Received: 30 December 2020 | Accepted: 31 December 2020

DOI: 10.1111/dth.14771

DERMATOLOGIC THERAPY WILEY

LETTER

Desquamative skin rash associated with temozolomide in a patient with glioblastoma

Dear Editor,

Glioblastoma (GBM) is the most aggressive brain tumor among adults. The standard of care treatment consists of surgery, radiotherapy, and chemotherapy with temozolomide (TMZ). TMZ inhibits DNA replication and leads to cell death. Drug eruptions due to TMZ often present a diagnostic challenge due to delayed onset and concomitant medications. We present a patient with GBM who developed a TMZ-induced desquamative skin rash.

A 58-year-old Caucasian female presented with progressive weakness in her left hand. Magnetic resonance imaging showed a right frontal cerebral brain lesion and biopsy revealed the diagnosis of GBM. The patient was started on dexamethasone for brain edema soon after her diagnosis. A month later she received a 6-week course of concurrent brain chemoradiation with oral TMZ, along with sulfamethoxazole-trimethoprim for PCP prophylaxis. The day after the patient finished the induction course and 12 days after she had discontinued dexamethasone, she developed erythema on the face that progressed to involve the rest of the body. The rash lasted for 3 weeks and improved after the patient was given methylprednisolone for 6 days. Sulfamethoxazole-trimethoprim (SMX)-TMZ was discontinued as it was suspected to be the cause of the drug reaction. Four weeks later, she began 6 cycles of maintenance therapy consisting of TMZ for the first 5 days of a 28-day cycle, along with dapsone for PCP prophylaxis. On the sixth day of the first cycle, the patient was admitted for diffuse erythema of the face, trunk, upper and lower extremities (Figures 1 and 2) that progressed to desquamation, particularly on the face, palms, and soles (Figures 3 and 4). There was no oral mucosa or eye involvement, respiratory symptoms, or fever. The rash cleared in 3 weeks with prednisone. Dapsone was discontinued due to potential drug eruption. However, 4 days after the patient finished the 5-day TMZ course of the second cycle, she again developed a generalized erythematous rash.

TMZ is an oral alkylating agent used to treat GBM multiforme.[1-3] Although generally well-tolerated, it is associated with adverse effects such as fatigue, myelosuppression, and convulsions.[2,3] Dermatologic side effects such as alopecia, desquamative skin rash, urticaria, Stevens-Johnson syndrome, and toxic epidermal necrolysis have also been reported.[2,3]

The diagnosis of TMZ-induced cutaneous eruptions is challenging since patients are often treated with systemic steroids for cerebral edema caused by the tumor or radiation therapy, which can delay onset.[4-6] This was true in our patient, with the rash developing 6 weeks after initiation of TMZ and 12 days after discontinuation of dexamethasone. There was initial concern that the prophylactic antibiotic may be the culprit, further complicating diagnosis, but it became clear that TMZ was the culprit upon rechallenge.

Two strategies have been described to minimize the adverse effects of TMZ and to prevent any interruption in treatment. The first strategy is pretreatment with systemic steroids prior to the TMZ dose.[2,5] The second is the 1-day desensitization protocol with very low doses of TMZ gradually increased every 30 minutes until the patient reaches a therapeutic dose.[2,5] The latter protocol successfully prevented recurrence of TMZ-induced drug eruption in our patient, with desensitization between the second and third cycles of chemotherapy. In conclusion, physicians should be aware of the cutaneous adverse effects of TMZ and recognize that the onset of cutaneous

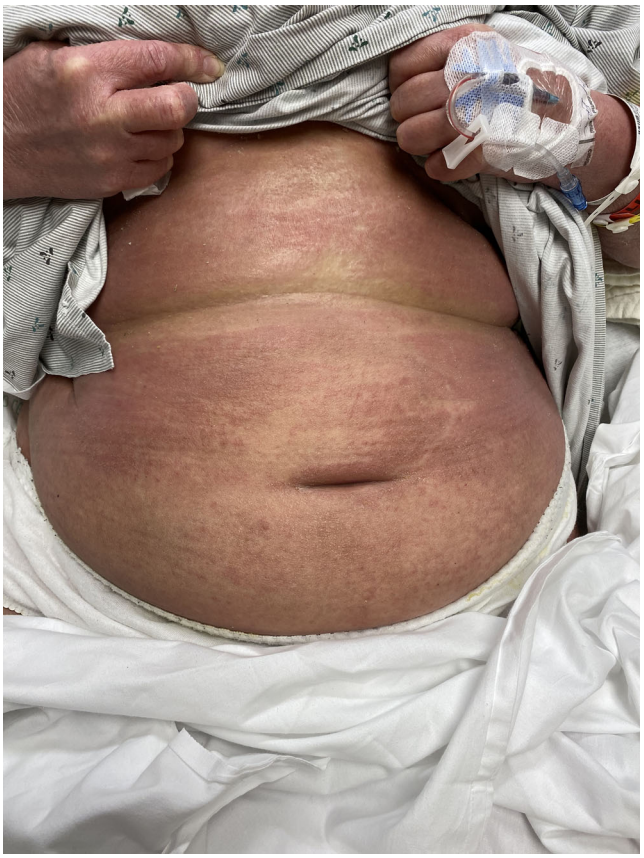

FIGURE 1 Widespread erythema on the chest and back 6 days after the patient completed her first 5-day maintenance cycle of temozolomide

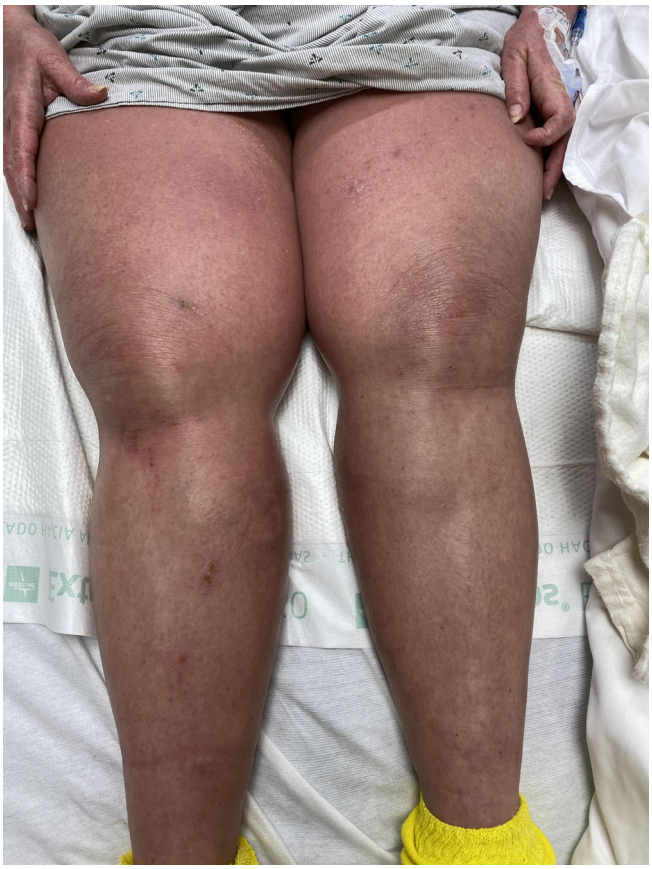

FIGURE 2 Diffuse erythema on bilateral lower extremities 6 days following first 5-day maintenance cycle of temozolomide

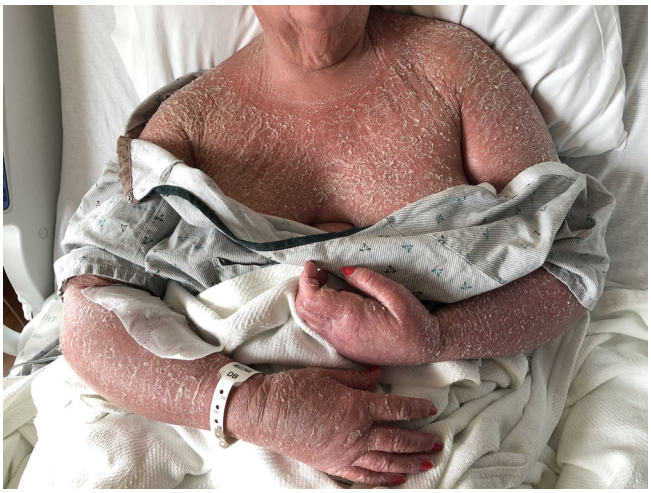

FIGURE 3 Erythema progressed to generalized desquamation on trunk and upper extremities 10 days after temozolomide treatment

eruptions may be delayed due to the immunosuppressive effects of concomitant steroids.

CONFLICT OF INTEREST

We confirm that the manuscript has been read and approved by all the authors, that the requirements for authorship as stated earlier in this document have been met, and that each author believes that the manuscript represents honest work.

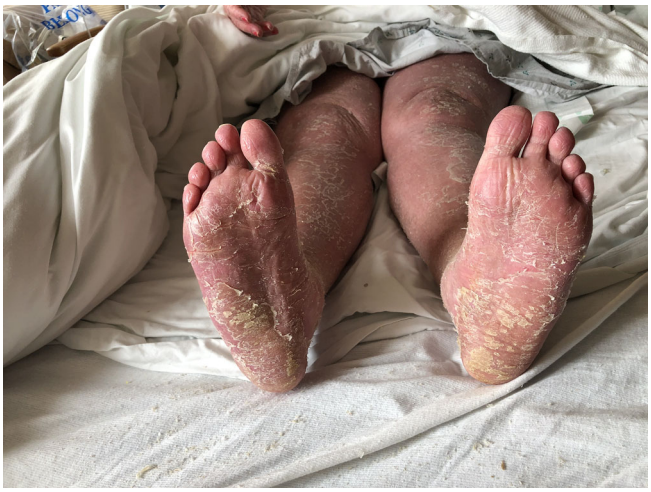

FIGURE 4 Severe plantar desquamation following temozolomide treatment

AUTHOR CONTRIBUTION

Mehdi Farshchian: Case review, Writing and revision of draft; **Redina Bardhi**: Writing and revision of draft; **Steven Daveluy**: Case review, Writing and revision of draft.

DATA AVAILABILITY STATEMENT

Data Availability Statement: Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Mehdi Farshchian[1]
Redina Bardhi[2]
Steven Daveluy[1]

[1]*Department of Dermatology, Wayne State University, Detroit, Michigan*
[2]*Wayne State University School of Medicine, Detroit, Michigan*

Correspondence
Mehdi Farshchian, Department of Dermatology, Wayne State University, 18100 Oakwood Blvd., Suite 300, Dearborn, MI 48124, USA.
Email: mfarshch@med.wayne.edu

ORCID

Mehdi Farshchian https://orcid.org/0000-0002-5386-9629

REFERENCES

1. Ostrom QT, Cioffi G. Haley Gittleman CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2012-2016. *Neuro Oncol*. 2019;21(Suppl 5):v1–v100.
2. Alonso-Llamazares A, Vega-Castro A, Beitia-Mazuecos JM, Mateo-Borrega B, Cardenas- Contreras R. Rapid desensitization with temozolomide in patients with delayed maculopapular rash. *J Investig Allergol Clin Immunol*. 2012;22(6):448-449.

3. Deluche SL, Touraine F, Clavère P. Two cases of cutaneous drug eruption associated with temozolomide therapy for glioblastoma. *Curr Oncol*. 2014;21(6):e779–781.
4. Virmani P, Chung E, Thomas AA, Mellinghoff IK, Marchetti MA. Cutaneous adverse drug reaction associated with oral temozolomide presenting as dermal and subcutaneous plaques and nodules. *JAAD Case Rep*. 2015;1(5):286-288.
5. Divekar R, Butterfield J, Maddox D. Successful rapid desensitization to temozolomide: A case series. *J Allergy Clin Immunol Pract*. 2016;4(3):545-546.
6. Pothiawala S, Hsu M-Y, Yang C, Kesari S, Ibrahimi OA. Urticarial hypersensitivity reaction caused by temozolomide. *J Drugs Dermatol*. 2010;9(9):1142-1144.