is illegal to post this copyrighted PDF on any website. Delirium in the Context of Zomisamide-Induced Toxic Epidermal Necrolysis

Samuel Reinfeld, DO^{a,*}; Christina I. Tejeda, MD^b; and Maju Mathew Koola, MD^c

S tevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are life-threatening adverse drug reactions characterized by widespread skin detachment and mucosal erosions.¹ While SJS/TEN is well documented in the literature, its association with neuropsychiatric complications is not firmly established. We present a case of zonisamide-induced TEN complicated by delirium with psychosis.

Case Report

A 40-year-old white married woman with a past medical history of obesity (body mass index: 30.8 kg/m²), asthma, and eczema, with no reported psychiatric or neurologic history was started on zonisamide 300 mg/d for weight loss (offlabel treatment). On the 16th day of treatment, she noted lip swelling and presented to the emergency department (ED). She was diagnosed with an allergic reaction, zonisamide was discontinued, and she was discharged on diphenhydramine. The next day, she wiped her lips and inadvertently removed lip skin. She returned to the ED, and the dermatology department was consulted. On physical examination, there were erythematous patches with several flaccid blisters and skin sloughing involving more than 50% of her body surface area. Skin biopsy showed full thickness epidermal necrosis consistent with TEN, and she was transferred to the burn unit. She was treated with intravenous immunoglobulin. During admission, her vital signs were significant for tachycardia (119 bpm) and intermittent fever ranging from 38.2°C (100.8°F) to 39.5°C (103.1°F). Her white blood cell count was within normal limits at 3.47 K/UL as were her electrolytes.

On day 2 of her admission, she had a sudden change in mental status. During the evening, she became confused and

^aDepartment of Psychiatry and Behavioral Health, Stony Brook University Renaissance School of Medicine, Stony Brook, New York

^cDepartment of Psychiatry and Behavioral Health, Cooper University Health Care, Cooper Medical School of Rowan University, Camden, New Jersey

*Corresponding author: Samuel Reinfeld, DO, Department of Psychiatry and Behavioral Health, Stony Brook University Renaissance School of Medicine, 101 Nicolls Rd, Stony Brook, NY 11794 (samuel.reinfeld@stonybrookmedicine.edu).

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was unaware of her surroundings. She believed she was on a snowy porch and attempted to elope. She received intravenous haloperidol 1 mg. The next evening, she experienced paranoia and visual hallucinations of her son being kidnapped. Oral haloperidol 5 mg was then administered by the primary medical team, which improved her symptoms. However, she still had fluctuations in consciousness and exhibited signs of agitation. The consultation-liaison psychiatry department was contacted to manage her agitation.

On psychiatric evaluation, the patient was lucid with no evidence of perceptual abnormalities. A diagnosis of delirium due to another medical condition was given (per *DSM-5* criteria),² and it was recommended to continue oral haloperidol 5 mg as needed for agitation and perceptual disturbances. She had no further episodes of altered levels of consciousness and required no subsequent doses of haloperidol. Her skin gradually improved with the treatment. She was discharged 18 days after admission and required no further psychiatric services.

Discussion

SJS and TEN are on a spectrum, differing only by percentage of epidermal detachment, with TEN being greater than 30%. The onset is typically 1–3 weeks after ingestion of the culprit medication. Skin findings are preceded by a prodrome of fever/malaise and present as painful, erythematous dusky plaques that progress to blisters and skin sloughing.¹ SJS/TEN is commonly associated with certain medications such as antiepileptic drugs (AEDs) and sulfonamide drugs. In this patient, it was induced by zonisamide, which is known to carry a higher risk of SJS/ TEN relative to other AEDs.¹ Zonisamide is a sulfonamide and is US Food and Drug Administration approved for the adjunctive treatment of partial seizures and is used off-label for weight loss.¹

Delirium is characterized as the acute onset of attention, awareness, and cognitive impairment, which tend to fluctuate over time. It is the most common psychiatric syndrome observed in hospitalized patients, with an incidence of 87% among critically ill patients.² Delirium is often multifactorial, and the proinflammatory state, severe pain, and ischemia that coincide with SJS/TEN are likely contributors, although there are no current studies linking the 2 conditions.

Zonisamide has been linked to psychosis and other mental disturbances.³ The case reports linking zonisamide and psychosis were of patients taking concomitant AEDs, which may indicate poorly controlled epilepsy as well as possible postictal or interictal psychosis.³ In addition, patients with

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^bDepartment of Dermatology, Stony Brook University Renaissance School of Medicine, Stony Brook, New York

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epilepsy (which our patient did not have) have a higher rate of psychosis.⁴ While our patient's delirium could be linked directly to zonisamide, it is more likely secondary to TEN, as she had discontinued the medication prior to her delirium.

directly to zonisamide, it is more likely secondary to TEN, as she had discontinued the medication prior to her delirium. In this case, the patient had elevated temperature and heart rate due to systemic inflammation, which spiked during her acute behavioral change.

There are limited publications of neuropsychiatric complications secondary to SJS/TEN. One report⁵ describes the case of a 61-year-old woman diagnosed with heparininduced SJS who presented with worsened insomnia, persecutory delusions, and visual hallucinations. This is the first case report, to our knowledge, of delirium due to zonisamide-induced TEN. It is important for the medical staff to understand the potential for delirium in patients with SJS/TEN.

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Patient consent: Verbal consent was received from the patient to publish the case report, and information has been de-identified to protect anonymity.

REFERENCES

- Teraki Y, Murota H, Izaki S. Toxic epidermal necrolysis due to zonisamide associated with reactivation of human herpesvirus 6. Arch Dermatol. 2008;144(2):232–235.
- 2. Thom RP, Levy-Carrick NC, Bui M, et al. Delirium. *Am J Psychiatry*. 2019;176(10):785–793.
- Abdoh M, Mersfelder TL, Melgar TA. Psychosis induced by zonisamide: a case report and review of the literature. Am J Ther. 2014;21(1):e15–e16.
- Cascella NG, Schretlen DJ, Sawa A. Schizophrenia and epilepsy: is there a shared susceptibility? *Neurosci Res.* 2009;63(4):227–235.
- Bidaki R, Saeidi SA, Zarch MB. Delirious state and agitation following heparin induced Stevens-Johnson syndrome. J Clin Diagn Res. 2017;11(5):VL01.