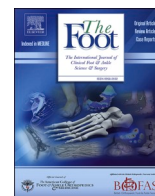




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## Case Report

## Foot manifestations in a patient with COVID-19 and Epstein-Barr virus: A case study

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## ABSTRACT

SARS-CoV-2 (COVID-19) is highly-contagious. It can lead to respiratory distress—and in some cases—death. Recent reports and observations have identified an association between COVID-19 and manifestations in the feet. However, there are very few reports that describe the course of these foot manifestations in any detail. The authors present a case study chronicling the progression of foot issues in a COVID-19 positive patient who also was positive for the Epstein-Barr virus.

SARS-CoV-2 (COVID-19) has already infected nearly five and a half million people throughout the world, and there have been nearly 350,000 deaths. [1] Anecdotal observations and case studies have proposed that COVID-19 affects the feet [2–14].

Because of the reduced access to tests for COVID-19 and false negative results from those that are currently available, a significant number of the case reports and observational studies conducted thus far include presumptive cases of individuals who are COVID-19-positive but lack definitive proof. To this end, researchers have considered signs and symptoms, and such factors as close contact with a person proven to have been COVID-19 positive [3,4,7].

Many of these reports have focused on cutaneous manifestations. Though not limited to the feet, Galvan Casas et al. classified these skin appearances as acral areas of erythema with vesicles or pustules (Pseudo-chilblain), other vesicular eruptions, urticarial lesions, maculopapular eruptions, and livedo or necrosis. Most reports of skin manifestations have not detailed the progression of the cutaneous issues, or whether there were other foot-related findings. One case study differed in not only describing the progression of the skin changes in the foot, but also documenting gait changes and pain symptoms [8].

Most prior reports have also focused on patients who were often only presumed or proven positive for COVID-19. Borghetti et al. caution practitioners that during the COVID-19 pandemic, it is important not to overlook other viral pathogens that mimic the symptoms of COVID-19 and may be the sole cause of a patient's problems or may be present concomitantly with COVID-19 or another disease [15].

This case study provides a description of the progression of foot manifestations in a patient in Spain who tested positively for COVID-19 and the Epstein-Barr virus (EBV), and may have also contracted parvovirus B19 (B19). The authors believe this may be the first detailed report of foot manifestations in a patient who had COVID-19, EBV and possibly B19.

## 1. Case study

This case concerns a 16-year-old female in Madrid, Spain. As a brief background, Spain reported its first confirmed COVID-19 case on January 31, 2020, and a state of emergency was declared March 14, 2020 when the government implemented a quarantine of its citizens [16].

The patient's history was negative for trauma, exposure to cold temperatures, or any health issues. She had no allergies, was not taking any medication, and denied cigarette use or vaping. However, she resided in a home with her 20-year-old sister, who on March 3, 2020, tested positive for active EBV and was also diagnosed with COVID-19. At the time, tests for COVID-19 were unavailable in the area, and the sister's diagnosis was based solely on her history and symptoms.

On February 25, 2020, the patient's sister developed a sore throat and then two days later, a fever. Her doctor prescribed Augmentin (amoxicillin and clavulanic acid). The next day, a rash appeared on her chest and abdomen, which the doctor thought was due to an allergic reaction to the Augmentin. The use of Augmentin was discontinued.

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From March 3 to the 8, the sister's rash spread to all areas of her body, including her hands, feet, and face. When she was found to be positive for EBV, she was diagnosed with active mononucleosis and COVID-19. The rash was treated with topical corticosteroids, which were of little help. The patient's sister's symptoms gradually resolved over the next 15 days.

Subsequently, the patient, residing with her sister, experienced a sore throat on March 6, soon followed by headache, diarrhea, and back pain. She was also prescribed Augmentin, and within three days, by March 9, all her symptoms resolved.

However, the next day, a rash appeared on the patient's chest, abdomen, and face, which was mildly itchy. This irritation gradually worsened, and by April 4, she was experiencing severe itching. The rash then spread to her toes, where it was also extremely irritating (Figs. 1 and 2).

On April 12, the patient and her mother consulted Dr. del Mar Ruiz Herrera, a podiatrist, via telemedicine. Dr. del Mar Ruiz Herrera advised the patient to be tested for COVID-19; however, no tests were available at that time. The podiatrist also prescribed the patient hydrocortisone cream 1% for her skin issues. The cream was beneficial, and the skin manifestations began to improve. Two days later, a pruritic rash appeared on some of the patient's fingers (Fig. 3).

On April 17, the patient was tested for COVID-19, EBV, Hepatitis B and C, mycoplasma pneumonia, syphilis, chlamydia, cytomegalovirus, and parvovirus B19. She was positive for EBV and parvovirus IgG, but all other tests, including COVID-19, were negative. On April 28, the patient tested positive for COVID-19 antibodies. Her final diagnosis was a co-infection of mononucleosis and COVID-19. It is unclear when she had B19, as it can be asymptomatic and may have occurred at an earlier time.

In early May 2020, the patient's rash completely resolved, with the cutaneous lesions on the feet disappearing last. The patient has had no further medical issues.

## 2. Discussion

This case study is one of the first to document the progression of the foot manifestations in a patient with COVID-19, EBV, and who also possibly had B19.

The case highlights the importance of considering other diseases in the presence of a patient suspected to have COVID-19. Other pathogens that may present with similar cutaneous manifestations include influenza virus, respiratory syncytial virus, enterovirus, bocavirus, adenovirus, and coronavirus (other than SARS-CoV-2) [15].

Chen et al. examined the incidence of EBV coinfection in COVID-19



Fig. 1. Skin manifestations on the toes of the left foot.



Fig. 2. Skin manifestations on the toes of the right foot.



Fig. 3. Skin manifestations on a finger.

patients and found that 56.5 % were positive for the EBV viral capsid antigen (VCA) IgM antibody, noting that these patients had a longer recovery time [17]. Morand et al. presented a case of a 55-month-old girl undergoing a liver transplant who had a confirmed co-infection of COVID-19 and EBV [17]. In the present case study, the timing of active EBV and COVID-19 in relation to each other is uncertain.

Though reports have suggested that COVID-19 causes skin manifestations in the feet, further research may refute this supposition. Also, since numerous diseases are known to cause cutaneous manifestations, including some that can affect the feet [18,19], it is not known if skin issues observed in COVID-19 patients are due to COVID-19 or the result of a co-infection, perhaps unrecognized. If other infectious agent are found to be present with COVID-19 they may be shown to be solely or in

combination responsible for the foot issues. In the case presented, both EBV and B19 are known to cause cutaneous manifestations, and as such, either one of these may have been the cause of the patient's foot issues, alone or in combination with COVID-19.

Further, this case study is of an adolescent, and at this time, research that has included younger patients suggests that in children, adolescents, and young people, COVID-19 may have a propensity for presenting in the feet and hands [2–6]. One of the larger observational studies, done by Recalcati, found that the skin manifestations mainly involved the trunk [20]. Unlike other studies cited herein, which involved young people and children with foot involvement, Recalcati's study was comprised entirely of adults and did not include any children.<sup>1</sup> Perhaps, further research will show an age association between COVID-19 and foot involvement.

Limitations of this case study include a lack of a biopsy, further laboratory investigations, vascular testing, and radiographs of the feet to determine if bone changes had occurred. There is the possibility that this patient's foot issues occurred at the time she was positive for COVID-19 by coincidence, and there could be another reason for lesions presenting in her feet. Further study is needed to better understand the effect of COVID-19 on the feet, including a consideration of how the foot practitioner should best treat these patients. Some focus should also be given to plotting the timing of foot manifestations in relation to COVID-19's more severe systemic effects, such as fever, to guide patients on what preparations, if any, should be implemented.

### 3. Conclusion

There is much work to be done to fully understand the effect of COVID-19 on the feet. The foot practitioner can play a key role in adding to the body of research on this subject, but conclusions should be cautiously drawn. This case highlights the progression of foot manifestations in a patient co-infected with COVID-19 and EBV, and possibly B19. However, for concrete conclusions and treatments to be established, further case studies and research is needed.

### Financial disclosures

None.

### Conflict of interest

None.

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<sup>1</sup> Sebastiano Recalcati (personal written communication, April 11, 2020).