Coronavirus COVID-19 and Relevance for Dermatologists – Are We Ready for the Battle?

Carsten Sauer Mikkelsen^{1,2}, Kristian Bakke Arvesen², Luit Penninga³, and Peter Bjerring²

¹Specialist in Dermato-venereology, Private Practice in Derma-

to-venereology, Brønderslev, Denmark, ²Specialist in Dermato-venereology, Research lab. Department of Dermato-venereology, Aalborg University Hospital, Denmark, and ³Specialist in Surgery, Ilulissat Hospital, Avannaa Region, Ilulissat, Greenland.

On December 31, 2019, the first registered case of "atypical ARDS/interstitial pneumonia" came from the Chinese city of Wuhan, Hubei. On February 11, 2020 the WHO officially announced the new name of the pathology associated with the coronavirus: COVID-19 (Coronavirus Disease 2019) (1). It is a new strain of RNA virus that has not previously been identified in humans.

afebrile initially (3).



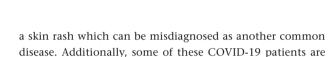
Data in the literature so far about skin manifestations in COVID-19 are very limited.

A group of dermatologists from Lecco in Italy collected data from 88 patients with COVID-19. Eighteen patients (20.4%) developed cutaneous manifestations. Eight patients developed cutaneous involvement at the onset, 10 patients only after hospitalization. The cutaneous manifestations seen were: erythematous rash (14 patients), widespread urticaria (3 patients), and chicken-pox like vesicles (1 patient). The skin on the trunk was the main involved region. Itching was

insignificant or absent and usually lesions healed in few days. Apparently, there was no correlation between skin symptoms and disease severity. It was concluded that skin manifestations related to COVID-19 infection are similar to those occurring during common viral infections (1).

A case report from Thailand presented a patient with a skin rash with petechiae. Because dengue is very common in Thailand and the patient also had low platelet

count, a clinical diagnosis of dengue was made by the first physician in-charge. In this case, the patient further presented respiratory problems and was referred to the tertiary medical centre. Other common virus infections that might cause fever, rash and respiratory problem were ruled out by laboratory investigation and the final diagnosis of COVID-19 infection was confirmed by RT-PCR (6). The group concluded it is a possibility that a COVID-19 patient might initially present with



More case reports from China present COVID-19 patients with urticaria as a clinical cutaneous manifestation (7).

Another study from Wuhan registered the clinical characteristics of 140 community-infected patients with COVID-19. It was found that the median age of all patients were 57 years old with almost 1:1 male:female ratio. Fever (91.7 %), cough (75.0%) and fatigue (75%), were the most common symptoms in COVID-19 patients. More than 1/3 of the patients had chest tightness or dyspnoea and gastrointestinal symptoms (nausea,

diarrhoea, and anorexia). CT scans or X-ray showed bilateral ground-glass and patchy opacity in 89.6% of the patients. No asthmatic patients were identified in this report, and only a few patients had self-reported drug hypersensitivity and urticaria. Other allergies such as allergic rhinitis, atopic dermatitis, and food allergy were not reported (8).

A retrospective study found 7 critical COVID-19 patients with acro-ischaemia

in a single centre in Wuhan. All patients had acro-ischaemia presentations including finger/toe cyanosis, skin bullae and dry gangrene. D-dimer, fibrinogen and fibrinogen degradation product (FDP) were significantly elevated in most patients. Prothrombin time (PT) were prolonged in 4 patients. D-dimer and FDP levels increased progressively when COVID-19 exacerbated, and 4 patients were diagnosed with definite disseminated intravascular coagulation (DIC). Six

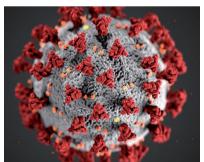


Foto: Alissa Eckert, MS; Dan Higgins, MAMS

patients received low molecular weight heparin (LMWH) treatment, after which their D-dimer and FDP decreased, but there was no significant improvement in clinical symptoms. Five patients died finally and the median time from acroischaemia to death was 12 days. It was concluded that hypercoagulation status in critical COVID-19 patients should be monitored closely, and that anticoagulation therapy should be considered in selected patients (9).

Conclusion

The data from studies concerning cutaneous manifestations in patients with COVID-19 varies a lot. Nevertheless, dermatologists should recognize the possibility that COVID-19 patients might present with only a skin rash initially, and should think of the possibility of the patient having Corona COVID-19 in order to prevent further transmission.

CUTANEOUS MANIFESTATION IN HEALTHCARE WORKERS FIGHTING CORONA COVID-19

In a study from China the skin damage among healthcare workers (HCW) managing corona virus COVID-19 was registered. The general prevalence of skin damages caused by enhanced infection-prevention measures was 97.0% among first-line HCW. The affected sites included nasal bridge, hands, cheek and forehead, and nasal bridge was the most commonly affected (83.1%). Among a series of symptoms and signs, dryness/tightness and desquamation were the most common symptom (70.3%) and sign (61.6%). The HCW who wore some medical devices longer than 6 h had higher risks of skin damages than those who did less time. The more frequent (>10 times/day) hand hygiene and longer time of gloves wearing could increase the risk of skin damages of the hands.

In conclusion, the study demonstrated that the prevalence of skin damages of first-line HCW was very high. Moreover, longer exposure time was a significant risk factor which highlights that the working time of first-line staff should be arranged reasonably. Besides, prophylactic dressings could be considered to alleviate device-related pressure injuries (10). The above information has been highlighted in a letter from AAD and suggestions for prevention are given for healthcare workers (HCW). HCWs fighting COVID-19 are prone to damage of both skin and mucosa barriers. In order to minimize skin and mucosa barrier breakdown, HCWs should adhere to standards on wearing protective equipment and avoid over-protection. At the same time, measures of skin care are recommended during work. AAD also provides professional advice on prevention and management of mild skin disorders. Nevertheless, timely referral to dermatologists is necessary if dermatoses are sustained or worsened gradually (11,12).

PATIENTS WITH CORONA COVID-19 SKIN DISEASES AND IMMUNOSUPPRESSIVE TREATMENT

The British Association of Dermatologists (BAD) has addressed potential issues regarding COVID-19 infection of patients who are taking medicines that affect the immune system such as biologic therapies and/or immunosuppressants (13). BAD inform patients taking a medication that targets their immune system that COVID-19 infection may pose a higher risk and therefore specific measures are advised. There are two categories of measures: shielding and very careful social distancing. Shielding is a measure to protect people who are at very high risk of severe illness if contracting (COVID-19) infection by minimising all face to face interaction between those who are extremely vulnerable and others. Shielding is a step up from very careful social distancing. People advised not leave their home for 12 weeks (current estimate until late June 2020). Asking people to stay at home and avoid contact is an intensified form of social distancing. For people taking drugs that target the immune system, very careful social distancing is advised by BAD.

Which category that applies to an actual patient depends on the medicine(s), age and what other medical problems the patient may have. The patient will be advised by the doctors prescribing their immune modulating drugs whether they are considered an 'extremely vulnerable' person needing to shield. BAD do not advise patients to stop their medicine without prior discussion with their dermatologist since stopping treatment could worsen their skin condition resulting in need for hospital treatment. Self-isolation applies if the patients have symptoms of COVID-19 infection or if the patient lives with someone who has symptoms. In this case they may NOT leave the house for 7-14 days. Many out-patient services are arranging for patients to be reviewed by telephone or online. The hospital departments contact patients to confirm these arrangements. Review and frequency of routine blood tests may become less often during this time but hospitals have made arrangements for easy access to bloods tests in their departments on a daily basis.

Patients on biologics will continue to receive their biologics via homecare delivery companies. BAD are not aware of any current stock- or delivery issues. Each hospital and GP practice will make its own arrangements for arranging repeat prescriptions.

BAD advice that dermatologists should only be starting or continuing patients on isotretinoin where the risks are outweighed by the benefits. This needs to be considered carefully in light of the need to reduce face-to-face consultations in the current pandemic, and the uncertainty of reliable follow-up/

monitoring over the coming months. Monitoring of side effects and blood monitoring, will need to be carried out as usual with remote consultations.

Skin cancer services should be attenuated to ensure that the following guidance is implemented according to BAD: Consider cancelling all elective surgeries. Consider deferring all surgical excisions of BCC, including Mohs micrographic surgery, for 3–6 months, with exceptions for highly-symptomatic lesions. Highly symptomatic lesions and those with potential for significant rapid growth could be considered for surgery. Consider deferring surgical excisions of squamous cell carcinomas (SCC), such as SCC *in situ* and small, well differentiated SCCs. Prioritise the following lesions: Rapidly-enlarging tumours, poorly-differentiated tumours, perineural tumours, ulcerated and symptomatic lesions; lesions in patients with significant risk factors (while balancing the risk of COVID-19 complications for these high-risk patients). Consider deferring treatment of melanoma *in situ* for 2–3 months.

REFERENCES:

- Recalcati SJ. Skin manifestations of coronavirus cutaneous manifestations in COVID-19: a first perspective. Letter to Editor. Eur Acad Dermatol Venereol 2020 Mar 26. doi: 10.1111/jdv.16387.
- Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020; 395: 507–513.
- 3. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395: 497–506.
- 4. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical character-

- istics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA 2020; 323: 1061–1069.
- Guan W, Ni Z, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020 Feb 28. doi 10.1056/ NEJMoa2002032. Epub ahead of print.
- Joob, B, Wiwanitkit, V. COVID-19 can present with a rash and be mistaken for Dengue. J Am Acad Dermatol 2020, Mar 22, doi: https://doi.org/10.1016/j.jaad.2020.03.036.
- Shubiao L, Linsong L, Zhiqiao Z, Xiao L, Jiang Z, Chen J, et al. Alert for non-respiratory symptoms of Coronavirus Disease 2019 (COVID-19) patients in epidemic period: A case report of familial cluster with three asymptomatic COVID-19 patients. J Med Virol 2020, March 19. doi: 10.1002/jmv.25776. [Epub ahead of print]
- Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy EAACI March 2020, doi: 10.1111/all.14238.
- Zhang Y, Cao W, Xiao M, Li YJ, Yang Y, Zhao J, et al. Clinical and coagulation characteristics of 7 patients with critical COVID-19 pneumonia and acro-ischemia. Zhonghua Xue Ye Xue ZA Zhi 2020 Mar 28;41(0).
- Lan J, Song Z, Miao X, Li H, Li Y, Dong L, et al. Skin damage among healthcare workers managing coronavirus disease-2019. J Am Acad Dermatol 2020 Mar 18: S0190-9622(20)30392-3. doi: 10.1016/j. jaad.2020.03.014. [Epub ahead of print].
- 11. Elston DM. Letter from the Editor: Occupational skin disease among healthcare workers during the Coronavirus (COVID-19) epidemic. J Am Acad Dermatol 2020 Mar. i: S0190-9622(20)30390-X. doi: 10.1016/j.jaad.2020.03.012. [Epub ahead of print]
- 12. Yan Y, Chen H, Chen L, Cheng B, Diao P, Dong L, et al. Consensus of Chinese experts on protection of skin and mucous membrane barrier for health-care workers fighting against coronavirus disease 2019. Dermatol Ther 2020 Mar 13:e13310. doi: 10.1111/dth.13310. [Epub ahead of print]
- British Association of Dermatology. Advice for Dermatology HCPs during Covid-19 Pandemic. Homepage BJD https://www.bad.org.uk/.