Dear Editor,

COVID-19 is currently one of the main causes of death worldwide. This virus affects mainly the lower respiratory system, but significant damage to other organs has been observed. Cutaneous manifestations related to the aforementioned viral infection have been reported with an incidence that ranges between 0.20% and 20%. The period between the appearance of cutaneous lesions and COVID-19 infection remains uncertain.1,2 With the information that exists, one can speculate that cutaneous manifestations of COVID-19 can be classified into two groups

Figure 1 In this graphic, patients with cutaneous manifestations (blue dots) and without cutaneous manifestations (green dots) are plotted according to their prognosis using clinical and biochemical variables. The red box represents patients with a P/F ratio >200 and CRP <11 mg/dL. The grey box represents patients with a P/F ratio >200 and CRP >11 mg/dL. The black box represents patients with a P/F ratio <200 and CRP >11 mg/dL.
depending on their physiopathological process: clinical characteristics similar to viral exanthems and cutaneous eruptions due to systemic consequences, especially vasculitis and thrombotic vasculopathy. Currently, the American Academy of Dermatology (AAD) is in the process of elaborating a registry with the most common cutaneous manifestations observed in patients with COVID-19. The most frequent ones are morbilliform exanthem (22%), pernio (18%), urticaria (16%), macular erythema (13%), vesicular eruption (11%), papulosquamous eruption (9.9%) and retiform purpura (6.4%).

In our centre, we performed a case-control study involving 97 hospitalized patients in non-critical care areas. We did a complete dermatological physical examination and measured biochemical inflammatory markers to all patients with a positive molecular test for SARS-CoV-2. Afterwards, we analysed our variables to correlate cutaneous manifestations with PaO2/FiO2 (P/F) ratio and biochemical inflammatory markers to determine prognosis and disease severity of COVID-19 infection.

We proceeded to dichotomize our population using a cut-off value for each variable to determine disease severity and poor prognosis. Such values were C-reactive protein (CRP) >11 mg/dL, total lymphocyte count <800 µL, D-dimer >1000 ng/mL, ferritin >500 mg/L, lactate dehydrogenase >245 UI/L and P/F ratio <200.

We sought the following cutaneous manifestations: morbilliform exanthem, urticaria, urticarial dermatosis, macular erythema, papular exanthem, skin necrosis, retiform purpura, vesicular lesions, pernio-like lesions and varicella-like exanthem. We found that the most frequent dermatological manifestation was papular exanthem (38%), followed by macular erythema (23%), morbilliform exanthem (16%) and retiform purpura (15%). We did not observe retiform purpura, vesicular lesions, varicella-like exanthem or pernio in our study population. The presence of these four cutaneous manifestations correlated with CRP values <11 mg/dL and a P/F ratio >200, with P values of 0.035 and 0.039, respectively, and a strength of association of 0.244 and 0.214, respectively (Fig. 1). Also, hospitalization time in patients with cutaneous lesions was slightly shorter (1.5 days) than in patients without skin lesions (Fig. 2).

We observed that cutaneous manifestations of SARS-CoV-2 infection are related to the severity of the disease depending on the presenting skin lesion. In our study, the most frequent dermatological manifestation was a papular exanthem, different to what is reported in other series, where the most common cutaneous lesion was a morbilliform exanthem.

Despite most case series worldwide report pernio as a common cutaneous manifestation, in our study none of our patients...
developed such lesion. This could be explained by the fact that we did not include paediatric patients, where pernio commonly manifests. Retiform purpura and skin necrosis are cutaneous manifestations that correlate strongly with severe COVID-19 infection; the Spanish Workgroup that studied 375 patients reported that individuals who developed these cutaneous manifestations have a mortality of 10%. Results obtained from our study are similar to what is reported in literature. In the database collected by the AAD, manifestations considered to be related with a favourable-intermediate prognosis were pernio, morbilliform exanthem, urticaria, macular erythema, vesicular eruption and papulosquamous eruption.

We conclude that dermatological manifestations in COVID-19 are relatively common. These could be useful as prognostic markers, especially in hospitals or primary healthcare centres with limited resources, since their relationship with the clinical severity of the disease depends on the type of dermatological manifestation.

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None.

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**Persistent maculopapular rash after the first dose of Pfizer-BioNTech COVID-19 vaccine**

*To The Editor,*  
The ongoing global pandemic COVID-19 led regulatory agencies to recently issue an emergency authorization for two effective COVID-19 vaccines from Pfizer-BioNTech and Moderna. Both vaccines use a novel technology of administering vaccination, namely a lipid nanoparticle-formulated, nucleoside-modified mRNA vaccine encoding the spike glycoprotein of SARS-CoV-2 for subsequent antigen presentation and immune system activation.

Although this novel vaccine technology is purported to be generally safe, the adverse effects and especially skin effects of mRNA vaccines are not yet completely characterized. In phase III clinical trial of Pfizer-BioNTech COVID-19 vaccine and in the first post-market morbi–mortality report, the main skin manifestations reported were anaphylaxis skin symptoms like urtica and diffuse erythematous rash and non-anaphylaxis allergic symptoms as an injection-site reaction, pruritus and rash without any semiological description. Recently, it was reported a case of a pruritic erythematous macular morbilliform eruption in a patient after each of the two injections of the Pfizer-BioNTech COVID-19 vaccine with spontaneous resolution in 24 h. Herein, we report a case of a different persistent maculopapular eruption onset for a few hours after the first injection of the Pfizer-BioNTech COVID-19 vaccine associated with liver damage, not described before.

A 55-year-old male hospital nurse, with no past medical history and no drug allergy, received the first dose of the Pfizer-BioNTech COVID-19 vaccine. Three hours after vaccination, the patient experienced injection-site soreness in the deltoid region with localized pruritic erythematous eruption which later spread on the face, trunk, upper extremities and thighs. During week 3, facing this persistent and unchanged eruption the patient presented at the dermatological consultation wondering about the safety of the second dose of vaccine. Clinical examination confirmed a maculopapular exanthema with 30% of body surface area involved (Fig. 1). Oral and genital mucosa was preserved and there was no fever, arthralgia or other systemic symptoms. HIV, HBV, HCV, CMV, EBV and measles serologies were negative and blood test only showed slight hepatic cytolysis (ASAT and GGT 2N). A punch biopsy was performed and haematoxylin and eosin-stained sections showed slight lymphocytic perivascular infiltrate, compatible with non-severe maculopapular toxi-dermia late biopsied.

It was decided not to perform the second dose because of the persistence of the rash, the liver damage and the known risk of more severe reaction after a first sensibilization, and the case was reported at the pharmacovigilance authority.

The rash persisted over a month with a gradual improvement over the days with dermocorticoid treatment in parallel with the improvement of liver enzymes.

The particular interest of our case is the early development of the rash with localized onset and its persistence over time with liver involvement, which led not to perform the second dose of vaccine. This is an example of the important role that healthcare providers and the dermatologists, in particular, play in the safety of these new vaccines by being vigilant in recognizing and reporting adverse events to the competent pharmacovigilance...