Letter to the Editor

Nail changes as manifestation of systemic disease in COVID-19 infection

To the editor

Skin is one of the most commonly affected organs by the SARS-CoV-2 infection. Different manifestations including skin, mucous membranes and hair have been reported. Until recently, not many articles incorporate nail manifestations of COVID-19. We conducted a literature search in Pubmed, Embase, The Cochrane Library, EBSCO and Google scholar databases regarding all the case reports and series of nail changes associated to COVID-19 infection. Included cases are summarized in Table 1.

A total of six case reports were found: two reported beau lines, two red half-moon nail sign, one onychomadesis and one a distal orange discoloration. Median age was of 53.5 years (range 37 to 89 years). Four patients were females and two males. Median time of onset of nail manifestations after the diagnosis of COVID-19 was of 56 days (range 2 to 112 days). The earliest manifestations were red half-moon nail sign, 2 and 14 days after diagnosis, and the latest the distal orange discoloration. Beau lines appeared after 28 and 98 days and onychomadesis after 84 days. Different COVID-19 symptoms were described, and the most frequently found was fever, which was present in four patients. After this, dyspnoea and cough were reported in three patients each. Other found symptoms were diarrhoea, anosmia, ageusia and sore throat. Of the six included patients, three required hospital admission and in one of these oxygen requirements were reported (red half-moon nail sign). The most commonly used treatment was hydroxychloroquine (3/6) and ceftriaxone (2/6). Other used therapies were methylprednisolone, lopinavir/ritonavir, oseltamivir and heparin.

Nails, like the rest of the skin, could provide important information regarding COVID-19 disease and systemic involvement. The exact pathogenesis of nail changes in patients with SARS-CoV-2 infection has not been completely understood. The red half-moon nail sign, which represents a transversal red band that surrounds the distal margin of the nail's lunula, could be associated to microvascular injury or to a procoagulant state connected to an inflammatory immune response. Because of the location, the distal subungual arcade's capillary network might be affected in these cases. Beau lines or transverse grooves in the nail plate can be caused by a temporary interruption of nail matrix growth. In more severe cases, an inhibition of the nail's proliferation causes a separation of the nail plate from the nail bed with an eventual shedding or onychomadesis. These alterations often occur after a systemic insult, such as infections, critical illnesses, drugs or autoimmune diseases. Lastly, no clear explanation for the transverse orange nail lesions has been found, but the shape of the discoloration favours a systemic illness. All of these findings have been previously described in Kawasaki disease, a disease that like COVID-19 has a vascular aetiology.

The published evidence regarding nail changes and COVID-19 is scarce, and no conclusion of the aetiology can be clearly made. We prompt authors to investigate and document nail changes as manifestations of COVID-19 infection.

Table 1 Summary of published case reports of nail manifestations in patients with COVID-19

| Authors                  | Number of patients | Gender | Age (years) | Nail manifestation | Time of onset (days) | COVID-19 symptoms                                      | Hospital admission | Oxygen requirement | Treatment for COVID-19 |
|--------------------------|--------------------|--------|-------------|--------------------|----------------------|--------------------------------------------------------|--------------------|--------------------|-----------------------|
| Alobaida et al. 2020³    | 1                  | M      | 45          | Beau lines         | 98                   | Diarrhoea, fever, and dyspnoea                         | No                 | NR                 | NR                    |
| Ide et al. 2020⁴         | 1                  | M      | 68          | Beau lines and leuconychia | 28                  | Fever, dyspnoea                                       | Yes                | NR                 | HCQ, 6-MP             |
| Méndez-Flores et al. 2020⁵| 1                  | F      | 37          | Red half-moon nail sign | 2                  | Anosmia, cough, fever                                 | No                 | No                 | NR                    |
| Neri et al. 2020⁵        | 1                  | F      | 60          | Red half-moon nail sign | 14                  | Fever, cough, dyspnoea, anosmia, ageusia              | Yes                | Yes                | HCQ, L/R, ceftriaxone, heparin |
| Tammaro et al. 2021⁶      | 1                  | F      | 89          | Orange discoloration | 112                 | Cough, asthenia                                       | NR                 | NR                 | NR                    |
| Senturk et al. 2020¹      | 1                  | F      | 47          | Onychomadesis      | 84                   | Sore throat                                           | Yes                | NR                 | HCQ, azithromycin, oseltamivir, ceftriaxone |

M, Male; F, female; NR, not reported; HCQ, hydroxychloroquine; 6-MP, methylprednisolone; L/R, lopinavir/ritonavir.
changes in COVID and post-COVID patients in order to obtain a panoramic image of COVID-19’s systemic manifestations. Nails can function as an alarm sign for physicians regarding systemic diseases, including COVID-19.

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