Revista da Sociedade Brasileira de Medicina Tropical
Journal of the Brazilian Society of Tropical Medicine
Vol.:56 | (e0008-2023) | 2023
https://doi.org/10.1590/0037-8682-0008-2023

Case Report

Post nirmatrelvir/ritonavir erythema multiforme in a patient with coronavirus disease infection

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ABSTRACT

Erythema multiforme (EM), an immune-mediated skin condition, can occur after infection or following the use of medications. In this study, we describe a patient who developed EM after nirmatrelvir/ritonavir administration. An 81-year-old woman presented with fever and dyspnea. Laboratory investigations showed positive coronavirus disease (COVID-19) based on polymerase chain reaction assay, and she received a 5-day regimen of nirmatrelvir/ritonavir. We observed development of EM after this treatment and initiated prednisone (1 mg/kg) therapy, which led to rapid improvement. Our study is the first to report EM in a patient with COVID-19, who received nirmatrelvir/ritonavir and showed a favorable response.

Keywords: COVID-19. Nirmatrelvir/ritonavir. Erythema multiforme.

INTRODUCTION

Erythema multiforme (EM), an immune-mediated condition involving the skin and mucous membranes[1,2], has an estimated prevalence of less than 1%[3]. EM predominantly affects women and adults aged 20–40 years[1]. The pathophysiology of this condition involves the production of immunocomplexes, which can be precipitated by infections or medications and injure small vessels in the skin and mucous membranes[4]. Lesions may be asymptomatic or may present with dysesthesia, and the mean duration varies from 1 to 4 weeks. EM is characterized by target lesions, which may present as macules, papules, or vesicles, mainly distributed on the hands, feet, knees, and elbows[1,5]. Treatment involves withdrawal of the possible causative agent in addition to corticosteroid therapy[1].

Coronavirus disease (COVID-19), an infection caused by the severe acute respiratory syndrome coronavirus 2[6] may present with cutaneous manifestations[7]. Antiviral medications, including nirmatrelvir/ritonavir are approved for treatment in patients at risk of adverse clinical evolution[8].

In this article, we describe a patient who developed EM after nirmatrelvir/ritonavir administration.

CASE REPORT

We searched the MEDLINE database via PubMed without any time restrictions. The following descriptors (bold), synonyms, natural language, and Boolean operators were used to cross-check the databases: MEDLINE (Medical Subject Headings [MeSH]:

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Authors' contribution: JWLT-J, JCJPF, LEGG: Conception and work design. JWLT-J, JCJPF, LEGG: Acquisition, analysis, or interpretation of data and work. JWLT-J, JCJPF, LEGG: Drafting the work. All authors were involved in the critical review of the manuscript for important intellectual content.

Conflict of Interest: All authors declare that they have no conflict of interest.

Financial Support: This study did not use funding from any specific source.

Received 19 January 2023 • **Accepted** 19 April 2023

search strategy (nirmatrelvir/ritonavir), (COVID-19), and (erythema multiforme). The search was performed on January 19, 2023.

An 81-year-old woman was admitted for evaluation of cough, fever, and mild dyspnea, which required supplemental oxygen inhaler use. COVID-19 polymerase chain reaction assay showed positive results 3 days after the onset of symptoms. Nirmatrelvir/ritonavir therapy was initiated 4 days after onset of symptoms and was continued for 5 days. An acute cutaneous eruption of reddish annular macules suggestive of EM was observed on the patient's arms the day following completion of the medication regimen (**Figures 1 and 2**). Histopathological examination of the lesions was not performed. Prednisone (1 mg/kg) therapy was initiated, which led to rapid improvement.

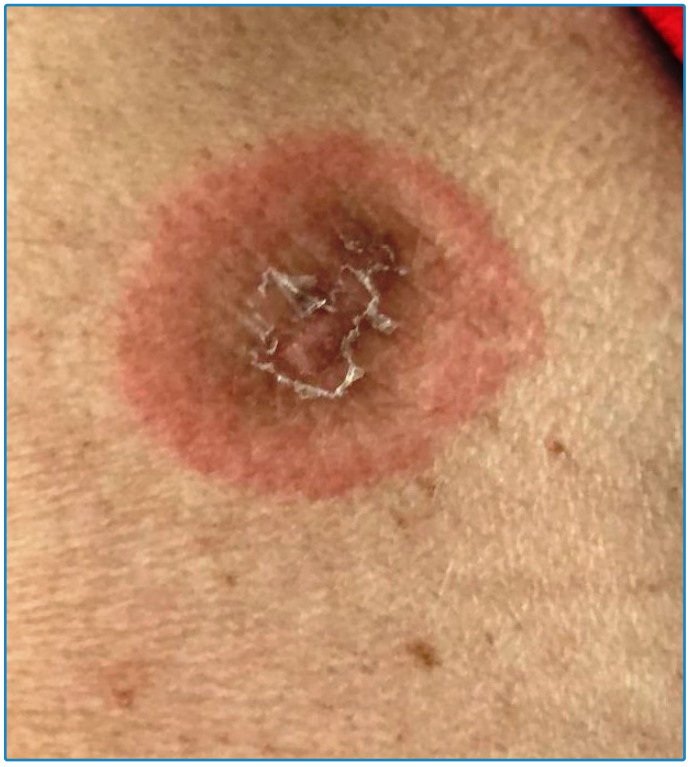

FIGURE 1: Photograph showing an erythematous maculopapular "target" lesion.

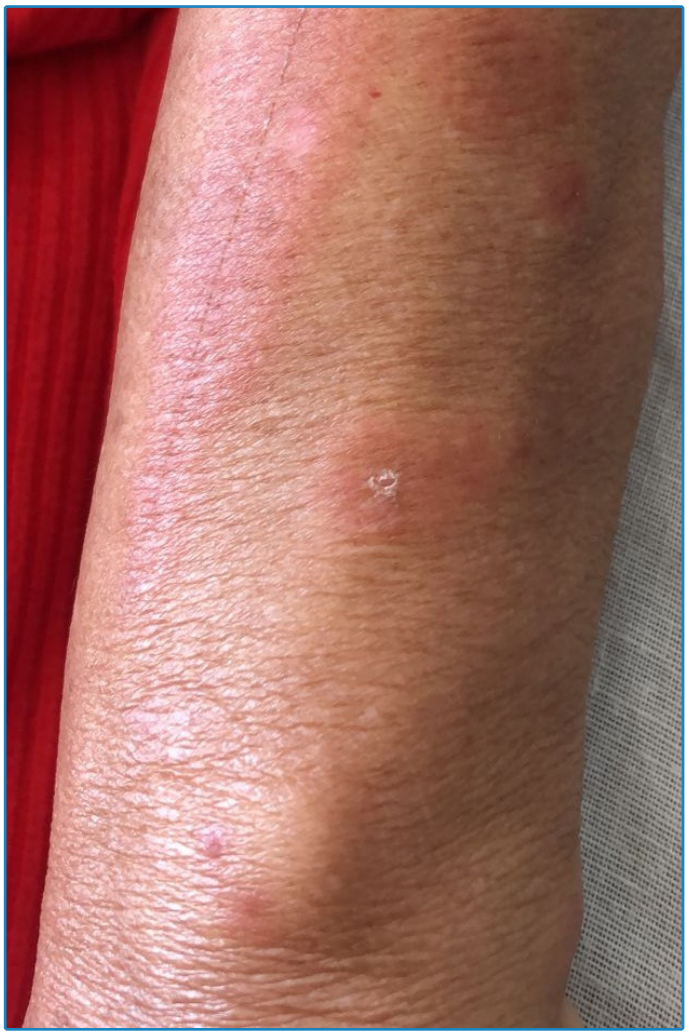

FIGURE 2: Photograph showing a macular "target" lesion.

DISCUSSION

To our knowledge, this is the first report of EM that showed a positive outcome in a patient with COVID-19, who was treated with nirmatrelvir/ritonavir.

Previous studies have reported EM after COVID-19 and lopinavir/ritonavir administration[9]. Likewise, EM associated with COVID-19 has been described in the medical literature, both in patients aged <30 years and in those aged >55 years[7].

Our patient did not undergo histopathological examination; however, the temporal relationship between the appearance of the lesion after medication initiation and improvement after discontinuation of therapy reinforces the contribution of nirmatrelvir/ritonavir to EM in this case. The Naranjo Adverse Drug Reaction Probability Scale[10] score in our patient was 5, which indicates a probable adverse reaction and strengthens our suspicion.

We could not differentiate whether EM was due to a viral infection or secondary to the use of the aforementioned medications in our patient, which serves as a limitation of this study.

CONCLUSIONS

In this case report, we describe a rare skin reaction following the use of nirmatrelvir/ritonavir. Our findings will serve as guidelines for early detection of this complication and can aid with the establishment of the most suitable treatment in such cases.

ACKNOWLEDGMENTS

We thank the patient and family.

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