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Cutaneous manifestations of COVID-19 in Mexican patients: A case series and review of literature

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Abstract

China officially recognized atypical pneumonia outbreak in December 2019; on 11 March 2020, the World Health Organization declared COVID-19 as a pandemic that is produced by a new coronavirus, named SARS-CoV-2, of rapid transmissibility, which can be asymptomatic, with mild to severe respiratory symptoms, and with cardiovascular, neurological, gastrointestinal, and cutaneous complications. Considering that the pandemic prolonged more than initially expected was prognostic, it is essential for the medical community to identify the signs and symptoms of COVID-19. Thus, this work's objectives were to present cases of cutaneous lesions observed in COVID-19 Mexican patients. We register cutaneous lesions in COVID-19 patients referred from internal medicine and otorhinolaryngology services to dermatology. We presented four interesting cases with cutaneous lesions, including exanthema morbilliform, urticaria, chilblains, ecchymosis, and facial edema, and review the available literature. The most frequent cutaneous markers are rash, chilblains, and urticaria. Skin lesions may be the first manifestation of COVID-19, accompany initial respiratory symptoms, or appear during the disease course. Symptoms associated with vascular changes (livedo reticularis and vasculitis) are considered of poor prognosis.

Keywords

COVID-19, SARS-CoV-2, rash, chilblain, urticaria, livedo reticularis, vasculitis

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Introduction

The disease called "acute cor pulmonale caused by coronavirus-2" (SARS-CoV-2) was initially described as a respiratory infection that produced severe pneumonia and presented a high transmission rate; the clinical condition was denominated COVID-19 (*CO*rona*VI*rus *D*isease 2019); clinical manifestations included cardiac, digestive, neurologic, and cutaneous signs, and severe complications included death. Thus, on 11 March 2020, COVID-19 was declared as a pandemic after a global spread.[1] The virus is globally expanding, with more than 92.3 million infected and 1.98 million deaths worldwide, and 1,570,000 confirmed cases and 137,000 deaths in Mexico, by 14 January 2021.

Cutaneous symptoms can be the first in appearance, accompany respiratory symptoms, or be subsequent. Given the limited number (in this pandemic) of internal medicine, emergency, and intensive care clinicians, it is critical that all physicians can identify signs and symptoms associated with COVID-19. Considering that Latin America is the current epicenter of the pandemic, and Europe presented the third wave of new cases, this article's objectives were, first, to present images of cutaneous lesions observed in COVID-19

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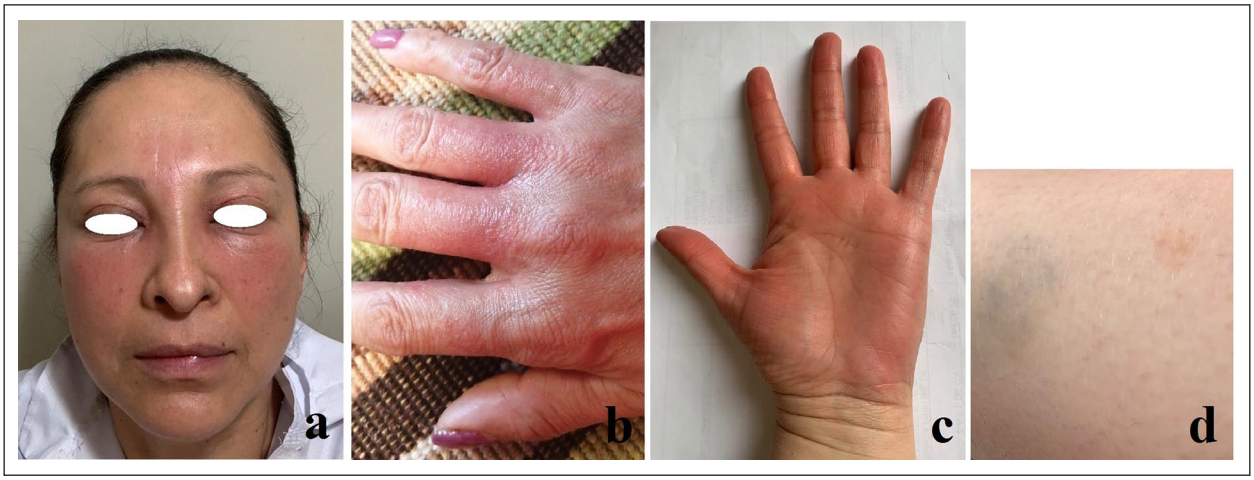

Figure 1. Case 1. (a) A 43-year-old female nurse with facial and eyelid edema. Case 2: A 45-year-old female with (b) chilblains, (c) hand edema and erythema (hand-in-glove), and (d) morbilliform erythema and ecchymosis.

patients and, second, to perform a review of the available literature on COVID-19 and skin manifestations.

We register cutaneous lesions in COVID-19-diagnosed patients referred by internal medicine and otorhinolaryngology (ORL) services. We review eight patients who presented cutaneous manifestations associated with COVID-19. According to the Helsinki Declaration of Human Rights, only four authorized the presentation of their pictures and details of their cases, given their written consent.

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Case 1

A female patient, 43-year-old nurse working in COVID area of the tertiary General Hospital, presented with facial edema and facial erythema (Figure 1(a)); after 48 h of evolution, she also presented odynophagia and general malaise; the COVID-19 test reported positive 2 days later. She was managed with rest at home and general measures, and no other complications were reported. After 15 days, decreased edema resulted in facial flaccidity and an aged appearance without other sequalae.

Case 2

In June 2020, a 45-year-old female lawyer presented to an ORL physician with general malaise, odynophagia, ageusia, and fever. COVID-19 was confirmed by polymerase chain reaction test (PCR) test. She was managed with rest at home and with antipyretic and analgesic medications. One week after diagnosis and an initial improvement in odynophagia, she developed cutaneous lesions characterized by morbilliform rash, edema, and erythema in hands and feet, and few ecchymoses in the abdomen, legs, and arms (Figure 1(b)–(d)); she also reported hemicrania headache, and distal pain. Initial laboratories only reported low levels of ketones and proteins in urine; hematic biometrics, clotting times, D-dimer, and C-reactive protein were in normal values. She received loratadine/betamethasone 5/0.25 mg VO twice a day with partial improvement, but 10 days later, the distal edema intensified and more ecchymosis was present. At this moment, laboratories reported blood in urine sample, with increased D-dimer and C-reactive protein; thus, prednisone 50 mg/day was started. She showed clinical improvement, and 4 weeks later, laboratory values returned to normal, but still intermittent hand erythema was present and she was continued in clinical observation by telemedicine consultation weekly until complete recovery 8 weeks later.

Case 3

Beginning March 2020, a 37-year-old female patient who had a recent voyage outside Mexico presented with fever, diarrhea, general malaise, and cutaneous distal erythema in toes (Figure 2(a)). Laboratory studies reported leukocytosis and denied bacterial or parasitic gastrointestinal infection. Thus, COVID-19 test was demanded and COVID-19 infection was confirmed. The patient was treated with hydric support, antipyretics, vitamin complex, and loratadine/betamethasone 5/0.25 mg. After 2 weeks, she was asymptomatic.

Case 4

In July 2020, a 39-year-old female consulted a general physician with odynophagia, pharyngeal erythema, geographic tongue, and general malaise. The PCR COVID-19 test confirmed COVID-19 suspicion. Also, her husband presented respiratory signs of COVID-19 and laboratory confirmation but without other signs. A few days later, she presented morbilliform erythema, finger paleness, and distal paresthesia and still had pharyngeal symptoms present (Figure 2(b) and

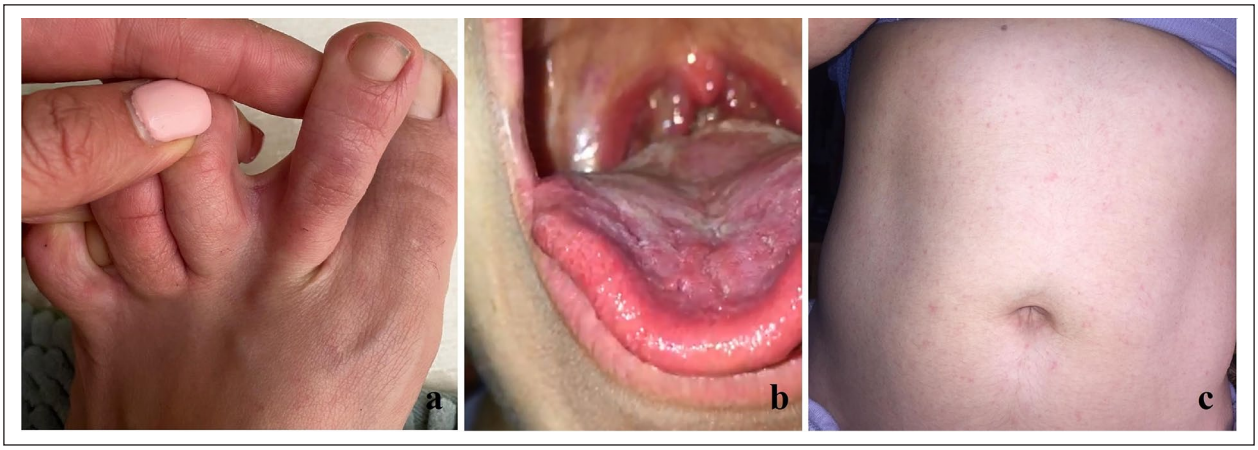

Figure 2. Case 3: (a) chilblains. Case 4: (b) pharyngeal hyperemia and (c) morbilliform erythema.

(c)). Thus, she was evaluated by a dermatologist, who after clinical and laboratory evaluation found no other causes of cutaneous symptoms more than COVID-19 infection. Rest at home, isolation, painkillers, and subsequent follow-up were indicated. In addition, blood count and D-dimer were demanded to complete the evaluation, but the patient did not return for the next appointment. Three weeks later, she was contacted by telephone and reported no cutaneous symptoms, but persistent odynophagia and pharyngeal pain.

Discussion

COVID-19 general aspects

COVID-19 is produced by SARS-CoV-2, a spherical virus which is single-stranded and has a positive-sense RNA of 30,000 bp; it belongs to the family Coronaviridae and is related to SARS-CoV and coronavirus isolated from bats.[2,3] It has structural proteins named spike (S), nucleocapsid (N), membrane (M), and envelope (E) and 16 nonstructural proteins.[4] SARS-CoV-2 compared with SARS-CoV and MERS-CoV has faster transmissibility, which is transferred from person to person, like influenza. The rapid spread is a well-proven fact, as well as transmission by asymptomatic carriers. SARS-CoV-2 was identified in feces and is thought to be a fecal–oral transmission. Symptoms appear 2–14 days after exposure. The infection may be asymptomatic or have symptoms that vary from moderate to severe, even causing death.[5,6] It affects people of any age, showing a more benign course in children and young people;[7] the highest mortality rate was observed in older men, especially those with comorbidities such as diabetes, cardiovascular or pulmonary diseases, obesity, and smoking.[8,9] Poor prognosis has been associated with organ damage produced by hyperinflammatory response.[10]

Coronavirus-2 uses the angiotensin-converting enzyme (ACE) type-2 (ECA2) to enter the tissues. ECA2 is overexpressed in patients with high blood pressure and diabetes mellitus, which could be associated with a worse prognosis.[11,12] ECA2 is found in many tissues, including the lungs, gastrointestinal system, and skin.[13]

The most common symptoms include fever, dry cough, general discomfort, anorexia, shortness of breath, rhinorrhea, ageusia, anosmia, chills, myalgia, and chest pain. Moreover, there may be gastrointestinal, cardiac,[14] neurological,[15] hematological, and cutaneous symptoms. Laboratory studies may find lymphocytopenia and thrombocytopenia, elevated liver function marker, and inflammation values.[16] Increases in the white count with lymphocytopenia, elevated prothrombin times, and elevated D-dimer, interleukin-6, C-reactive protein, and procalcitonin are considered poor prognosis.[17]

Dermatosis can occur in 20% of COVID-19 cases, precede the general or respiratory symptoms, and present together with these or during the disease course.[18,19] There are dermatoses directly associated with the infectious process by COVID-19, such as rash and urticaria.[20] The present case series only showed skin manifestations associated with COVID-19 in patients that they general condition not demanded hospital management and were evaluated by the dermatologist in external consultation; it is interesting that all patients are middle-aged women, with an average of 41 years. Two of them had other family members positive for COVID-19 but without skin symptoms. Nevertheless, it is important to remember that some skin manifestations have been reported in complicated patients and are associated with poor prognosis.

Cutaneous manifestation associated with COVID-19 (literature review)

Erythema multiforme. Lesions like erythema multiforme were reported more frequently in patients in the age range of 58–77 years. It first affects the trunk and later spreads to face and arms. Lesions may be erythematous papules or dark center erythematous violaceous plaques, or target lesions

characteristic of erythema multiforme.[9]

Exanthema maculopapular. This is the most frequent dermatosis in COVID-19, in patients of any age, presenting jointly or a few days after general symptoms.[21,22] In infants, it can start on the face and extend to the trunk and limbs, similar to that of roseola from which it differentiates.[23] Among the differential diagnoses, in adults, are dengue, Zika, scarlet fever, cytomegalovirus, and so on.[24,25]

Vascular Lesions. Admission of SARS-CoV-2 to cells using ACE leads to the accumulation of angiotensin II, which may contribute to lung damage and vascular dysfunction. Vascular lesions include violaceous maculae, livedo reticularis, nonnecrotic purple, necrotic purple lesions, chilblain, and so on. Livedo reticularis occurs in 6% of patients; it has been associated with poor prognosis and progression to progressive ischemia. Chilblain affects 19% and frequently appears after general and respiratory symptoms. Chilblain as data of SARS-CoV-2 is more frequent in children and young adults and is associated with mild disease and good prognosis but may be accompanied by itching and mild local pain, respiratory and gastrointestinal symptoms, and increased D-dimer, as described in case 3.[26,27]

Urticaria. Erythematous plaques were reported in 19% of patients with COVID-19. They may or may not be accompanied by pyrexia, and it could be the first manifestation of COVID-19, even without other symptoms. These patients can infect others and must remain isolated. Most COVID-19 patients with hives evolved favorably with antihistamines, antipyretics, and general measures. We agree with Abuelgasin et al. in relation to treatment; thus low-dose prednisolone should be considered on an individualized case.[28] Urticaria was associated with high mortality, up to 2%.[29,30]

Eruption vesicular. It is described among the five most frequent skin lesions associated with COVID-19, occurs in middle-aged patients, appears before other symptoms, and is associated with intermediate severity of the disease.[18,31] It is found in eruptions formed by vesicles, papules, and pustules; grouped in plates; and frequently located in the trunk, plants, and palms. Differential diagnoses include herpes simplex, herpes zoster, varicella zoster, HIV, and parvovirus B19, among others.[32]

Conclusion

The most frequent cutaneous markers in COVID-19 patients are rash, chilblains, and urticaria. Skin lesions may be the first manifestation of COVID-19, accompany initial respiratory symptoms, or appear during the disease course. Symptoms associated with vascular changes such as livedo reticularis, purpura, and vasculitis are considered of poor prognosis.

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Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

Ethics declaration

Clinical images included in this article were authorized by the patient's written consent, according to the Helsinki Declaration, 1975.

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Informed consent

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article

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