Annular lichenoid eruption following treatment with casirivimab/imdevimab for COVID-19

Netana H. Markovitz, MD,[a] Elisabeth Pedersen, MD, PhD,[b] Dana L. Sachs, MD,[b] and Scott C. Bresler, MD, PhD[b,c]

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INTRODUCTION

Antiviral treatments for COVID-19 are increasingly being developed and utilized.[1] Delayed hypersensitivity reactions have been reported in a small percentage of patients who receive casirivimab/imdevimab (REGN-COV2).[2] To our knowledge, lichenoid hypersensitivity reactions have not yet been described.

CASE REPORT

A 53-year-old female with a history of hypertension, hypercholesterolemia, hypothyroidism, traumatic brain injury, and breast cancer in remission presented with a rash on her right arm 1 week following treatment with REGN-COV2 for a moderately symptomatic case of COVID-19. She met eligibility criteria for the investigational therapy REGN-COV2 due to her history of breast cancer and severity of COVID-19 symptoms. She had completed the two-part Moderna vaccination approximately 2 weeks prior to receiving REGN-COV2. Her history was pertinent for allergies to penicillin and procaine, which had resulted in an unspecified rash. Her medication list included other drugs for chronic diseases including losartan (7 years), atorvastatin (3 years), levothyroxine (5 years), and zonisamide (4 years). She had been taking these medications consistently without noted issues. She reported no over-the-counter medications and had not taken any other prescription or over-the-counter treatments for COVID-19 prior to the onset of the eruption. Dietary supplements included a multivitamin and iron, but otherwise no other vitamins, supplements, or herbal preparations. With the exception of the COVID-19 vaccine, she had not received any new vaccinations over the past 2 years. Her presenting rash consisted of edematous well-demarcated targetoid to annular and arcuate erythematous plaques on the right arm (Fig 1, *A*), right palm (Fig 1, *B*), and lower legs. The eruption had spontaneously improved approximately 1 mo following antibody administration and subsequently resolved with triamcinolone cream. Approximately 2 mos later, a similar rash reappeared in the same locations on the right arm (Fig 1, *C*) and right palm (Fig 1, *D*). A punch biopsy of the right elbow lesion was obtained, which demonstrated lichenoid interface dermatitis with occasional eosinophils, consistent with a lichenoid hypersensitivity reaction (Fig 2). The rash subsequently improved with clobetasol ointment.

Abbreviations used:

FDE: fixed drug eruption
REGN-COV2: casirivimab/imdevimab

DISCUSSION

Lichenoid drug eruptions have been described following various medications such as antimalarials,

From the University of Michigan Medical School, Ann Arbor, Michigan[a]; Michigan Medicine Department of Dermatology, Ann Arbor, Michigan[b]; and Michigan Medicine Department of Pathology, Ann Arbor, Michigan.[c]

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Correspondence to: Netana H. Markovitz, MD, 1301 Catherine st, Ann Arbor, MI, 48109. E-mail: netanamarkovitz@gmail.com. Twitter handle: @NetanaMarkovitz.

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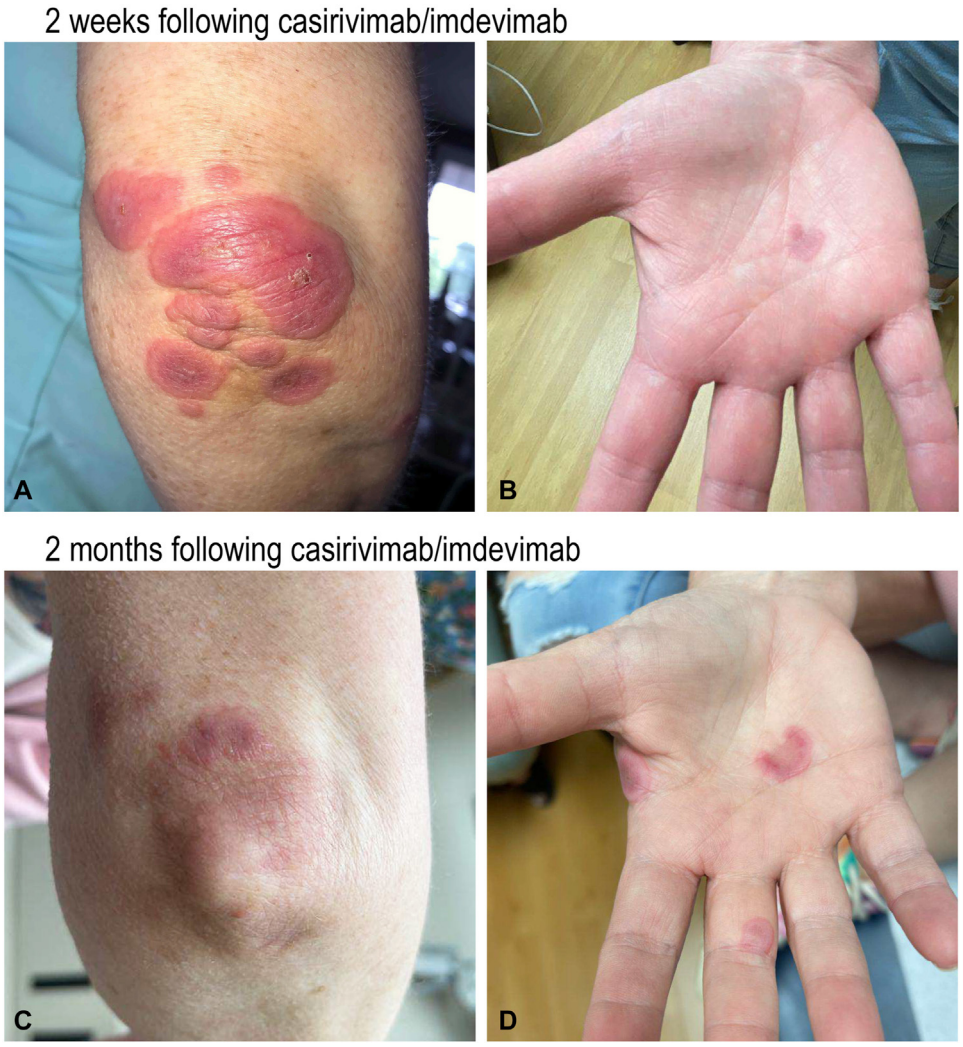

Fig 1. Edematous well-demarcated targetoid to annular erythematous plaques with dusky centers 2 weeks (**A** and **B**) and 2 months (**C** and **D**) following casirivimab/imdevimab (REGN-COV2) administration. *Left*: posterior right elbow; *right*: right palm

diuretics, antibiotics, immune checkpoint inhibitors, and more.[3] However, to our knowledge, this is the first report describing lichenoid drug eruption following administration of REGN-COV2. Casirivimab and imdevimab are two SARS-CoV-2 neutralizing human IgG1 antibodies, respectively, that prevent viral entry into cells via inhibition of the spike protein,[2] given as a single dose either subcutaneously or intravenously. The combination has been associated with a lower rate of hospitalization in high-risk patients with mild to moderate COVID-19, and its use has become widespread.[1]

Several morphologic presentations of lichenoid drug eruptions have been described including classic lichen planus-like, photo-distributed, eczematous, and others.[3] These drug eruptions often lack clinical features of lichen planus such as Wickham striae and oral/nail involvement.[3] Lichenoid drug eruptions can further be differentiated from other lichenoid disorders based on clinical history and histopathologic features.[3] Lichenoid drug eruptions typically have a longer latency period than usual hypersensitivity reactions, with the potential for presentation even up to 1 year following exposure.[3] These lesions may be the result of continuous, small volume exposure or a single, large volume acute exposure.[3] Lichenoid drug eruptions may disappear entirely or be recurrent.[3] Our patient presented 1 week following drug administration, and though initially resolved, the rash recurred approximately 2 mo later in the same areas, in addition to the development of new lesions. It is challenging to precisely explain why the rash recurred and worsened in the absence of reexposure to REGN-COV2. The mean half-life for both casirivimab and imdevimab has been estimated at 25 to 37 days,[2] which is consistent with the

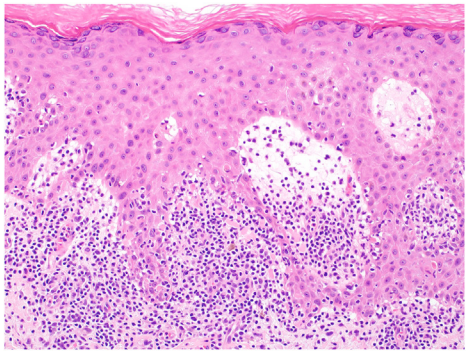

Fig 2. A punch biopsy specimen revealed a lichenoid infiltrate with interface change, epidermal hyperplasia, and mild papillary dermal edema. Occasional pigment-laden macrophages and eosinophils were present (hematoxylin-eosin stain; original magnification: ×200).

monthslong duration of the eruption and provides a potential explanation for our patient's late recurrence of symptoms after cessation of topical steroids. In addition, the patient had undergone several subsequent interventional procedures for back pain and a surgery in the subsequent months, during which she may have received a medication or treatment that contributed to a flare of the rash.

While lichenoid drug eruptions are typically reported in small-molecule drugs, lichenoid reactions to biologics such as adalimumab,[4] dupilumab,[5] and ixekizumab[6] have been reported and may occur as rapidly as 1 week after exposure.[6] Interestingly, this patient's rash also had several features of fixed drug eruption (FDE), appearing as well-circumscribed annular lesions that recurred in a consistent location, as well as histopathologic features that were compatible with FDE.[7] FDE typically appears 1-2 weeks after exposure to a medication and may appear in the same location as soon as 24 hours after reexposure and most commonly occurs due to exposure to nonsteroidal anti-inflammatory drugs, tetracyclines, trimethoprim-sulfamethoxazole, and acetaminophen.[7] None of these medications had been taken prior to time of rash appearance or recurrence, and none of her other chronic medication schedules would necessarily explain a new-onset FDE.

It is also possible that the rash was triggered by an undisclosed medication or other unclear trigger. Of note, she had two doses of the Moderna COVID-19 vaccine 3 weeks apart, the second of which was administered approximately 2 weeks prior to REGN-COV2. While several cutaneous eruptions have been reported in response to COVID-19 vaccination, lichenoid eruptions appear to be rare.[8]

While the mechanism of these eruptions is incompletely understood, it is thought to involve persistent activation of CD8 autocytotoxic T lymphocytes against epidermal cells.[9] REGN-COV2 are two SARS-CoV-2 neutralizing human IgG1 antibodies that prevent viral entry into cells via inhibition of the spike protein.[2] Although cutaneous manifestations of COVID-19 itself are widespread, these most commonly include pernio-like acral lesions, morbilliform rash, urticaria, vesicular eruptions, and vaso-occlusive lesions,[10] and rarely a lichenoid dermatitis.

Our patient's rash was self-resolving and was ultimately successfully treated with a short course of topical clobetasol ointment. However, these drug eruptions typically do resolve with cessation of the causative agent and may be treated with watchful waiting. Further study is needed to delineate the prevalence of cutaneous reactions to REGN-COV2.

Conflicts of interest

None disclosed.

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