Photosensitive Lichenoid Drug Eruption Due to Zonisamide

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ABSTRACT

Zonisamide is a sulfonamide anticonvulsant now being increasingly used in the management of seizure disorders. We report possibly, the first case of a photosensitive lichenoid drug eruption due to zonisamide in a middle-aged male.

Key Words: Anticonvulsant crossreactivity, lichenoid drug eruption, zonisamide

INTRODUCTION

Zonisamide is a synthetic 1,2-benzisoxazole-3-methanesulfonamide with anticonvulsant properties. We report possibly, the first case of a lichenoid drug eruption due to the administration of zonisamide in a middle-aged male.

CASE REPORT

A 41-year-old male, shopkeeper by occupation, presented with itchy lesions over the malar area of the face, dorsum of the nose, and V area of the chest since the past 7 weeks. There was no history of other cutaneous lesions or orogenital involvement. The patient gave a history of a head injury 6 months back, after which he received tablet phenytoin 300 mg daily. Within 8 weeks of starting phenytoin, he developed redness with mild scaling all over the body in view of which the treating neurophysician stopped the offending drug, and the patient was administered symptomatic treatment with complete resolution of the rash and itching within 2 weeks. He was further started on zonisamide 100 mg once a day, 7 weeks after which he developed the current symptoms. He denied any drug allergies in the past. Personal and family histories were not contributory.

General examination of the patient was normal. On cutaneous examination, there were ill-defined violaceous plaques on the centrofacial area of the face, including the bilateral supraciliary areas, malar areas, dorsum of the nose, area above the upper lip, the lower lip, and the V area of the chest [Figure 1]. Rest of the cutaneous examination including the oral cavity, palms, soles, scalp, nails, and hair was normal.

A diagnosis of drug-induced photosensitive lichenoid eruption was entertained.

Hematological investigations such as complete blood count, liver function tests, renal function tests, and urinalysis were normal. A biopsy from the papule on the V area of the chest showed the presence of epidermal atrophy, basal cell vacuolization, melanin incontinence, and civatte bodies in the epidermis with a band-like infiltrate of lymphocytes at the dermoepidermal junction [Figure 2a and b]. These features were consistent with a diagnosis of lichen planus.

On clinicopathological correlation, a final diagnosis of zonisamide-induced photosensitive lichenoid drug eruption was made. The patient was advised, sunscreens, avoidance of sunlight and topical steroids. Zonisamide was replaced by sodium valproate, and there was gradual but significant decrease in the lesions over a follow-up of 6 months. Rechallenge test was advised but was refused by the patient in view of generalized nature of the eruption.

Causality assessment was carried out using the Naranjo scale and the World Health Organization – Uppsala Monitoring Centre Criteria after which we came to the conclusion that zonisamide was a probable (Naranjo score 5) cause of this adverse drug reaction.

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DISCUSSION

Lichenoid drug eruptions are common cutaneous adverse reactions known to be associated with gold, antimalarials, thiazides, sulfonylureas, heavy metals, antitubercular drugs, nonsteroidal anti-inflammatory drugs, phenothiazines, etc.\(^1\)

The exact etiology of lichenoid drug eruption is unknown. The drug is recognized by the body as nonself, and it incites a T-cell mediated autoimmune damage to the basal keratinocytes. After stopping the drug, the altered keratinocytes are cleared and that leads to resolution of the rash.\(^2\)

Zonisamide is a newer sulfonamide anticonvulsant. Eruptions have been reported in 1–2% of Japanese patients who take zonisamide with drug-induced hypersensitivity syndrome and toxic epidermal necrolysis being the major manifestations. HLA-A*02:07 is proposed as a potential biomarker for zonisamide-induced Stevens–Johnson syndrome/toxic epidermal necrolysis in Japanese individuals.\(^3\) No such data are available currently for Indian patients. Furthermore, it is not known if the same genetic basis applies to lichenoid drug eruption due to zonisamide.

Patients with a previous allergic episode to sulfonamide-containing drugs are at a higher risk for developing a skin eruption. Lymphocyte toxicity assay is advocated to predict a possible reaction to zonisamide when sulfonamide sensitive patients are administered the drug.\(^4\)

There is also a possibility of cross-reactivity of anticonvulsants since both zonisamide and phenytoin belong to the same class of aromatic anticonvulsants.

There is a 40–60% possibility of recurrence of rash when one patient is changed from one aromatic anticonvulsant to another.\(^5\) Recent observations have revealed an ambiguous association between HLA-B*1502 allele and cross-reactivity of aromatic anticonvulsants.\(^5\) Although we are unsure whether the same hypothesis holds true in this case, the possibility cannot be completely negated.

Lichenoid drug eruption mimics lichen planus clinically with the presence of violaceous papules and plaques over the trunk and extremities in association with the history of drug ingestion. The eruption usually begins weeks to months after initiation of the offending drug. The lesions are more psoriasiform, and even exfoliative dermatitis can occur. There is the absence of Wickham’s striae. Oral involvement is rare. Long lasting deep hyperpigmentation and skin atrophy occur after resolution.

In contrast to idiopathic lichen planus, the cellular infiltrate in cases of drug induced lichenoid eruption tends to be pleomorphic, less dense, present in the mid as well as deep perivascular location with the presence of eosinophils. There is focal parakeratosis with focal interruption of the granular layer with the cytoid bodies that are situated higher up in the granular and the cornified layer.\(^6,7\)

These features are more commonly seen in nonphoto distributed lichenoid eruption than in photo distributed lichenoid drug eruption.\(^8\) Hence, even though the biopsy specimen in our case was consistent with classical lichen planus, considering the time – event relationship, distribution, and regression of the skin lesions on withdrawal of the drug, we arrived at the final diagnosis of lichenoid drug eruption due to zonisamide.

As zonisamide is being increasingly used for seizure disorders, clinicians should be aware of the possibility of a lichenoid drug eruption occurring as a rare adverse event.
Cessation of the causative drug remains the mainstay of the treatment for lichenoid drug eruption. Mild cases may be managed by topical corticosteroids and systemic antihistamines while in severe cases, administration of systemic corticosteroids may be required.[9] In cases of hypersensitivity to an aromatic anticonvulsant, other aromatic anticonvulsants and lamotrigine should be avoided, and agents with low allergenic potential such as benzodiazepines, levetiracetam, and gabapentin are probably safe for use.[10]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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