

Their course was mostly mild and self-limiting. Only one patient with urticaria (nr. 45) required intravenous steroid treatment.

With regard to the urticarial manifestations, Polyethylene glycol-2000 (PEG-2000), an excipient of the vaccine, may play a role. In fact, PEG contained in several drugs can produce immediate hypersensitivity reactions¹ and cases of urticaria have been reported.² Moreover, PEG is investigated as possible responsible for the rare cases of anaphylaxis induced by *BioNTech/Pfizer* vaccine.^{3,4}

The question of completing the vaccination cycle, after urticaria triggered by the first dose, remains open. We preferred to avoid exposure to the second dose, because it is currently unclear whether it should be regarded as a risk factor for anaphylaxis, although the timing of onset after exposure is not consistent with a type I Ig-E mediated reaction. Regarding the other observed reactions, it must be admitted that FDE represents a stereotypic reaction induced by drugs, but it is rarely induced by vaccines.⁵ Conversely, pityriasis rosea has been reported after vaccinations or drug use.^{6,7} It appears remarkable that urticarial, pityriasis rosea-like rashes or chilblain-like changes have been frequently reported during or after COVID-19.^{8–10} For two patients (nr. 45–46), a swab and a serological test for SARS-CoV-2 resulted negative. For the remaining cases, we cannot exclude with certainty a contagion with SARS-CoV-2 shortly before or after the vaccine injection.

In conclusion, cutaneous adverse reactions triggered by *Comirnaty*®-*BioNTech/Pfizer* are seldom but appear similar to those reported during SARS-CoV-2 infections. Limitations of this study include the use of self-reported data. However, the reporting subjects were largely healthcare workers, and therefore, the reliability of data can be considered high. In addition, all the reports show a temporal relation with the vaccine, but this does not allow us to conclude that a true causal link exists.

The exact biological mechanisms underlying cutaneous effects after this mRNA COVID-19 vaccine have still to be elucidated, and further studies based on larger cohorts are needed to better understand them.

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References

- Cox F, Khalib K, Conlon N. PEG that reaction: a case series of allergy to polyethylene glycol. *J Clin Pharmacol* 2021; **61**: 832–835.
- Gökay SS, Çelik T, Sari MY *et al*. Urticaria as a rare side effect of polyethylene glycol-3350 in a child: case report. *Acta Clin Croat* 2018; **57**: 187–189.
- Garvey LH, Nasser S. Anaphylaxis to the first COVID-19 vaccine: is polyethylene glycol (PEG) the culprit? *Br J Anaesth* 2021; **126**: e106–e108.
- Blumenthal KG, Robinson LB, Camargo CA *et al*. Acute allergic reactions to mRNA COVID-19 vaccines. *JAMA* 2021; **325**: 1562–1565.
- Sako EY, Rubin A, Young LC. Localized bullous fixed drug eruption following yellow fever vaccine. *J Am Acad Dermatol* 2014; **70**: e113–e114.
- Drago F, Ciccarese G, Parodi A. Pityriasis rosea and pityriasis rosea-like eruptions: how to distinguish them? *JAAD Case Rep* 2018; **4**: 800–801.
- Atzori L, Pinna AL, Ferrel C, Aste N. Pityriasis rosea-like adverse reaction: review of the literature and experience of an Italian drug-surveillance center. *Dermatol Online J* 2006; **12**: 1.
- Zhao Q, Fang X, Pang Z *et al*. COVID-19 and cutaneous manifestations: a systematic review. *J Eur Acad Dermatol Venereol* 2020; **34**: 2505–2510.
- Visconti A, Bataille V, Rossi N *et al*. Diagnostic value of cutaneous manifestation of SARS-CoV-2 infection. *Br J Dermatol* 2021. **184**: 880–887.
- de Masson A, Bouaziz J-D, Sulimovic L *et al*. Chilblains is a common cutaneous finding during the COVID-19 pandemic: A retrospective nationwide study from France. *J Am Acad Dermatol* 2020; **83**: 667–670.

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Heterogeneous red–white discoloration of the nail bed and distal onycholysis in a patient with COVID-19

Editor

The severe acute respiratory syndrome, coronavirus 2 (SARS-CoV-2) disease (COVID-19) that emerged in China, was declared a pandemic on 11 March 2020, by the World Health Organization.¹ Numerous cutaneous symptoms such as pseudopernio, maculopapular, vesicular and urticarial rashes, livedoid or purpura-like vascular rashes, erythema multiforme-like rashes have been reported in COVID-19.² There are also case presentations mentioning nail symptoms related to COVID-19. Reports include half-moon-shaped transversal red bands;³ Beau lines;⁴ leukonychia in addition to Beau lines;⁵ and red half-moon nail



Figure 1 Heterogeneous red–white discoloration (yellow circles) and onycholytic areas surrounded by erythema (yellow arrows) in the distal part of the nail.

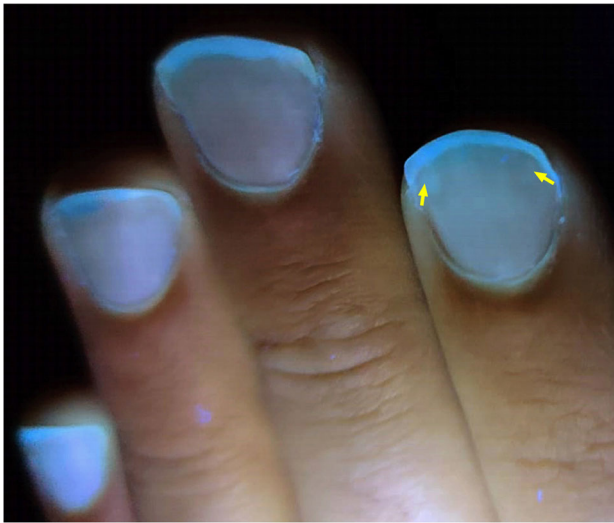


Figure 2 Onycholytic areas (yellow arrows) in the distal part of the nail in the Wood's lamp examination.

signs.⁶ This case report describes nail symptoms detected in a patient who applied to the dermatology outpatient clinic.

A 23-year-old male patient applied to the dermatology outpatient clinic with a complaint of discoloration in his nails. He stated that he had been isolated at home with the diagnosis of COVID-19 together with his parent and sister and had complaints of fever, sore throat and joint pain, but used no medications, 4 months ago. He also remarked that a red–white discoloration occurred in his nails during the disease, and he noticed a whiteness on the edge of his nails one month later.

There was no history of trauma, disease or medication use. In his dermatological examination, heterogeneous red–white discoloration in all his nails, and two round onycholytic areas surrounded by erythema in the distal part of the second nail on the left hand were detected (Fig. 1). In the Wood's lamp examination, onycholytic areas were observed only in the distal part of the second nail on the left hand only (Fig. 2). This clinical picture detected in the case reminded to Terry's nail, and it was wanted to be presented because it could be associated with COVID-19.

Terry's nail is a type of apparent leukonychia described as having a ground-glass appearance in the whole nail, loss of lunula and a pink discoloration in the nail distal. Although Terry's nail can also occur with the normal ageing process, it can be an indicator of diseases such as cirrhosis, chronic kidney failure and congestive heart failure.⁷ The overgrowth of connective tissue due to the change in nail bed vascularity has been held responsible for the incidence. Telangiectasia in the distal band has been reported in the nail bed biopsy.⁸

In the case presented here, heterogeneous red–white discoloration and distal onycholytic areas have been detected in the whole nail. In patients with COVID-19, it has been stated that pericapillary oedema, dilatation, folding and density decrease in capillaries have been detected in nail-fold examinations by videocapillaroscopy.⁹ The role of COVID-19 could not be clearly evaluated in this patient; however, heterogeneous red–white discoloration in the nail bed has been associated with possible oedema and inflammation. In biopsies taken from cutaneous lesions associated with COVID-19, there have been reports of epidermal characteristics such as acantholysis, multinuclear ballooned keratinocytes, dyskeratosis and necrosis and histopathological features such as dermal vascular damages including lymphocytic vasculitis and, endotheliitis especially in the presence of severe thrombosis.¹⁰

In the patient, a nail biopsy could not be taken due to cosmetic apprehension. It was considered that round onycholytic areas surrounded by erythema reminiscent of the psoriasis nail could be an indication for a localized microvascular damage. This nail image, which has not been previously reported, should be presented as it may be associated with COVID-19.

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References

- Jin Y, Yang H, Ji W *et al*. Virology, epidemiology, pathogenesis, and control of COVID-19. *Viruses* 2020; **12**: 372.
- Daneshgaran G, Dubin DP, Gould DJ. Cutaneous manifestations of COVID-19: an evidence-based review. *Am J Clin Dermatol* 2020; **21**: 627–639.
- Neri I, Guglielmo A, Virdi A, Gaspari V, Starace M, Piraccini BM. The red half-moon nail sign: a novel manifestation of coronavirus infection. *J Eur Acad Dermatol Venereol* 2020; **34**: e663–e665. <https://doi.org/10.1111/jdv.16747>
- Alobaida S, Lam JM. Beau lines associated with COVID-19. *Can Med Assoc J* 2020; **192**: E1040.
- Ide S, Morioka S, Inada M, Ohmagari N. Beau's lines and leukonychia in a COVID-19 patient. *Intern Med* 2020; **59**: 3259.
- Mendez-Flores S, Zaladonis A, Valdes-Rodriguez R. COVID-19 and nail manifestation: be on the lookout for the red half-moon nail sign. *Int J Dermatol* 2020; **59**: 1414.
- Abdullah L, Abbas O. Common nail changes and disorders in older people: diagnosis and management. *Can Fam Physician* 2011; **57**: 173–181.
- Witkowska AB, Jasterzbski TJ, Schwartz RA. Terry's nails: a sign of systemic disease. *Indian J Dermatol* 2017; **62**: 309–311.
- Natalello G, De Luca G, Gigante L *et al*. Nailfold capillaroscopy findings in patients with coronavirus disease 2019: Broadening the spectrum of COVID-19 microvascular involvement. *Microvasc Res* 2021; **133**: 104071.
- Kaya G, Kaya A, Saurat JH. Clinical and histopathological features and potential pathological mechanisms of skin lesions in COVID-19: review of the literature. *Dermatopathology* 2020; **7**: 3–16.

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Androgenetic alopecia in women and men is not related to COVID-19 infection severity: a prospective cohort study of hospitalized COVID-19 patients

To the Editor,

The ongoing outbreak of COVID-19 has posed significant threats to international health. The first biologic step of potential infectivity of COVID-19 is the priming of the spike proteins by transmembrane protease, serine 2 (TMPRSS2). TMPRSS2 cleave angiotensin converting enzyme 2 for augmented viral entry and thus is regarded as essential for viral spread and pathogenesis in the infected hosts.^{1,2} Androgen receptor activity is considered as a requirement for the transcription of the TMPRSS2 gene and no other regulatory element of the TMPRSS2 promoter has been described in human to date.³ Thus, this led us to hypothesize

that variations in the androgen receptor gene may predispose male COVID-19 patients to increased disease severity.

Through a prospective study, 116 hospitalized patients due to severe COVID-19 infection (confirmed with viral nucleic acid testing) were involved in the study. Lung high-resolution computed tomography (HRCT) findings as well as laboratory data, and disease outcome including discharge, intensive care unit (ICU) care, intubation and death, were recorded for each patient. hyper-androgenic skin manifestations including androgenetic alopecia (AGA), acne severity, seborrheic dermatitis and hirsutism were examined by a dermatologist. Severity of AGA was assessed using Hamilton scale and Ludwig scale for male and female patients, respectively. Patients with immunosuppressive conditions and anti-androgenic medication were excluded. Analyses were carried out by Statistical Package for Social Sciences computer software (SPSS version 16, Chicago, IL, USA).

Totally, 118 confirmed COVID-19 patients including 61 men (51.7%) and 57 women (48.3%) with mean age of 60.45 ± 15.99 (ranging 18–100) years were investigated. All the patients were symptomatic. Triad of dyspnoea, cough and fatigue were the most common symptoms that were recorded in 100 (84.7%), 78 (66.1%) and 57 (48.3%) patients, respectively. Twenty-nine patients (24.4%) had all the symptoms of the triad (Table 1).

Chest HRCT showed abnormalities in 115 patients (97.4%) whom all of them had more than one involved lobe. Lesions were inclined to distribute in the lower lobes. Right inferior (92.3%) and right middle lobes (61.0%) were the most and the least affected lobes, respectively. Combination of ground glass opacification and consolidation which was presented in 65 patients (55.1%) was the most involved pattern.

Androgenetic alopecia was present in 45 men out of 61 (73.7%) including 13 (28.8%) severe AGA (Hamilton scale >5), 22 (48.8%), moderate AGA (Hamilton scale 3–4) and 10 (22.2%) mild AGA (Hamilton scale 1–2). In total, 32 women out of 57 (56.1%) had AGA including 2 (6.2%) severe AGA (Ludwig score advanced and frontal), 14 (43.7%) moderate AGA (Ludwig score 2–3) and 16 (50.0%) mild AGA (Ludwig score 1). Both the mortality rate and AGA severity were significantly higher in patients over 60 years old ($P = 0.003$ and 0.020 , respectively). AGA was significantly higher in men than women ($P = 0.045$). AGA severity did not show any significant correlation with HRCT severity, neither with patients' ICU care, intubation and expire in both genders. Similarly, other hyper-androgenic manifestations did not significantly correlate with disease outcome and HRCT severity (Table 2).

Among disease outcomes, ICU care, intubation and death were recorded in 48 patients (40.7%), 16 (13.6%) and 22 (18.6%) patients, respectively. Mortality rate was 18.0% among males (11 patients) and 19.3% among women (11 patients). No