

CONTACT POINT

Ethosuximide-induced Stevens-Johnson syndrome/toxic epidermal necrolysis overlap confirmed by patch testing in a child

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KEYWORDS: ethosuximide, patch test, Stevens-Johnson syndrome, toxic epidermal necrolysis

Anticonvulsants, used widely to treat epilepsy in children, may cause nonimmediate T-cell-mediated life-threatening cutaneous adverse reactions as Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN).^{1,2} Aromatic anticonvulsants are among the most frequent culprits in pediatric SJS/TEN.^{1,2} Ethosuximide, a nonaromatic antiepileptic, has been rarely implicated in SJS/TEN, with only six cases of SJS and two cases of TEN reported, exclusively in children, as its main indication are absence seizures.¹⁻⁴

1 | CASE REPORT

A 4-year-old boy diagnosed with SJS/TEN overlap exhibited severe mucosal erosions and skin blisters on the face and trunk after the onset of ethosuximide (Figure 1). The patient had myoclonic generalized epilepsy after neonatal sepsis, global developmental delay, and failure to thrive. Because daily medication (clonazepam, sodium valproate and levetiracetam) was unable to control absence seizures, levetiracetam was replaced by ethosuximide 40 mg/kg/day twice daily (500 mg/day). After 15 days, the patient developed SJS/TEN overlap, and both ethosuximide and sodium valproate were withdrawn. In an intensive care unit, the patient received intravenous immunoglobulin (2 g/kg, 1 day) and high-dose systemic corticosteroids (methylprednisolone, 10 mg/kg/day, 3 days). He recovered without sequelae after 3 weeks but epilepsy control was suboptimal under clonazepam.

Three months after recovery, patch tests were performed with a reduced baseline series and several antiepileptic drugs including carbamazepine, diphenylhydantoin, lamotrigine, sodium valproate, diazepam at 2%–10% pet. (Chemotechnique Diagnostics, Vellinge, Sweden), topiramate, and levetiracetam at 10% in pet. (prepared at the hospital), as well as ethosuximide (Zarontin, capsule gel). A small drop of the gel was tested “as is,” and the content of the capsule was diluted in pet. to achieve an active drug concentration of 10%. Allergens in IQ Ultra chambers were applied on the back and readings on day 3 revealed strong positive reactions (2+) for the two concentrations of ethosuximide (Figure 2). The remaining allergens tested negative. Patch tests with the same ethosuximide preparations were performed on 13 healthy individuals, with negative results. Sodium valproate was later re-introduced without adverse reactions.

2 | DISCUSSION

There is no reliable in vitro test for the prompt identification of culprit drugs in severe nonimmediate cutaneous adverse drug reactions. Patch testing has demonstrated weak sensitivity in SJS.^{1,2} However, for specific drugs, such as carbamazepine, sensitivity can be up to 62.5% and its use is supported when there is a clear benefit of the diagnostic information obtained.⁵ In all ethosuximide-induced SJS/TEN cases reported so far, patch testing was performed in only one patient, also at a 10% concentration, with a negative result but a positive drug-induced lymphocyte transformation test.³

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FIGURE 1 Severe mucosal erosions as well as skin blisters in the face and trunk



FIGURE 2 Positive patch test to ethosuximide ("as is" and 10% in pet., day 3)

Safety considerations regarding the use of patch testing in SJS/TEN have been raised, but many studies have confirmed its safety in this setting.⁵ The present report demonstrates the role of patch

testing in the diagnostic confirmation of this severe reaction, although more reports are needed to know its real sensitivity in severe T cell-mediated adverse drug reactions induced by ethosuximide.

ACKNOWLEDGMENT

No funding sources to declare.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

AUTHOR CONTRIBUTIONS

Ana Matos: Conceptualization; data curation; writing - original draft; writing-review & editing. **Jóni Carvalho:** Conceptualization; data curation; writing - original draft; writing-review & editing. **Rebeca Calado:** Conceptualization. **Tiago Gomes:** Conceptualization. **Leonor Ramos:** Conceptualization. **Margarida Gonçalves:** Conceptualization; writing-review & editing.

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How to cite this article: Matos AL, Carvalho J, Calado R, Gomes T, Ramos L, Gonçalves M. Ethosuximide-induced Stevens-Johnson syndrome/toxic epidermal necrolysis overlap confirmed by patch testing in a child. *Contact Dermatitis.* 2021;1-2. <https://doi.org/10.1111/cod.13928>