

LETTERS TO THE EDITOR

Bilateral foot ulcers in a COVID-19 patient under favipiravir treatment

Dear Editor,

Coronavirus disease 2019 (COVID-19) affects many organs and systems including skin. COVID-19-associated cutaneous manifestations are very heterogeneous and recently they have been classified into two main groups: inflammatory/exanthematous lesions and vasculopathic/vasculitic lesions.¹ Necrotic skin ulcers were rarely reported in patients with COVID-19.

Herein, we present a 59-year-old female patient administered to emergency room with large foot ulcers. The ulcers started as painful erythematous macules. Soon after, she developed tender

non-hemorrhagic bullae on erythematous patches and large ulcers. Two days before the lesions, the patient had severe myalgia, headache, cough, and mild fever. Her nasopharyngeal swab real-time reverse-transcription-polymerase-chain-reaction (RT-PCR) test was positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). She was diagnosed with COVID-19 and favipiravir treatment was prescribed. The patient had diabetes mellitus (DM) and has been using oral anti-diabetic drugs+insulin treatment for more than 10 years. Dermatological examination revealed purpuric patches with non-hemorrhagic bullae on the left sole and right heel

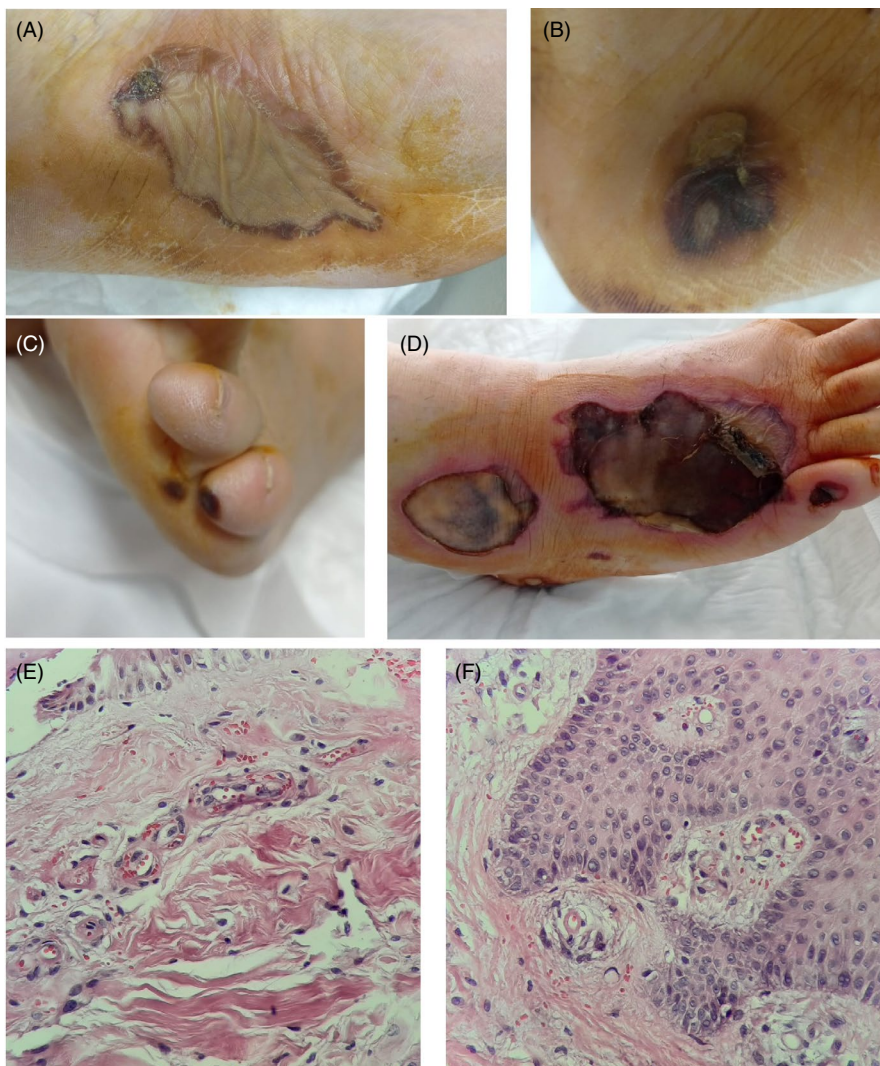


FIGURE 1 Purpuric patches with non-hemorrhagic bullae on the left sole and right heel (A and B), palpable brown papules on the fifth toe and left sole (C), and multiple sharply circumscribed necrotic ulcers on the right foot (D), thickening of capillary walls and erythrocyte extravasation in skin biopsy (E and F)

Written informed consent was obtained from the patient.

(Figure 1A and B), palpable brown papules on the fifth toe and left sole (Figure 1C), and multiple sharply circumscribed necrotic ulcers on the right foot (Figure 1D). Antinuclear antibodies, rheumatoid factor, extractable nuclear antigen (ENA) panel (Ro, La, Sm, RNP, Scl-70, Jo1), c3, and c4 were negative. Skin punch biopsy showed thickening of capillary walls and erythrocyte extravasation. (Figure 1E and F).

The exact mechanism of vasculopathic/vasculitic lesions of patients with COVID-19 is unknown, and there are many theories including vascular occlusion, inflammation, and complement-mediated damage of vascular walls.¹ Additionally, a SARS-CoV-2 PCR positivity was shown in skin biopsies of patients with COVID-19 and vasculitis suggesting a local effect of the virus on vascular walls.² Although histopathological changes in skin biopsy of our patients were not enough for diagnosis of a true vasculitis, thickening of capillary walls and erythrocyte extravasation suggested a possible vasculopathic component in the pathogenesis of skin ulcers in our patient.

Favipiravir-induced vasculitis was also considered in our patient. Many mucocutaneous side effects associated with anti-COVID-19 treatments have been identified. The morphology and frequency of the eruption varies among different treatment regimens. Maculopapular rash is one of the most frequent drug-induced cutaneous reaction in COVID-19 patients. There are other well-known cutaneous side effects of anti-COVID-19 drugs but, to the best of our knowledge, necrotic skin ulcers associated with favipiravir treatment have not been reported before.³ Although the ulcer developed after the administration of favipiravir, the skin biopsy did not show any pathological changes that can support drug reaction.

Our patient had DM and it is well known that diabetic patients have a high risk of developing foot ulcers secondary to ischemia, neuropathy, and endothelial damage.⁴ Despite the long history of DM, our patients developed foot ulcers for the first time. In our opinion, DM acted as a possible facilitating factor, not as a primary cause of ulcers in our patient.

Foot ulcers are rare in patients with COVID-19 but in patients with additional risk factors such as DM, ulcers could be seen more frequently than normal population.

KEYWORDS

COVID-19, foot, ulcer

CONFLICT OF INTEREST

None declared.

DATA AVAILABILITY STATEMENT

Data not available.

Yıldız Hayran¹ 

İlke Diren Albayrak¹

Devrim Tuba Öcalan²

Akın Aktaş¹

¹Department of Dermatology, Ankara City Hospital, Ankara, Turkey

²Department of Clinical Pathology, Ankara City Hospital, Ankara, Turkey

Correspondence

Yıldız Hayran, Department of Dermatology Ankara City Hospital, Üniversiteler, Bilkent Blv. No:1, 06800 Çankaya/Ankara, Turkey.

Email: yildiz_kantarci@yahoo.com

ORCID

Yıldız Hayran  <https://orcid.org/0000-0003-1942-7285>

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