Figure 2 (a,b) Erythematous purpuric lesions associated with secondary blistering of the toes; (c) 14 days later, the lesions had resolved without treatment.

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References

1 Crowson AN, Magro CM. Idiopathic perniosis and its mimics: a clinical and histological study of 38 cases. *Hum Pathol* 1997; **28**: 478–84.
2 Alramthan A, Aldaraji W. A case of COVID-19 presenting in clinical picture resembling chilblains disease. First report from the Middle East. *Clin Exp Dermatol* 2020;**45**: 746–8..
3 Piccolo V, Neri I, Filippeschi C *et al*. Chilblain-like lesions during COVID-19 epidemic: a preliminary study on 63 patients. *J Eur Acad Dermatol Venereol* 2020;**34**: e291–3..
4 Kolivras A, Dehavay F, Delplace D *et al*. Coronavirus (COVID-19) infection induced chilblains: a case report with histopathological findings. *JAAD Case Reports* 2020;**6**: 489–92..
5 Ip DK, Lau LL, Leung NH *et al*. Viral shedding and transmission potential of asymptomatic and paucisymptomatic influenza virus infections in the community. *Clin Infect Dis* 2017; **64**: 736–42.

Erythema multiforme-like eruption in patients with COVID-19 infection: clinical and histological findings

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Cutaneous manifestations in patients with COVID-19 infection are increasingly being reported. Several patterns have been described since the initial report by Recalcati,[1] including erythematous maculopapular,[1] urticarial,[1,2] chickenpox-like,[1,3] purpuric periflexural,[4] transient livedo reticularis,[5] and acroischaemic or chilblain-like lesions.[6,7]

Table 1 Clinical and laboratory findings of the four patients with erythema multiforme-like eruption.

Patient	Sex	Age, years	Days after symptoms[a]	Days after treatment[a]	Drugs	Microbiological tests	Worsening of laboratory parameters[b]
1	F	63	19	16	L/R, H, A, Cs, Ce	Not performed	Elevation of CRP and D-dimer
2	F	77	16	11	L/R, H, A, Cs	Negative for HIV, EBV, CMV, VZV, HSV, *M. pneumoniae*, syphilis	Not performed
3	F	58	24	15	L/R, H, A, Cs, Ce	Not performed	Elevation of D-dimer; decrease in lymphocyte count
4	F	69	19	10	L/R, H, A	Negative EVB for HIV, EBV, CMV, VZV, HSV, *M. pneumoniae*, syphilis. HSV PCR found in vesicle swab	Elevation of CRP and D-dimer; decrease in lymphocyte count

A, azithromycin; Ce, ceftriaxone; Cs, corticosteroids; CMV, cytomegalovirus; CRP, C-reactive protein; EBV, Epstein–Barr virus; H, hydroxychloroquine; HIV, human immunodeficiency virus; HSV, herpes simplex virus (PCR multiplex); LR, lopinavir/ritonavir; *M.*, *Mycoplasma*; VZV, varicella zoster virus. [a]Days from the onset of COVID-19 symptoms and from the start of treatment to the appearance of cutaneous lesions, respectively; [b]worsening of laboratory parameters at the time of skin lesions, compared with those at the time of discharge.

We report the observation a new pattern with erythema multiforme (EM)-like lesions in four hospitalized patients with COVID-19 infection.

All four patients were women, with a mean age of 66.75 years (range 58–77 years). Mean interval between the onset of COVID-19 symptoms to the appearance of cutaneous lesions was 19.5 days (range 16–24 days). One patient developed the skin rash during hospitalization, while the remaining three patients had been previously discharged after clinical, analytical and radiological improvement, and a negative COVID-19 PCR test.

These three patients returned to the emergency department because of the skin rashes at 6, 7 and 4 days after discharge, respectively. Laboratory tests at the time of presentation showed worsening of one or more parameters (C-reactive protein, D-dimer or lymphocyte count), compared with those at the time of discharge. However, none of the patients presented recurrence of clinical symptoms of COVID-19. Microbiological studies were performed in two patients, which excluded other infectious diseases (Table 1). In all patients, the skin lesions had begun as erythematous papules on the upper trunk, which progressively turned to erythematoviolaceous patches with a dusky centre, and a pseudovesicle in the middle. Typical EM targetoid lesions were observed in two patients. Lesions coalesced markedly on the back, and then spread to the face and limbs within 1 week, without involvement of the palms or soles (Fig. 1). These patients underwent oral cavity examination, which revealed palatal macules and petechiae.

Histological examination was similar in all patients, revealing a normal basket-weave stratum corneum, and mild to moderate spongiosis in epidermis. The dermis showed dilated vessels filled with neutrophils, extravasation of red blood cells, and lymphocytic perivascular and interstitial infiltrate. Basal vacuolar changes with interface dermatitis were observed in one patient, and lymphocytic exocytosis in another (Fig. 2). All patients were treated with systemic corticosteroids with progressive resolution of the skin lesions within 2–3 weeks.

We are facing challenging times in dermatology. New information and details of cutaneous manifestations possibly related to COVID-19 are emerging every day. Further studies are needed to evaluate whether these lesions are associated with the virus, the drugs used or any other conditions. EM is linked to infectious agents in 90% of cases, while drug-associated EM is reported in < 10%. Herpes simplex virus and *Mycoplasma pneumoniae* are the main agents, but other viruses have been reported, such as adenovirus, coxsackievirus and parvovirus B19.[8] We suggest that this EM-like or target-like exanthem might be another pattern of exanthem associated with COVID-19 infection. Recent articles have also reported targetoid lesions in exanthems of patients with COVID-19 infection.[9,10] In addition, the presence of pseudovesicles and enanthem are two clues that suggest an infectious cause rather than a drug reaction. However, we cannot positively exclude the involvement of the various drugs administered to the patients. To our knowledge, this is a first observation that will require further investigation.

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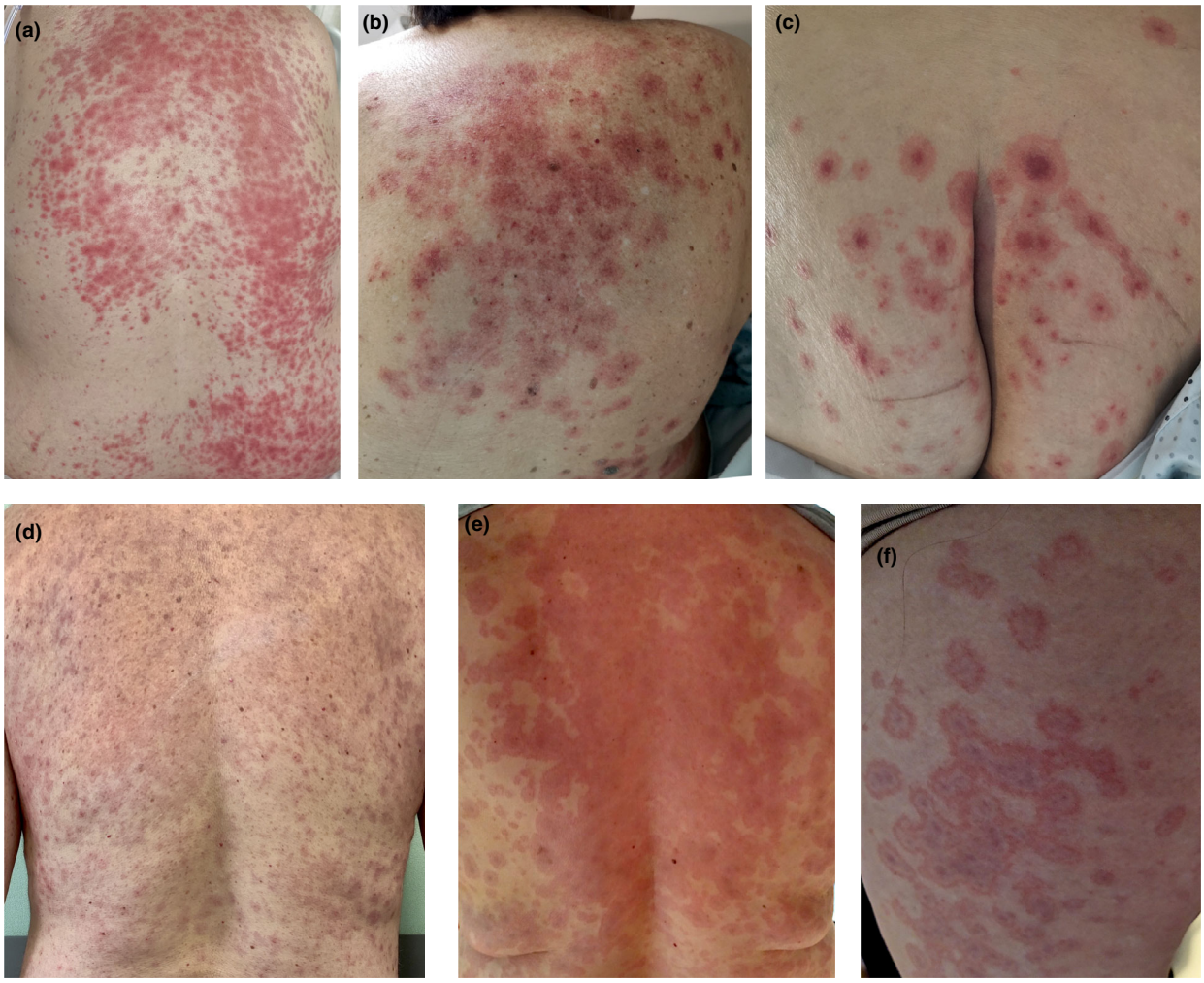

Figure 1 Clinical presentation of erythema multiforme (EM)-like exanthem in (a) Patient 1; (b) Patient 2; (d) Patient 3; and (e) Patient 4 showing coalescing erythemato violaceous patches with a dusky centre, some of them with pseudovesicles in the middle, located on the back. Typical EM targetoid lesions were observed on (c) the buttocks of Patient 2 and (f) the thigh of Patient 4.

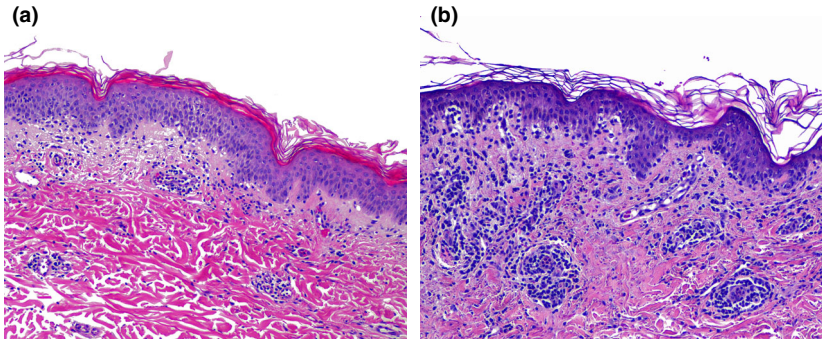

Figure 2 (a) Histological examination of Patient 1 showed normal basketweave stratum corneum, mild to moderate spongiosis and lymphocytic exocytosis in the epidermis, while the dermis showed dilated vessels filled with neutrophils, extravasation of red blood cells, and lymphocytic perivascular and interstitial infiltrate. (b) Patient 3 had basal vacuolar changes with interface dermatitis.

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References

1 Recalcati S. Cutaneous manifestations in COVID-19: a first perspective. *J Eur Acad Dermatol Venereol* 2020; **345**: e212–e213.https://doi.org/10.1111/jdv.16387

2 Fernandez-Nieto D, Ortega-Quijano D, Segurado-Miravalles G *et al.* Comment on: Cutaneous manifestations in COVID-19: a first perspective. Safety concerns of clinical images and skin biopsies. *J Eur Acad Dermatol Venereol* 2020. https://doi.org/10.1111/jdv.16470

3 Tammaro A, Adebanjo GAR, Parisella FR *et al.* Cutaneous manifestations in COVID-19: the experiences of Barcelona and Rome. *J Eur Acad Dermatol Venereol* 2020. https://doi.org/10.1111/jdv.16530

4 Jimenez-Cauhe J, Ortega-Quijano D, Prieto-Barrios M *et al.* Reply to "COVID-19 can present with a rash and be mistaken for dengue": petechial rash in a patient with COVID-19 infection. *J Am Acad Dermatol* 2020. https://doi.org/10.1016/j.jaad.2020.04.016

5 Manalo IF, Smith MK, Cheeley J, Jacobs R. A dermatologic manifestation of COVID-19: transient livedo reticularis. *J Am Acad Dermatol* 2020. https://doi.org/10.1016/j.jaad.2020.04.018

6 Fernandez-Nieto D, Jimenez-Cauhe J, Suarez-Valle A *et al.* Characterization of acute acro-ischemic lesions in non-hospitalized patients: a case series of 132 patients during the COVID-19 outbreak. *J Am Acad Dermatol* 2020. https://doi.org/10.1016/j.jaad.2020.04.093

7 Piccolo V, Neri I, Filippeschi C *et al.* Chilblain-like lesions during COVID-19 epidemic: a preliminary study on 63 patients. *J Eur Acad Dermatol Venereol* 2020. https://doi.org/10.1111/jdv.16526

8 Sokumbi O, Wetter DA. Clinical features, diagnosis, and treatment of erythema multiforme: a review for the practicing dermatologist. *Int J Dermatol* 2012; **51**: 889–902.

9 Amatore F, Macagno N, Mailhe M *et al.* SARS-CoV-2 infection presenting as a febrile rash. *J Eur Acad Dermatol Venereol* 2020. https://doi.org/10.1111/jdv.16528

10 van Damme C, Berlingin E, Saussez S, Accaputo O. Acute urticaria with pyrexia as the first manifestations of a COVID-19 infection. *J Eur Acad Dermatol Venereol* 2020. https://doi.org/10.1111/jdv.16523

Cutaneous manifestations in COVID-19: familial cluster of urticarial rash

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Coronavirus disease (COVID-19) is a new infectious disease that is rapidly spreading across the world. Many clinical manifestations of the virus have been described, and new symptoms are emerging, but only a few cases of skin manifestation have been described since the pandemic was announced by the World Health Organization in March.[1,2]

Common clinical features of COVID-19 reported include fever, cough, myalgia, fatigue, headache, shortness of breath and diarrhoea.[1]

Some reports have suggested that skin manifestations are present in up to 20.4% of patients with COVID-19, and reports suggest a wide range of skin conditions being related to the virus, including widespread urticaria, morbilliform rash, erythematous rash, chickenpox-like vesicles, purpuric rash, dusky acrocyanosis, dry gangrene, petechiae rash coexisting with thrombocytopenia, transient livedo reticularis and red papules on fingers resembling chilblains.[2–5] Unfortunately, some of these reports do not have clinical pictures to show the relation between COVID-19 and the skin manifestations.

We report a family of five members living in the city of Monterrey, Mexico who tested positive for COVID-19, as a result of one of the members becoming infected during a trip to New York in February 2020. All five patients had anosmia, ageusia, chills and dizziness, and two of them had skin manifestations associated with COVID-19.

Patient 1 was a 50-year-old woman, and Patient 2 was a 20-year-old woman, who was the daughter of Patient 1. Both patients had a bilateral disseminated rash on the shoulders, elbows, knees and buttocks, characterized by erythematous annular and irregular weals on the skin that appeared suddenly and disappeared within < 24 h (Fig. 1). The rash appeared after the cough and fever appeared. Neither patient had any history of similar lesions, and no trigger factors other than the viral context were identified. No other clinical or laboratory examinations were positive.

A diagnosis of urticaria associated with COVID-19 was made. Both patients were treated with antihistamines and moisturizers, and 48 h after treatment was started the urticaria resolved.

Although urticarial rash is the most common skin manifestation described in COVID-19 infection, cases can be classified into two groups: those related to the virus and those associated with complications and management.[5]