular exanthema	drug-induced or a direct reaction to a viral infection	7–11 days	47%	severe	trunk	pruritus	more than 20 days after the first symptoms of COVID-19; simultaneously or immediately after other symptoms of the disease	2%	other viral rashes and drug-induced skin reactions	23, 24, 27, 36
Urticarial eruptions/rash	drug-induced or "cytokine storm"; nonspecific mast cell activation, direct endothelial damage, antigen-antibody deposits, activation of complement, activation of the kinin pathway	6–8 days	16–19%	moderate to severe	trunk and extremities	pruritus	onset concurrently with systemic symptoms	2%	drug-induced skin reactions	34, 38, 39, 50
Vasculopathic lesions										
A diverse group: asymptomatic patients, sparse patients, intensive care unit patients										
Lesions may result from: coagulation disorders and consequently microemboli, which may lead to disseminated intravascular coagulation (DIC) in severe cases; vasculitis due to small vessel occlusion, a neurogenic, microthrombotic mechanism mediated by immune complexes										
Livedo (livedo reticularis + livedo racemosa) or necrosis	secondary to COVID-19-induced thrombotic vasculopathy	variable	6%	more severe	extremities	pain, burning, itching	at any time during SARS-CoV-2 infection differential symptoms	10%	antiphospholipid syndrome, lupus erythematosus cutaneous panniculitis, cryofibrinogenemia,	23, 26, 27, 80–83
Ischemic acral lesions: chilblain-like + acral ulcers	without cold exposure or other predisposing substrates	2–8 weeks	pseudo-chilblain – 19%; 19–40% of adults with a milder course, in 16% of those hospitalized	chilblain mild to asymptomatic course; an acral ulcer occurs in critically ill patients	toes	pain, itching, cold sensation	on average after 9 days, frequently late in the after other symptoms, even after a recovery period	lack of data	Cold injuries, systemic lupus erythematosus	23, 24, 27, 36, 84, 85

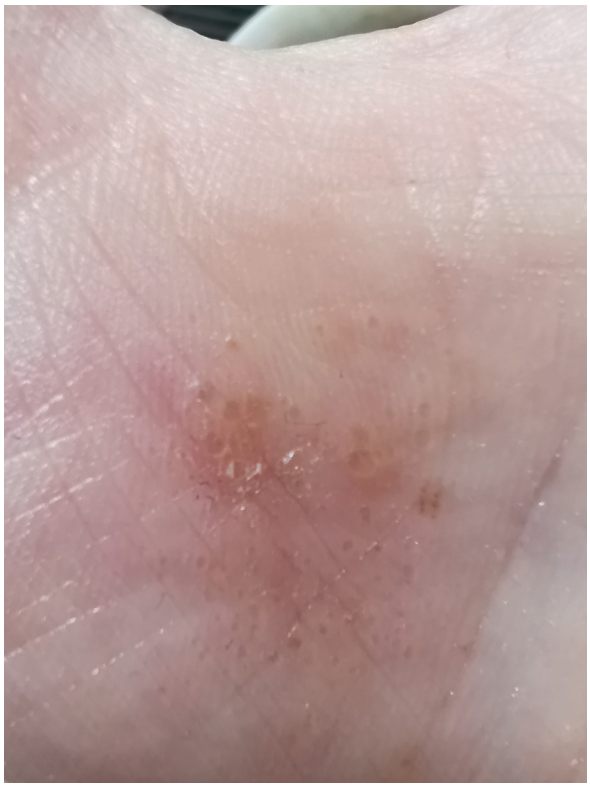

Figure 2. Contact dermatitis located on the palm.

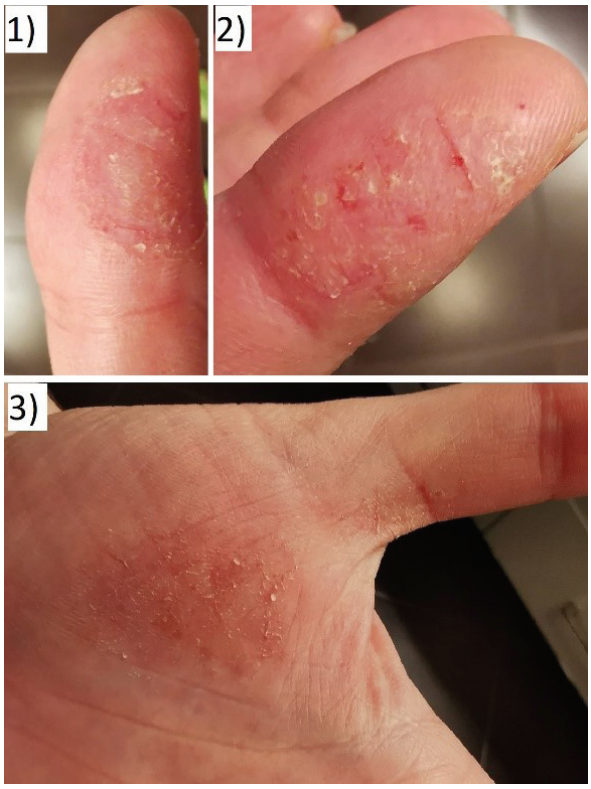

Figure 3. Atopic dermatitis flare - hand eczema.

fly or pear shape, rapidly progressing from hyperpigmentation to necrosis [35].

Other cutaneous manifestations were also observed that may be due to factors such as disinfectant-induced contact dermatitis/emphysema (**Figure 2**), telegonous alopecia, alopecia areata, nail changes, Raynaud's phenomenon-like lesions, and bedsores in hospitalised patients [27,36].

An important aspect to raise regarding skin lesions is atopic dermatitis (AD). During the COVID-19 pandemic, an increase in the frequency of exacerbations of atopic dermatitis with mild clinical severity was observed [37]. **Figures 2** and **3** show an example of cutaneous manifestations of SARS-CoV-2 infection in a patient with atopic dermatitis. The course and severity of AD are determined by many factors, including genetic, environmental, and immunological. AD patients develop type I immune hyperreactivity and increased production of Th2-type cytokines (such as IL-4, IL-5 and IL-6). SARS-CoV-2 infection can also result in an increased immune response, leading to the overproduction of inflammatory mediators (specifically TNF-α, IL-1, IL-8, and IL-6, as in AD). In COVID-19, as in AD, a comparable immune effect is observed in the form of increased overproduction of cytokines, which may lead the organism to perceive SARS-CoV-2 infection as another exacerbation of AD [38].

Skin lesions caused by treatment

The differential diagnosis of skin lesions should also consider adverse skin reactions caused by pharmacotherapy during COVID-19. Selected medications are discussed below.

Systemic glucocorticosteroids commonly used in hospital treatment could cause adverse cutaneous events such as pruritus, burning, erythema, oedema, fissures, urticaria, papulopustular lesions, telangiectasia or purpura [39,40].

Most guidelines recommend using anticoagulants, and according to some studies, adjunctive therapy with low molecular weight heparin (LMWH) may be associated with lower patient mortality [41]. However, LMWH use may be related to heparin-induced skin necrosis at the injection site or a distance, manifesting as erythematous plaques, necrotic ulcers, hemorrhagic blisters, and petechiae. Cases of fixed erythema after

enoxaparin administration have also been reported [42,43]. Side effects of antiretrovirals, such as ritonavir or lopinavir, may manifest as maculopapular rash, exfoliative erythroderma, Stevens-Johnson syndrome or toxic epidermal necrolysis, or scleroderma-like lesions, annular erythema and pruritus, urticaria or drug eruptions [39,40]. A symptom related to remdensivir may be a maculopapular rash [40,42,43]. Rush, including urticaria and pruritus, are the cutaneous side effects of Sotrovimab [44].

Tocilizumab is a humanised monoclonal antibody against IL-6 receptors and can potentially cause pruritus, *psoriasiform dermatitis*, maculopapular rash, urticaria and pustular eruptions [39,40]. Anakinra, on the other hand, may cause a generalised urticarial rash [40]. Cutaneous side effects of baricitinib and the other Janus kinase inhibitors include urticaria, rashes and palmoplantar pustulosis-like eruption. An overview of the drugs and potential skin lesions is shown in **Table 2**.

Other medications that can affect the skin and are currently of decreased importance in managing COVID-19 are interferon, oseltamivir, colchicine, azithromycin, and antimalarials.

As can be shown, multiple medications administered to patients with COVID-19 may affect the emergence of skin lesions, which may complicate the differential diagnosis between lesions caused by treatment and those caused by SARS-CoV-2 infection.

Finally, an important aspect is the effect of COVID-19 vaccination on the onset or exacerbation of skin diseases. Thus, reports exist on new cases of lichen planus and exacerbation of symptoms of this disease. The underlying mechanism needs to be clarified. So far, reports in the literature indicate that vaccination affects the induction of Th1 cell responses and, consequently, the secretion of cytokines that may cause the development of this disease [45]. For a detailed explanation of the expression of the immune system after vaccination against COVID-19, an example described in the context of the development of lymphomas will be used. The exact mechanisms of T-cell lymphomas induced by mRNA vaccines against COVID-19 are still unknown. However, in this case, it is also considered that these vaccines may have the ability to stimulate the immune system and thus over-activate immune responses. However, there are reports that mRNA vaccines against COVID-19 induce continuous stimulation of T and B cells, which may cause a high inflammatory response.

Consequently, this may lead to lymphoma or accelerate its progression [46]. It is worth emphasising that exacerbation of AD after COVID-19 vaccination was not observed, and neither was there any such correlation when patients were treated with biotechnology drugs such as sarilumab. In addition, no correlation has been found between the specific type of COVID-19 vaccine and AD exacerbation. Post-vaccination flare-ups of AD symptoms such as pruritus (usually mild and temporary) have been observed; however, no significant adverse effects have been noticed [45,47].

Pressure ulcers in COVID-19

Pressure injuries are among the most common aftermaths of prolonged confinement to bed. It is estimated that around 33.6% of patients with COVID-19 in a prone position develop pressure ulcers. On the other hand, pressure injuries in patients in a supine position tend to be rarer because they appear only in around 12% [48]. Among the iatrogenic risk factors for the appearance of pressure ulcers are the use of over two vasopressors, long-term mechanical ventilation, and the need to spend over two days in bed with

Table 2. Drug-induced skin lesions.

Drug	Possible skin lesions
Systemic glucocorticosteroids	Pruritus, erythema, urticaria, purpura
Low molecular weight heparin (LMWH)	Necrosis, erythema
Antiretrovirals (e.g. ritanavir)	Maculopapular rash, Exfoliative erythroderma, Stevens-Johnson syndrome
Tocilizumab	Pruritus, Psoriasiform dermatitis, urticaria
Anakinra	Generalized urticarial rash
Janus kinase inhibitors	Urticaria, rash

a pressure redistribution system [49]. Comorbidities strongly associated with the development of pressure injuries include hypertension, type-2 diabetes and obstructive lung diseases, e.g. asthma and COPD — furthermore, both patients with low BMI and severely obese are more likely to manifest pressure injuries. What is additionally crucial is the fact that COVID-19 itself may be a risk factor for developing pressure injuries [50]. It is based on a few factors. The first of them is low oxygen saturation on arrival at the hospital. It leads to local ischemia, which accelerates ulcer pain due to the accumulation of metabolites such as lactic acid [51]. Another element of the development of ulcers and its prognosis in COVID-19 is cytokine storm. High concentrations of interleukins, especially interleukin-6, cause prolonged inflammation. This is also may lead to local ischemia and more muscular pain related to ulcers [52]. Endothelial dysfunction, described extensively previously, may also impact the emergence of bedsores. The next factor which may be associated with the risk of pressure ulcers is comorbidities admitted to the ICU. Patients with advanced COVID have additional illnesses such as coronary disease or diabetes [53]. These conditions increase the risk of pressure ulcers [54,55] and are adverse prognostic factors in COVID treatment [56,57].

Furthermore, prone positioning, also used in patients with COVID-19 disease, is linked to a 3-fold increase in pressure-related injuries compared with supine positioning [58]. The need for medical equipment such as ECMO (extracorporeal membrane oxygenation) cannulas and endotracheal tubes is also a significant factor in increasing the risk of developing bedsores and other skin lesions. The skin at the site of insertions is vulnerable to infection and mechanical injury. In addition, pressure on the skin caused by passing cannulas may also lead to skin damage. Examples of ECMO injuries and pressure sores are presented in **Figures 4** and **5**.

Together, the elements mentioned above result in the necessity of additional care for patients with COVID-19. However, pressure ulcers are very challenging conditions. Treatment costs are incredibly high, forcing medical equipment to introduce prevention in the first place. It includes the rotation of patients, usage of pressure redistribution points in medical devices and additional strategies [60]. However, studies show that even intensive care personnel must learn about prevention methods for pressure ulcers [61]. This should concern officials in improving education and searching for more straightforward prevention techniques. Among them, one very promising is the usage of dressings in the form of foam and hydrocolloids. They were proven to be very effective and also relatively cheap [62].

Furthermore, studies of hydrogels based on zwitterion suggest they may also be used to treat pressure ulcers [63]. Another potential treatment for pressure injuries is heparin. Heparin is proven to be an effective drug in the prevention of hypoxia in COVID-19 [64], which was already mentioned as one of the most essential factors of pressure ulcers. However, there are reports that usage of heparin may not affect hypoxia in patients admitted to ICU [65].

Finally, one of the aftermaths of pressure ulcers is facial scars. As of the first half of 2022, there are not many reports about the frequency of this condition. However, first-case reports show that this may be a crucial problem in the following years [66].

Skin Failure in COVID-19

Another critical skin condition appearing in ICUs is skin failure. It is defined as the loss of integument associated with hemodynamic instability and/or additional organ failure [67]. The. The pathophysiology of this process is complex and should differ from pressure ulcers. Skin failure may occur independently from pressure ulcers or as a complication [68]. The most critical factors contributing to integumentary breakdown are hypoperfusion combined with hypothesised destruction of autosomes (i.e. areas of skin vascularised by one artery) and severe organ dysfunction contributed to other illnesses (e.g. myocardial infarction, shock, cerebrovascular incidents, etc.). Additionally, skin failures can be divided into two categories: acute, which most commonly occurs in ICUs and end-of-life, which mostly happens among terminally chronically ill patients [69].

Similarly to pressure ulcers, there is a strong relationship between COVID-19 and skin failure [70]. Besides the mechanisms mentioned above

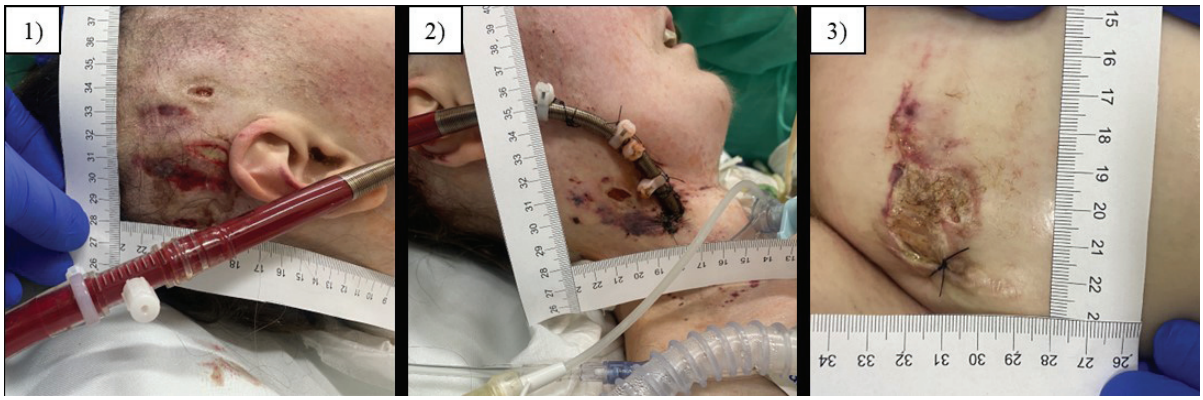

Figure 4. ECMO-induced skin lesions: 1) pressure ulcers in the area of the head resulting from the position of the VV ECMO cannula; 2) skin lesions around the cannula of VV ECMO with sores on the auricle; 3) skin lesion after removal of VV ECMO cannula in the groin area.

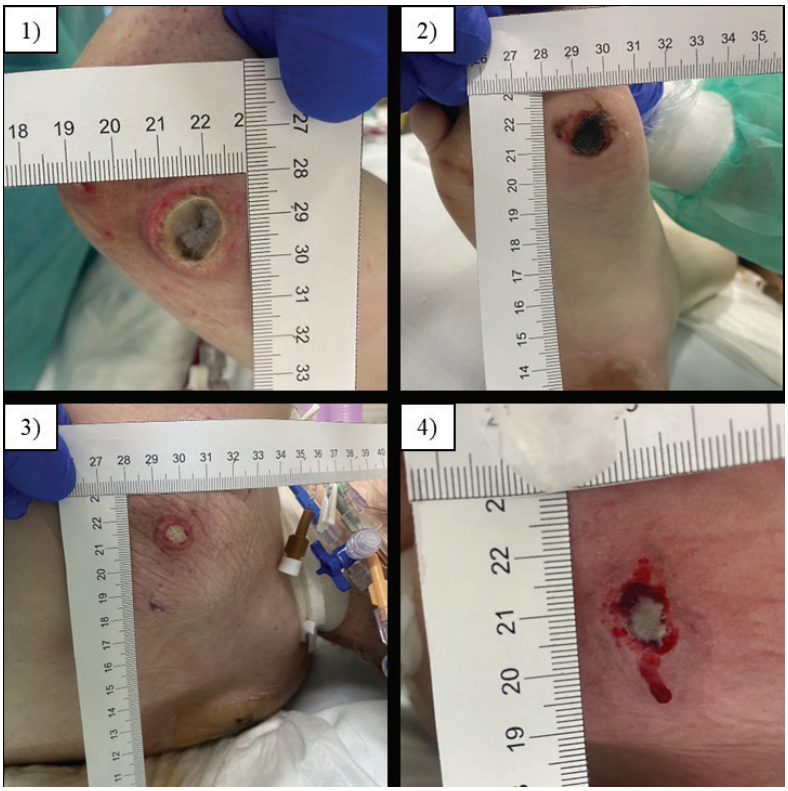

Figure 5. Pressure ulcer located in 1) the elbow region, 2) the sole, 3) the scapular region, and 4) the scapular region.

in pressure ulcers, there are also unique factors of COVID-19 that contribute to the development of skin failure. The first of them is vasculitis, which attacks small vessels of the skin. It is one of the most common complications both in COVID-19 and ICUs [71,72].

Contrary to Kawasaki-like, cutaneous vasculitis is common among adult patients [73]. Other risk factors for developing skin failure in COVID-19 are coagulopathy and complement-related microthrombosis. These are responsible for skin ischaemia and critical organ failures [27]. Furthermore, it is worth emphasising that the appearance of microthrombi might be associated with COVID-19, and their occurrence may be associated with an acute disease [74].

Unfortunately, it is hard to estimate the exact number of patients with skin failures because it is difficult to differentiate them from other skin conditions in ICUs.

Understaffing and quality of care

The hypothetical pathomechanism of decubitus ulcer formation is based on systemic processes leading to skin ischemia [75]. However, it is worth noting that other determinants of pressure ulcer problems include staff deficiency, worker exhaustion, and the practice of bedsores prophylaxis.

Medical personnel, including nurses, physiotherapists, and other medical professionals, have a significant role in preventing pressure sores [61].

The COVID-19 pandemic impacted previously underfunded health care, which resulted in shortages, especially at the beginning of the COVID-19 pandemic, not only of personal protective equipment for medical personnel but also a shortage of hospitals and hospital beds [76,77].

In addition, SARS-CoV-2 has shed light on medical staffing deficiencies that had already occurred before its onset [77].

During the COVID-19 pandemic, additional factors affected the reduction in the number of medical personnel; for example, in Poland, due to the restriction of work to one workplace, increased worker morbidity from COVID-19 at the peak of the pandemic, employee rotations, and retirement [77].

Personnel deficiencies, in particular, could impact the development of pressure sores, even more so in pronated patients, since it takes 4–6 workers to reposition a patient each time [58]. Moreover, patients with severe courses of COVID-19 require special care due to their condition and the number of medical procedures performed, resulting in greater staffing requirements.

Studies conducted in the USA, Canada, and some European countries [78] have shown that adequate nursing staffing affects hospitalised patients' outcomes and the shorter duration of hospital stays. Furthermore, the staffing level of nurses in hospitals is a determinant of the quality of nursing care [78].

Preventing pressure sores requires interdisciplinary collaboration, but the care process is critical.

Due to the hiring of volunteers, soldiers, medical students, and immigrants without waiting for the formalities of nostrification, calling people retired, and the insufficient time to educate newcomers, it is not sure whether these workers were adequately prepared to prevent pressure injuries [77,79]. It is essential to emphasise that knowledge regarding avoiding and caring for pressure ulcers is specialised. Thus, it is questionable that in such a limited period, with a deficiency of staff, training in this area would be provided sufficiently, especially since it has been shown that even ICU staff may have inadequate cognisance regarding methods of preventing bedsores [61].

Another aspect that could affect the development of decubitus ulcers is the inability of family members or relatives to be involved in hygiene routines, including preventive care for pressure ulcers, due to restrictions or prohibitions on visiting healthcare facilities.

Skin biopsy as a diagnostic method

Analysis and evaluation of skin lesions extended by tissue examinations can simplify the diagnosis and prognosis of patients infected with SARS-CoV-2. Cutaneous punch biopsy proposed by Laurence et al. appears to be a practicable and well-promising diagnostic instrument for detecting COVID-19 incidence and predicting the course of the disease [74]. Although the study was conducted on a small number of subjects (15 with severe/critical COVID-19 and 6 with mild/moderate COVID-19), the results are nevertheless promising. In their study, the severity of COVID-19 correlated with microthrombi. They observed the presence of microthrombi in patients with severe COVID-19, while these were undetectable in samples from subjects with a mild or moderate course. The formation of microclots may lead to cutaneous minification. The above indicates that skin lesions and their evaluation with tissue examination could help assess the condition of a patient with COVID-19 before severe symptoms develop, identifying patients at high risk of acute disease and, consequently, may allow for earlier implementation of appropriate treatment.

Discussion

As time passes and more cases are analysed, knowledge of the disease caused by SARS-CoV-2 is expanding.

Skin lesions are observed in patients during COVID-19 and are increasingly described.

It should be kept in mind that some of the observed lesions may be due to pharmacotherapy. To differentiate between lesions induced during the disease and those resulting from the implemented treatment, it would be necessary to discontinue the drugs suspected of causing skin lesions, which would entail discontinuation. In patients hospitalised for SARS-CoV-2 infection, multiple drugs are used simultaneously. Thus, in the case of an adverse skin reaction, it seems essential to consult a consultant allergist for treatment of acute skin symptoms and a possible diagnosis of hyperresponsiveness to the medications.

Finding the cause may contribute to the proper treatment of skin lesions; therefore, it seems necessary to consider implementing dermatological and allergological consultations.

Cutaneous manifestations may also be the single symptom of COVID-19, which may facilitate the diagnosis of this disease. The mechanism of skin lesions is unclear because it is difficult to determine their cause. They may result from a superposition of several factors, such as coagulopathy, other viral infections, or medication-related dermatoses. It seems necessary to extend the diagnostics of skin lesions during COVID-19 in order to understand their pathogenesis. Inadequate care due to staff shortages or inadequate education may lead to the development of pressure sores. Implementing solutions that could protect both patients and staff in the event of future pandemics would seem imperative.

The compilation of skin lesions presented in this paper may be useful in diagnosing COVID-19, indicating the need for testing for SARS-CoV-2 in the absence of other symptoms, early diagnosis of lesions, and patient prognosis for some of the lesions described.

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Conflict of interest statement
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