

CASE REPORT

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Intravenous Immunoglobulin in the Treatment of Lamotrigine- Induced Toxic Epidermal Necrolysis

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ABSTRACT

Toxic epidermal necrolysis is a potentially life-threatening disease, which needs necessary treatment.

We present a 12 years old female who was a known case of idiopathic generalized tonic-clonic convulsion and presented with fever, diarrhea and generalized erythematous eruption after 2 weeks of being under treatment with maintenance doses of Lamotrigine (LTG) and Valproate (VPA). The eruption led to more than 90% epidermal detachment of the total body surface area. However, she made a full recovery with few negligible sequelae regarding the severity of her disease and the symptomatic therapy and Intravenous Immunoglobulin (IVIG) administration which started soon after the bullae appeared.

While IVIG might be beneficial in the treatment of TEN, controlled studies are needed to evaluate the efficiency of IVIG compared to other modalities.

Key Words: Intravenous immunoglobulin; Lamotrigine; Toxic epidermal necrolysis.

INTRODUCTION

Toxic epidermal necrolysis (TEN) as the severe form of Steven Johnson syndrome (SJS) is a potentially life threatening disease characterized by severe mucosal erosion and widespread erythematous rash with positive Nickolsky sign and epidermal detachment. In SJS epidermal detachment involves less than 10% of total body skin area. TEN is defined as a detachment greater than 30% and SJS-TEN as detachment of 10 to 30%.¹⁻³ Mortality rate of TEN is mentioned to be about 30-35 %.⁴

Graft versus host disease and infection with *Mycoplasma pneumonia* are mentioned as the cause of TEN, but it is mostly a drug induced disease.

Anticonvulsants, sulfonamides and some nonsteroidal anti-inflammatory drugs are reported as the most common causes of TEN.⁴

Lamotrigine (LTG) is a relatively new anticonvulsant being used for different types of epilepsy. The most common adverse reaction leading to discontinuation of LTG has been rash. The need to discontinue the therapy was reported in 3% of adults in a clinical trial.⁵ Most rashes are benign however, the incidence of rash associated with hospitalization in a clinical trial with LTG was three of 1000 (0.3%) in adults and one of 100 (1%) in children.⁶ Excessive initial dose or rate titration

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and combination of LTG with valporate (VPA) are factors which increase the risk of LTG rashes.^{6,7}

Different treatments including steroids, IVIG, cyclosporin, plasmaphoresis have been suggested for TEN, but there is still debate on their use.⁸

Our patient was a girl with the most severe form of eruptive disease following use of LTG. She made full recovery with supportive care and IVIG treatment.

CASE REPORT

Our patient was a 12 years old female, who was a known case of idiopathic generalized tonic -clonic convulsion on treatment with VPA and Topiramate, however, her convulsion was not controlled. In the treatment plan, Topiramate was substituted with LTG. It was started with 25 mg of LTG and increased to 100 mg /day when finally her convulsion stopped. She did not experience any convulsion for 2 weeks on treatment with LTG and VAP. However, after those two weeks she presented with diarrhea, fever and generalized erythematous rash. Her medications were discontinued immediately and an intermittent IV diazepam was started to control her convulsion. The next day, confluent bullae appeared all over her body except her skull.

She was transferred to the PICU. During the following three days, all blisters ruptured and her condition deteriorated with a high grade fever, low blood pressure and confusion state. All cultures including blood, urine and wound were sent to the laboratory and antibiotic and supportive care including fluid therapy; albumin, proper skin care, eye drops and mouth wash were started. She was neutropenic and anemic, and the inflammatory index (CPR> 192 mg/l) was high. Other lab tests including liver function test and electrolytes were normal. IVIG was commenced on the 4th day of her admission with 400 mg/Kg/day for four days. Her general condition was better during the second week and she did not have any convulsion on benzodiazepines over this period. Reepithelialization began on her leg about one week after the first dose of IVIG, and covered her whole body during the next 10 days and she was discharged with a good condition. A patch of hair loss, some hypopigmentation on her skin and some nail loss were the sequelae of TEN.

DISCUSSION

Previous studies showed that skin rash was the most common adverse reaction to LTG and it was much more common in pediatric age group. Guberman et al. showed that children had at least three folds increase risk of developing serious rash (SJS, TEN) compared to adults.⁶ Two factors appeared to increase the risk including exceeding the recommended initial dose and the titration rate and combination with VPA.^{6,7}

Although LTG was started cautiously for our patient due to her repeated convulsions, it was increased more rapidly when compared to the recommended dose. It was also added to VPA which accounts as an additional risk factor. She developed skin rash 2 weeks after cessation of her convulsion on the maintenance dose of 100 mg/ day of LTG.

The cornerstone of treatment for TEN is fluid replacement, nutritional support, surveillance and aggressive treatment for infection.⁹ The administration of corticosteroids in treatment of TEN is still controversial.^{10,11} The role of cyclosporine, plasmaphoresis, IVIG and cyclophosphamide has been studied for treatment of SJS and TEN. Treatment with IVIG has shown promising outcome.¹²⁻¹⁵ A recent study on the pathogenesis and therapeutic options for TEN showed that the hallmark of SJS/TEN was epidermal cell apoptosis, which may be mediated through keratinocyte Fas-FasL interaction or through cytotoxic T-cell release of perforin and granzyme B. IVIG contains anti-Fas antibodies which can inhibit apoptosis.¹² A retrospective study on 8 patients with TEN and 4 patients with SJS-TEN treated with 1.5-2 g/kg of IVIG indicated a 91.6% survival rate and no adverse reaction to IVIG.¹³ In another study seven patients with SJS were treated with IVIG and showed no blisters within 24 to 48 hours after IVIG administration.¹⁴ A report by Manglak indicated the efficacy of low dose of IVIG (0.05-0.1 gm/kg/day) in treatment of TEN.¹⁵

IVIG was commenced with a dose of 400 mg/kg for 4 days for our patient, 2 days after appearance of her bullae. Epithelialization started one week later. She recovered completely within 10 days. It can not be concluded that reepithelialization was directly due to IVIG concerning a prospective open trial on 34 patients showing no measurable effect on the progression of detachment or on the speed of reepidermalization with IVIG.¹ However, it suggests the necessity of a con-

trolled study to evaluate the efficacy of IVIG in treatment of SJS and TEN.

In conclusion, we presented in an epileptic child with TEN who was being treated concomitantly with LTG and VPA. She made a full recovery without any serious sequelae with supportive care and IVIG. Our case suggests that IVIG is safe and might be beneficial in the treatment of TEN. Controlled studies are needed to rationally evaluate the efficiency of IVIG compared to other modalities.

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