Lamotrigine and Toxic Epidermal Necrolysis

D.		Vukelić ^a
D.		Božinović ^a
G.		Tešović ^a
I.		Dobrić ^b
D.		Lončarić ^b
I.		Knezović ^a
M.		Skerlev ^b

^aUniversity Hospital for Infectious Diseases and ^bDepartment of Dermatovenereology, Zagreb Clinical Hospital and Zagreb University School of Medicine, Zagreb, Croatia

Key Words

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D. Vukelić, MD, University Hospital for Infectious Diseases 'Dr. Fran Mihalević, Mirogojska cesta 8, CRO-41000 Zagreb (Croatia)

Cutaneous rash is one of the commonest adverse events associated with lamotrigine, especially among patients already taking valproic acid. The risk of developing severe skin reactions including toxic epidermal necrolysis (TEN) is low [1]. We describe a patient with myoclonic epilepsy receiving valproate who developed TEN 14 days after initiating lamotrigine therapy. A male child aged 22 months was admitted to the Department of Pediatric Infectious Diseases on December 27, 1996 with a 3-day history of fever and rash. He was the first child in a 3-member family, born after an uncomplicated 40-week gestation. He had a history of viral meningoencephalitis at the age of 4 months. Treatment-resistant myoclonic epilepsy developed after the meningoencephalitis. Since valproate treatment resulted only in a poor control of epilepsy, lamotrigine was added on December 11, 1996, at an initial dose of 1 mg/kg/day increased after 10 days to 2 mg/kg/day. During this period of combined therapy, the patient became seizure free, but fever and a maculopapular rash developed on the 14th day of therapy and

the patient was admitted to the pediatric intensive-care unit (PICU). On admission the child appeared very sick, severely dehydrated, prostrated with high fever (39.8 °C) and with a sunburn-like rash covering two thirds of the skin surface which rapidly evolved to blisters. Lamotrigine was then discontinued, but the eruption worsened and TEN involved the conjunctivae, oral cavity and trachea. A skin biopsy was done which confirmed the diagnosis of TEN. Histologically, necrotic keratinocytes within the epidermis, vacuolar alteration of the basal layer and subepidermal blisters were present. The clinical course of illness was protracted and complicated by a nosocomial *Enterobacter cloacae* infection. After 4 weeks in the PICU, the patient recovered totally.

A cutaneous rash develops in about 5% of patients starting lamotrigine [1]. The risk of developing TEN is very low [1], although a fatal outcome of TEN occurring under treatment

with lamotrigine was reported in a patient previously treated with carbamazepine [2]. The incidence of a rash is increased in patients receiving concomitant valproate therapy [1]. Valproate inhibits lamotrigine metabolism and alters the half-life of lamotrigine by as much as 100% [3]. Therefore, the gradual increase in the lamotrigine dose in patients already receiving valproate therapy is advised. Most of the patients reported developed skin reactions within 2 weeks after starting lamotrigine that is compatible with the development of immune sensitization [4]. In previous studies lamotrigine was well tolerated and effective for various types of seizure [5]. We suggest that lamotrigine should be considered as a cause of unexplained cutaneous rashes, particularly in patients where lamotrigine therapy is combined with sodium valproate.

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