

## Levetiracetam induced toxic epidermal necrolysis: A fatal outcome

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**Abstract:** *Toxic Epidermal Necrolysis (TEN) is a rare, life-threatening dermatological manifestation which usually develops after intake of some culprit drugs. These drugs often belong to antibiotics, sulfonamides, non-steroidal anti-inflammatory drugs (NSAIDs) and anti-convulsants. We here report a fatal case of an elderly male patient who developed TEN soon after the intake of levetiracetam.*

**Keywords:** *Levetiracetam, anticonvulsant, Toxic Epidermal Necrolysis*

### Introduction

Levetiracetam is an analogue of piracetam. It is used as an adjunct in the treatment of partial seizures with or without secondary generalizations in adults and children aged 4 years and over. <sup>(1)</sup> It appears to be safe and effective; its exact therapeutic profile has yet to be determined. <sup>(2)</sup> Its therapeutic index appears to be high and the commonest of the adverse effects are asthenia, dizziness and drowsiness. <sup>(3)</sup> Cutaneous drug eruptions to antiepileptic drugs (AEDs) used for seizure prophylaxis can range from a maculopapular eruption to severe Stevens-Johnson syndrome or toxic epidermal necrolysis.<sup>(4)</sup> Anticonvulsants are the commonest group of drugs causing SJS and TEN in several earlier reports. <sup>(5)</sup> Serious adverse drug reactions such as SJS, TEN and SJS-TEN overlap in children are caused by antibiotics, NSAIDs and anticonvulsant. The mortality rate is higher in the TEN groups. <sup>(6)</sup>

### Case Report

A 60 years old male patient was hospitalized following complaints of fever, headache, vomiting, hiccups with myoclonic seizures since 15 days. He also had history of pulmonary tuberculosis (PTB) 3 years back which was recovered after treatment. On MRI investigation of brain, sub-acute non hemorrhagic right middle cerebral artery territory infarct was found. The patient was hospitalized in the intensive care unit where the treatment was started with oral levetiracetam 500mg twice a day. The other concomitant drugs were oral clindamycin and ibuprofen-paracetamol combination. On the 6<sup>th</sup> day of drug intake, reaction in the form of skin peeling started from the right shoulder, spreading throughout the body in the next 3 days i.e. on the 9<sup>th</sup> day. After worsening of patient's condition, he was shifted to other hospital where he was diagnosed Levetiracetam induced TEN with more than 30% body surface area (BSA) skin detachment. Severe desquamative bullous eruptions developed with involvement of whole body and oral mucosa. The patient was put on ventilator and concurrently treatment with antibiotics such as imipenem, teicoplanin & other i.v. fluids was started. On the 12<sup>th</sup> day of suspected drug intake, the patient expired.

### Discussion

Serious dermatological reactions, including Stevens Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) in both children and adults treated with levetiracetam are reported. The median time of onset is reported to be 14 to 17 days, but cases have been reported at least 4 months after initiation of treatment. <sup>(7)</sup> On January 21, 2011, the US Food and Drug Administration (USFDA) registered levetiracetam on the list of Drugs under safety monitoring for the risk of SJS and TEN. <sup>(8)</sup> In addition to the adverse reactions reported during clinical studies, TEN, SJS, Erythema multiforme and alopecia have been reported in post marketing experience. Data are insufficient to support an estimate of their incidence in the population to be treated. <sup>(9,10)</sup> In this case, dechallenge was negative and rechallenge was not performed. Moreover, the other concomitant drugs were clindamycin and ibuprofen-paracetamol

combination which also have few isolated reports on causing TEN. Thus, the causality assessment in this case is 'possible' as per WHO-UMC causality categories.



**Fig 1:**



**Fig 2:**

### **Conclusion**

In this case, it is clear that the second line anticonvulsant drug, although thought to be safer than first line drugs might still have some potential to cause serious dermatological reactions when used concomitantly with drugs like ibuprofen and other antibiotics which already have well established adverse dermatological manifestations in literature. Therefore, precautions must be taken while using anti-convulsants concomitantly with other NSAIDs combinations.

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