

SKIN DISORDERS IN COVID-19 PANDEMIC

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The corona virus family are viruses with ARN. The genomic and phylogenetic analysis of the coronavirus subfamily which causes the COVID-19 disease is a beta coronavirus which determines the severe acute respiratory syndrome. The SARS-CoV-2 virus bounds to the angiotensin converting enzyme 2 (ACE2) through spike protein. The severity spectrum of the symptomatology varies from mild to severe – critical. Among comorbidities associated with the infection severity are cardiovascular diseases, diabetes mellitus, pulmonary diseases, kidney diseases, obesity and cancer. The cutaneous manifestation patter of the COVID-19 disease includes rash, morbilliform, pernio-like acral lesions, vesicular eruptions, urticarial eruptions, maculopapular eruptions, retiform purpura. Dermatological conditions encountered during the COVID-19 pandemic are also caused due to personal protection equipment, lack of proper personal care or lack of proper hand hygiene.

Keywords: skin, COVID-19, dermatologic manifestations.

INTRODUCTION

The COVID-19 disease has it's starting point in the Wuhan city from China, towards the end of the year 2019. The virus quickly spread through China becoming an epidemic. After the virus started affecting more and more countries, on 11th of March 2020 the World Health Organization officially declared the COVID-19 spread a pandemic. The incubation period is 14 days on average, most of the cases showing symptoms in 4 to 5 days from exposure¹. Pneumonia is the most frequent manifestation of SARS-CoV-2 infection followed by fever, cough, myalgia, headache, dyspnea, loss of smell or taste, diarrhea and nausea. The gold standard for COVID-19 diagnostic is the real time polymerase chain reaction (RT-PCR) which shows the presence of the virus through viral genetic material amplifications techniques. The presence of SARS-CoV-2 ARN in the nasopharyngeal and pharyngeal exudate from collected samples indicates the presence of the COVID-19 disease².

Regarding the impact of age as a factor, all age groups shown to be affected by the disease. However in the case of older people with comorbid-

ities such as diabetes mellitus, cardiovascular diseases, hypertension, pulmonary diseases, cancer and obesity, the COVID 19 disease has a higher severity form.

CUTANEOUS MANIFESTATIONS OF SARS-CoV-2 INFECTION

The frequency of cutaneous manifestations varies between 0.2 and 20%. The time after exposure for these symptoms to appear in COVID-19 is difficult to assess. The associations between the infection severity and cutaneous manifestations is yet unclear. The possibility of some cutaneous symptoms to come as an adverse reaction to the medication used for treatment is not yet excluded³. A close collaboration between dermatologists and dermatopathologists is required for a proper differentiation between cutaneous manifestations caused by COVID-19 and cutaneous reaction which have as trigger ingested pills or other dermatological affections⁴.

Most frequently encountered cutaneous patterns are: morbilliform rash, pernio like lesions, livedo reticularis like, livedo racemose like, urticaria like, varicella like lesions⁵.

The morbilliform rash manifest itself at the trunk and proximal parts of the members while having a distribution pattern similar to viral exanthemas.

The pernio-like lesions pseudo chilblain acral presents itself as purpuric or erythematous-violaceous patches at hand digits level, elbows, feet fingers with or without edema or pruritus⁶. Pernio is a superficial vascular inflammatory response which frequently appears acral as a result of low temperature exposures⁷. Their description was done in absence to cold exposure or to pathologies associated with perniosis. The resolution can appear in 2 to 8 weeks. There is no treatment guide for pernio-like lesions associated with the COVID-19 disease. High potency corticosteroids applied topic can be useful in the case of lesions which cause discomfort. The pathogenesis of these lesions is a primary inflammatory process⁸. Electronic microscopy shows the presence of viral SARS-CoV-2 particles in endothelial cells of cutaneous biopsies of a group of pediatric patients and it suggests a vascular injury caused by the virus as a potential pathogenic mechanism⁹. Several cases of pernio-like lesions were registered for test subjects positive for IgM or IgG for SARS-CoV-2 infection and negative for polymerase chain reaction (PCR) which might indicate an ulterior stage in the infectious process¹⁰. Pernio-like lesions were observed in both symptomatic and asymptomatic patients¹¹. Pernio is mostly idiopathic or caused due to the base disease, such as lupus erythematosus and antiphospholipid syndrome⁸. Cases of cutaneous vasculitis were also observed for symptomatic patients. The prothrombic status and the coagulopathy can contribute as factors in the microvascular thrombosis pathogenesis and the laboratory parameters changed include D-dimer and elevated fibrinogen¹².

Livedo reticularis like. Such vascular lesions were reported at COVID-19 patients. Symmetric cutaneous vasculitis was reported for patients with systemic manifestations of the SARS-CoV-2 infection in which livedo reticularis like transitory cutaneous eruptions appeared¹³.

Livedo-racemosa-like. Retiform purpura and necrotic vascular lesions were associated with the COVID-19 severity. The histopathological and immunohistochemical analysis of the cutaneous biopsies show a pattern of microvascular lesions mediated by the complement in both the affected skin as well as in the healthy one¹². The thrombotic vasculopathy and change of clotting laboratory

parameters were also reported in severe cases of COVID-19¹⁴.

Urticaria like lesions. Erythematous-edematous urticarial, papules were described at patients with COVID-19 with light pruritus as accompaniment. Palm and plantar crusting was also observed. Antihistamines can be used to reduce the pruritus¹⁵.

Varicella like eruptions (vesicular eruptions). Vesicular eruptions were reported, varicella-like eruptions associated with COVID-19 disease, micro papules and vesicles which appear between 4 and 30 days from the COVID symptomology disappear in 10 days. There is no causality between vesicular rash, antiviral treatment and other treatments used⁴.

Multisystem inflammatory syndrome in children. Atypical Kawasaki disease was described in children in an Italian study. The symptomology includes polymorphic rash, erythema and induration of hands and feet, conjunctivitis and oral mucositis¹⁶.

COVID-19 disease manifestation among children are mild. However, in rare cases, children can present severe cases which are different from the adults⁷.

In a study published by The Lancet which took place in UK during April 2020, similarities with Kawasaki disease were observed, the children having fever, gastrointestinal symptoms (abdominal pain, diarrhea, vomiting), erythematous rash, conjunctivitis, mucous membrane implication, respiratory symptoms, neurocognitive implications (lethargy, headache, confusion), sore throat, myalgia, hand and feet edema, arrhythmia, lymphadenopathy¹⁶.

CONDITIONS RELATED TO DERMATOLOGIC CARE

Dermatological affections caused by personal protection equipment or prevention methods for limiting the SARS-CoV-2 spread lead to skin injury. The most exposed are health care workers which take care of COVID-19 infected patients due to their prolonged wearing of the COVID-19 protection medical equipment (over 6 hours) and thus the risk of skin damage increases. Masks, face shields, protective goggles and gloves create pressure, abrasion and maintain a moist environment which leads to afflictions at cheek level, hands, forehead and nose. Personal protection equipment induced injuries include erythema, maceration, fissuring, desquamation, papules, erosions which lead to pain and itching. Furthermore, the personal protection

equipment leads to aggravation of preexisting dermatological condition¹⁷.

For preventing cutaneous injuries due to the protection equipment, creams which reestablish the lipidic film as a cutaneous protection barrier should be constantly used.

Hand hygiene related dermatitis. Hand hygiene is a key factor in preventing the SARS-CoV-2 spread. Hand eczema is a condition frequently found in the cases of health care workers and it's caused by excessive hand washing and prolonged use of protection gloves. The frequency of irritative contact dermatitis can be reduced through usage of mild soaps with glycerin and the use of emollient creams, washing using mildly warm instead of hot water and by following the use of alcohol based disinfectants with application of emollient creams. Another pathology frequently encountered during the pandemic is acne which presents itself in mild to severe forms and which can appear de novo or can be aggravated by mask wearing. The pressure applied by the mask creates ecchymosis while also favoring the multiplication of bacteria through maintaining a moist environment. Rosacea condition can become aggravated and it can be complicated via bacterial spreading-impetiginized. Perioral dermatitis can take severe forms due to the moist environment favored by mask wearing.

DERMATOLOGIC THERAPEUTIC CONSIDERATIONS

There were a few cases where improvements of SARS-CoV-2 severe symptoms were shown after administering treatment for psoriasis and psoriasis arthritis with monoclonal antibody Guselkumab, which targets the p19 subunit of interleukin IL-23¹⁸. These observations show a potential beneficial role in preventing the cytokine storm triggered by SARS-CoV-2. The profile of the cytokines involved in the hyperimmune response from the severity of SARS-CoV-2 is formed from IL-6, IL-1, TNF- α , IL-7, INF- γ . Successful attempts to suppress the hyperimmune response were done with biologic therapy. IL-6 is associated with vascular leakage, activation of complement and coagulation cascades, cardiomyopathy and disseminated intravascular coagulation (DIC) symptoms associated with COVID 19 disease. Interferon gamma associated flu-like symptoms with fever, dizziness, headache. Tumor necrosis factor alpha cause malaise, watery diarrhea, vascular leakage, lung injury and production of acute phase proteins.

In August 2020, the Lancet magazine publishes an article about the therapy with anti-IL6 in severe cases of COVID-19. Tocilizumab which is used in treatment of psoriasis arthritis, giant cell arteritis is a recombinant humanized monoclonal antibody of IgG1 class against IL-6 receptor, and is used successfully on patients with severe symptoms of COVID-19. The exclusion criteria were coexistent infection other than COVID-19, use of glucocorticoid, history of allergic reactions to monoclonal antibodies, gastrointestinal conditions that may predispose to bowel perforation, hematological, liver or renal function impairment¹⁹.

Moreover there were clinical trials with biological agents which directly targeted the IL-6 inhibitor pathway such as siltuximab.

The optimal treatment for the COVID-19 disease has not been established yet.

APPROACH TO PREVENT SARS-CoV-2 INFECTION

The control of the infection in order to reduce COVID-19 transmission is done through covering of the nose, mouth and eyes, fast identification and isolation of COVID-19 suspects, the use of personal protection equipment in the case of health care workers and the use of disinfectants.

Self-prevention and self-assessment tools are important factors in the conduct of each person in order to diminish the transmission risk and for controlling the infection spread²⁰.

Having dedicated trial tents for patients which presents themselves in medical units further contributes to limiting the spread of the virus.

Assuring medical assistance during the pandemic through telemedicine/teledermatology to limit the risk of transmission. Teledermatology allows the opportunity for medical personnel to evaluate patients while limiting their exposure. Methods of implementation can be a video conference or having a phone call followed by pictures of the dermatological affections sent via phone.

Telemedicine is currently an option for dermatologists; however concerns were raised regarding intimacy and security of the telemedicine system.

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