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CASE REPORT

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Eculizumab-related drug reaction in a patient with neuromyelitis optica

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Abstract

Eculizumab is approved for treatment of antibody positive neuromyelitis optica, myasthenia gravis, and hematologic disorders like paroxysmal nocturnal hemoglobinuria. Drug rash has not yet been reported as a side effect of eculizumab. We report a case of a cutaneous drug reaction soon after introduction of eculizumab therapy in a patient with refractory neuromyelitis optica. Clinicians should be aware of a drug reaction as a possible adverse reaction to eculizumab.

KEYWORDS

drug reaction, eculizumab, neuroimmunology, neuromyelitis optica

1 | INTRODUCTION

Eculizumab is a fully humanized monoclonal blocking antibody to complement protein C5 that inhibits cleavage to C5a and C5b, thus preventing terminal complement complex C5b-9 and formation of the membrane attack complex.[1] Eculizumab was FDA-approved in 2020 for the treatment of neuromyelitis optica (NMO) after it was shown to be effective in reducing relapse frequency in highly clinically active, aquaporin-4 immunoglobulin G (AQP4-IgG)-positive NMO.[2] Commonly reported side effects (>10%) include upper respiratory infections and headache. A life-threatening desquamating rash and hyperammonemia following the administration of eculizumab for paroxysmal nocturnal hemoglobinuria (PNH) has been reported.[3] Cutaneous adverse drug reactions can range from self-limited cutaneous eruptions such as maculopapular exanthema to severe cutaneous drug reactions. Severe cutaneous adverse reactions are rare, potentially life-threatening, and T-cell-mediated hypersensitivity reactions.[4] Certain drugs can induce autoantibodies rather than cause an autoantibody-associated disease. The information available suggests eculizumab is unlikely to do this.[5] We report a patient with refractory NMO who developed a cutaneous drug reaction following intravenous eculizumab administration. This information will be useful to clinicians, given the expanding clinical uses of eculizumab in diseases such as atypical hemolytic uremic syndrome (aHUS), PNH, and myasthenia gravis.[6–8] Eculizumab has also been used for lupus nephritis-associated thrombotic microangiopathy in systemic lupus erythematosus patients.[9]

2 | CASE PRESENTATION

A 75-year-old woman with AQP4-IgG-positive NMO was started on weekly intravenous eculizumab following suboptimal response to rituximab with mycophenolate mofetil. Soon after the third infusion, she developed an itchy skin rash involving all extremities that progressed over the subsequent days despite diphenhydramine therapy. Due to the progression of the rash, the infusions were discontinued after the fourth one. Her medical history

included discoid lupus erythematosus (DLE) in remission for 30 years and Sjogren's syndrome.

Her physical examination was remarkable for NMO-related deficits (numbness and weakness from the chest down, hyperreflexia, and left eye blindness) and the skin rash. All extremities were involved by well-defined, coin-shaped, erythematous papules with varying size and scaling (Figure 1). Her mucous membranes, nails, scalp, and hair were unaffected. A dermatology evaluation confirmed the clinical impression of this being a drug rash, as did subsequent pathology. Skin biopsy of the left leg revealed a vacuolar interface dermatitis (characterized by vacuolization at the dermal-epidermal junction and lymphocytic inflammation of the epidermis and dermis). Epidermal hyperplasia and dyskeratotic keratinocytes were also present. The preponderance of inflammation over epidermal necrosis favored a medication reaction over erythema multiforme. Findings typical of drug-induced cutaneous lupus (basement membrane thickening and mucin deposition) were absent.

Serological studies showed the absence of antinuclear, anti-double-stranded deoxyribonucleic acid, and anti-histone antibodies. Anti-Ro/Sjogren syndrome A and anti-La/Sjogren syndrome B antibodies were positive.

She was placed on 50 mg of oral prednisone four times a day for 4 days with tapering. Prompt clinical improvement was noted with complete resolution at 5 months.

3 | DISCUSSION

Cutaneous adverse drug reactions usually start 12–24 h after exposure.[4] A temporal relationship between the introduction of eculizumab and development of skin rash suggests a relationship between them.

A study evaluating the immunogenicity of eculizumab found zero of 75 patients with PNH on eculizumab developed human antihuman antibodies.[5]

Our knowledge of eculizumab-related drug reactions is limited, and further research is needed to better understand the pathophysiology. Importantly, there is little evidence documenting autoimmune response to IgG2/IgG4 monoclonal antibody therapy. Eculizumab's use in disorders like NMO, aHUS, PNH, and myasthenia gravis makes it important for clinicians to be aware of its potential to cause severe skin reactions. It is possible that this patient's history of other autoimmune disorders (DLE and Sjogren's syndrome) played a role in her reaction, which is important given that this is common in patients with NMO.

AUTHOR CONTRIBUTIONS

Rishi Sharma: Conceptualization; data curation; methodology; writing – original draft; writing – review and editing. **Moises Romo:** Data curation; writing – original draft; writing – review and editing. **Flavia Nelson:** Conceptualization; data curation; investigation; methodology; supervision; writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST

Rishi Sharma: None. Moises Romo: None. Flavia Nelson: Dr. Nelson Research support: NIH, Institute of translational Neuroscience, University of Minnesota, The Frank J. and Eleanor A. Maslowski Charitable Trust. Dr. Nelson has received honoraria for participation in Advisory Boards with Genentech, Novartis, Sanofi, Bristol Myers Squibb, Roche and TG therapeutics.

DATA AVAILABILITY STATEMENT

The raw/processed data required to reproduce the above findings cannot be shared at this time due to legal/ethical reasons.

ETHICAL APPROVAL

The patient has been de-identified. Any images used do not permit the identification of the individual. Otherwise, there are no ethical concerns in this manuscript. There was no ethics approval required for this manuscript.

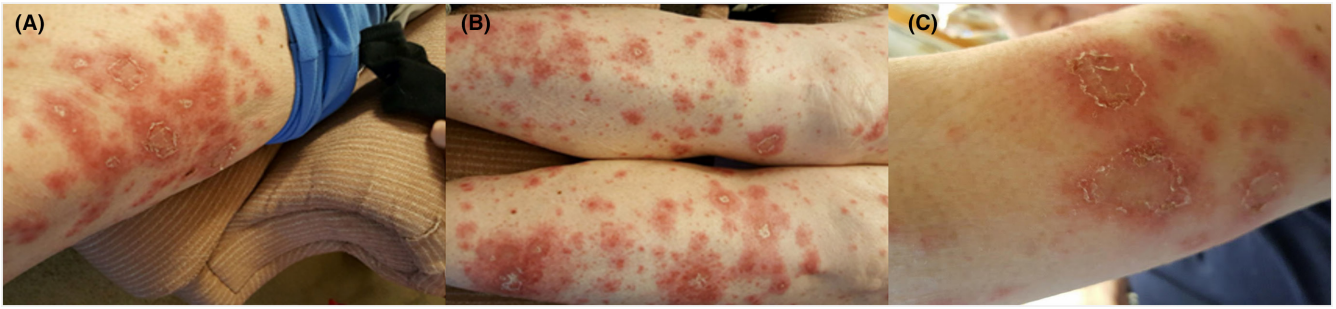

FIGURE 1 Cutaneous drug reaction lesions. Left thigh (A), legs (B), and left arm (C) showing skin rash characterized by erythematous papules and plaques of varying size with extensive scaling.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy and with institutional guidelines.

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