CASE REPORT

Anticonvulsant Hypersensitivity Syndrome associated with Carbamazepine Induced Toxic Epidermal Necrolysis A Rare Case Report in an Epileptic Child

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ABSTRACT

Reporting the case of a seven-year-old boy with complaints of painful exfoliation and blistering of skin involving around 40% of body's surface area alongwith high grade fever (102 F). Detailed history revealed that he was started on tablet Carbamazepine a month ago for Epilepsy, which was well tolerated for the first two weeks, however after the dose was increased, cutaneous and systemic symptoms began to appear. There are very few case reports of Toxic Epidermal Necrolysis in paediatric population related to the use of Carbamazepine. Hence, importance of cautious use and prompt recognition of side effects must be realized in children.

Key Words: Carbamazepine, Epilepsy, Exfoliation, Stevens johnson syndrome, Toxic epidermal necrolysis

How to cite this article: Zahoor M, Anticonvulsant hypersensitivity syndrome associated with carbamazepine Induced toxic epidermal necrolysis, a rare case report in an epileptic child. Ann Jinnah Sindh Med Uni. 2021;7(2):79-81

DOI: https://doi.org/10.46663/ajsmu.v7i2.79-81

INTRODUCTION

Toxic Epidermal Necrolysis (TEN) is a rare and life threatening condition with 30% mortality rate[1]. It is characterized by erythema, necrosis and extensive sloughing of epidermis, involvement of mucous membranes and systemic symptoms[2]. Etiological factors for TEN are several, however, the most common ones are adverse drug reactions[3]. In 3% of individuals treated with Carbamazepine, cutaneous reactions were seen which included diffuse erythema, exanthematous rash, urticaria, purpuric petechiae or a mucocutaneous syndrome, any of which can occur from day eight to day sixteen after the treatment has been started[4]. Nevertheless, the majority of data in this regard comprises adult cases. Therefore, keeping in mind the paucity of literature on this issue in paediatric age group, the case is being reported to emphasize the importance of careful use and anticipation of adverse effects related to Carbamazepine in children.

CASE:

A seven years old boy weighing 25 kg came to the Emergency department with presenting complaints of rashes and peeling of skin for the past seven days and fever for two days. Parents reported that the rashes first appeared on the child's hands and upper limbs, but later on progressed to the whole body. Initially, the mother applied coconut oil on the rashes but condition worsened and skin started to slough off painfully. At this point, the child developed high grade fever, and became unable to eat due to painful ulcers in the mouth, and thus, brought to the emergency room.

On further history taking, it was learned that the Child also had two episodes of fits in the past three months for which he was being investigated at a private hospital and one month ago, the final diagnosis of epilepsy was made. Tablet Carbamazepine (200 mg) was started as treatment. Initially, half a tablet was given twice daily for two weeks which was well tolerated. However, after two weeks, the dosage increased to one tablet twice daily and it was nearly at that time when the cutaneous symptoms began.

The child is the second issue of a consanguineous marriage and there is no history of any allergies or skin diseases in the patient or his family.

At the time of admission, the child was febrile (Temp 102 F). Other vitals were stable. Local examination showed Erythema and Exfoliation of skin on face and crusting and erosions of lips (Figure 1). Skin of eyelids was also involved and eye opinion was sought from

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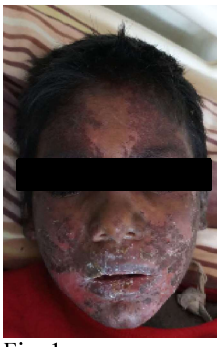
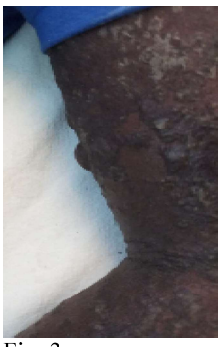


Fig. 1


Fig. 2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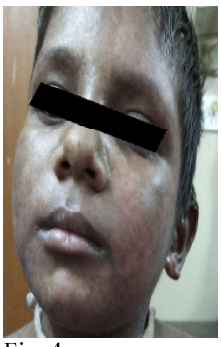
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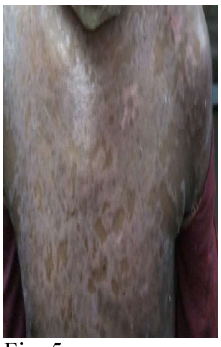
Fig. 5

Note: All photographs of patient are being shared after obtaining consent from parents.

Ophthalmologist who documented no evidence of corneal ulceration, keratitis, or uveitis. On trunk and upper limbs, the maculopapular rashes progressed to bullous eruptions, alongwith extensive areas of epidermal necrosis (Figures 2 and 3). Around 40% of the body's surface area was affected. Nikolsky's Sign was positive (slight rubbing of skin results in Exfoliation of most outer layer).

Complete blood count, renal and liver function tests, and electrolytes were within normal range. ESR was raised (40mm/hr). Estimation of adverse drug reaction was done using Naranjo Scale[5] which turned out to be seven in this case, indicating probable adverse drug reaction.

The child was admitted to the ICU. Carbamazepine was stopped immediately. Fluid resuscitation was done initially with Ringer's Lactate and later with half strength Dextrose Saline. Samples taken from blood and skin swabs were sent for culture sensitivity. Injection Hydrocortisone (2mg/kg/dose) was given 12 hourly for five days. Broad spectrum parenteral antibiotics Piperacillin+ Tazobactum along with Linezolid were administered for five days. Injection Paracetamol for fever and injection Ketorolac for pain relief was given. Parenteral nutrition was ensured. Antibiotic ointments and saline soaked sterile pads were used for eyes. Magic mouthwash comprising normal saline, betnisol, nystatin, antacid, and diphenhydramine was dispensed. Potassium permanganate solution and saline wash was used for local cleaning of wounds on body after which Fusidic Acid was applied. Combined preparation containing liquid paraffin and white soft paraffin was applied all over the body. Posture of the child was changed frequently on sterile bed sheets. Child showed signs of improvement with these measures and was afebrile after four days of admission. Culture reports for blood and skin swab came negative. Peeling of skin stopped, pain and fever subsided. He was discharged on the 12th day. At his follow up visit after one week, skin lesions showed marked re-epithelialization, oral ulcers had healed and there were no signs of secondary infections (Figures 4 and 5).

DISCUSSION

Toxic Epidermal Necrolysis (TEN) and Stevens Johnson Syndrome (SJS) are two forms of the same life-threatening skin condition occurring as a result of an immune mediated hypersensitivity reaction[6]. In SJS, less than 10% of body surface area (BSA) is involved, whereas, it is more than 30% in TEN. If BSA involvement is between 10-30%, overlapping SJS/TEN is considered[7]. In our patient, around 40% of the body surface area got involved after two weeks of Carbamazepine initiation, at the time of dosage increase.

To predict the risk of death in a patient with TEN, Bastuji-Garin et al has described a SCORTEN scale, which takes different parameters into account at the time of hospital admission like age, malignancy, percentage of epidermal detachment, heart rate, blood urea, glucose, and bicarbonate levels. A score more than five is associated with 90% mortality rate[8]. In our patient, the score was one which coincided with 3.2% mortality rate and that explains the excellent progress which was seen in that child.

In literature review, about management of children with TEN, initial treatment comprising withdrawal of suspected drug, admission in an intensive care/burn unit, and supportive therapy with fluid resuscitation, nutritional support, and prevention of infections is recommended. Furthermore, systemic therapy such as systemic steroids, intravenous immunoglobulins, Cyclosporine, Plasmapheresis, and Tumour Necrosis Factor (alpha) inhibitors are the treatment options whose safety and efficacy still needs to be confirmed through studies[9]. In our patient, alongwith the supportive treatment, we administered systemic steroids and the outcome was better. However, it was clearly elaborated

by McPherson et al in a summary of British Association of Dermatologist's guidelines that for SJS/TEN in children, the best way to manage this potentially life threatening condition is still unknown, and need for data collection and standardization of treatment exists[10].

This case has been reported to highlight the association of TEN with Carbamazepine, as there is a paucity of literature on this issue in paediatric population. It is essential to prescribe Carbamazepine cautiously, and equally important to not use other aromatic anti-convulsants in a patient who already has an adverse skin reaction with Carbamazepine due to the phenomenon of cross reactivity. We started our patient on Levetiracetam and the child is doing fine with that. Also, it is of utmost importance to discuss the possible adverse drug reactions before the initiation of the treatment as in this case, parents did not seem to be aware of the condition and continued to give the medicine and deal the skin rashes with home remedies before seeking medical attention.

Conflict of interest: None

Acknowledgement: The author would like to thank the parents of the child for giving their consent to publish the photographs of their child in a medical journal for educational purpose.

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