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Case Report

Sodium valproate induced Stevens Johnson syndrome and hepatitis in a pediatric patient: a case report

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ABSTRACT

Stevens Johnson syndrome is a life threatening IgE mediated hypersensitivity reaction affecting the skin and mucous membranes and should be considered in any child who has been on antiepileptic medication. A case of Stevens Johnson Syndrome and hepatitis following treatment with sodium valproate is presented. A 2 year old female pediatric patient suffering from atonic seizures and myoclonic seizures was treated with sodium valproate monotherapy. The patient reported skin peeling and rash since 15 days and yellowish discoloration of sclera since 7 days. Her laboratory investigations revealed abnormal hemoglobin levels, blood urea and liver function. Based on physical examination and laboratory findings it was diagnosed that she was suffering from sodium valproate induced Stevens Johnson Syndrome with hepatitis. The score of toxic epidermal necrosis (SCORTEN) criteria score was 1. She was treated with antihistamines, iron folic acid and topical liquid paraffin lotion.

Keywords: Stevens Johnson syndrome, Hepatitis, Sodium valproate, SCORTEN

INTRODUCTION

Valproic acid (VPA) has been used in clinical practice since the 60's, with a relatively favourable safety and efficacy profile. Pancreatitis, hepatotoxicity and teratogenicity are the most significant adverse drug reactions.[1] Valproate-induced hepatotoxic effects are also more typical in paediatric populations, particularly infants younger than 2 years.[2]

SJS is a rare dermatological emergency characterised by epidermal necrosis involving both skin and mucous membranes. There is overlap with toxic epidermal necrolysis (TEN), with differentiation according to the extent of skin involvement. SJS is categorized by involvement of <10% of the body surface area, TEN by involvement of >30%.[3] SJS/TEN have been observed with more than 100 drugs. Common culprits are antimicrobials, antiepileptic drugs and non-steroidal anti-inflammatory agents (NSAIDs).[4]

SCORTEN is an illness score that has been developed to predict mortality in SJS and TEN cases. It uses seven independent risk factors to predict the risk of death: Age, malignancy, heart rate, epidermal detachment, serum urea, glucose and bicarbonate at admission.[5] The risk of dying from SJS/TEN depends on the score.

CASE REPORT

A 2 year old female child, weighing 8kgs was admitted in pediatric department with chief complaints of peeling of skin, exfoliating macula popular rash involving mucous membrane all over the body since 15 days and yellowish

discoloration of sclera since 7 days. Her past medical history revealed that she was suffering from atonic seizures and myoclonic seizures with starring of eyeballs. She was prescribed with sodium valproate syrup 5ml, twice daily one month ago. She had no history of similar complaints and adverse drug reactions previously. Antenatal history revealed that her mother was not suffered from diabetes mellitus, eclampsia, thyroid problem.

Her post natal history revealed that there are no episodes of neonatal seizures and neonatal jaundice. Her family history reveals that there were no similar complaints in siblings. They belong to class-IV according to modified Kuppuswamy socioeconomic scale. On investigation, complete blood cell count showed low haemoglobin levels (5.8gm/dL). Liver function tests were done and found to be abnormal (ALT 58 IU/L;AST 154 IU/L; Total bilirubin 7mg/dL; conjugated bilirubin 6mg/dL). Causality assessment was determined using Naranjo's algorithm. Causality assessment using Naranjo's criteria revealed that sodium valproate was the probable cause (overall score 8) of the adverse drug reaction (ADR).

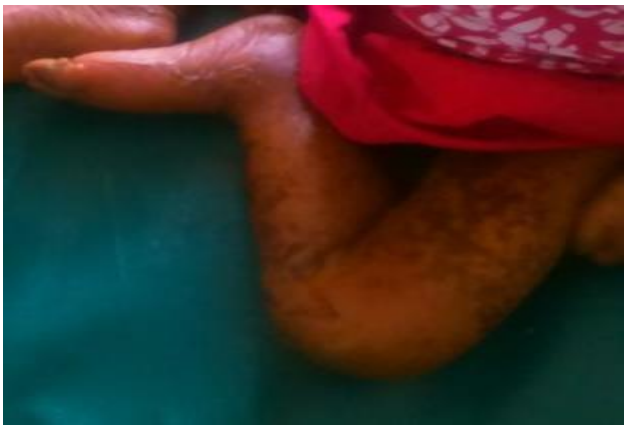

Figure 1: Peeling of skin.

Treatment was initiated with syrup lactulose 3ml twice daily, syrup iron folic acid 3ml twice daily, capsule vitamin A and D 5omg once daily, syrup Avil 2ml twice daily and liquid paraffin lotion for external application. On the 12th day of the treatment, bilateral edema of legs was observed. Injection magnesium sulphate 1.7ml Intramuscular route was added. There is no improvement in the patient condition; the patient was referred to dermatology department to take care of.

DISCUSSION

As a result of its broad spectrum of efficacy, valproate could be the drug of choice for most children with newly diagnosed epilepsy, like idiopathic generalized epilepsy, epilepsies with prominent myoclonic seizures or with multiple seizure types, and photosensitive epilepsies.[6] The SANAD (Standard and New Antiepileptic Drugs) trail indicated that valproate is the most effective and best tolerated first line AED for patients with Idiopathic Generalized epilepsy, including Juvenile Myoclonic Epilepsy, compared against lamotrigine and topiramate.[7]

Hepatic failure has been reported usually within 6months of treatment. So clinical and laboratory monitoring is recommended periodically. Its use must be discontinued immediately if condition occurs. Pediatric patients under age 2 years are at increased risk and should be used cautiously as monotherapy.

The abnormality in liver function tests clearly depicts the hepatotoxicity of valproate where in the values of total bilirubin and conjugated bilirubin is extremely abnormal. Parents should be informed to report the signs /symptoms of hepatotoxicity. Important nonspecific symptoms include malaise, lethargy, anorexia and vomiting.

Stevens Johnson Syndrome is a life threatening adverse drug reaction characterized by skin detachment <10% body surface area, maculo popular rashes and rash all over the body. Risk for the development of SJS/TEN with antiepileptics is largely confined to initial 8 weeks.[4]

Causality assessment was performed using Naranjo's causality assessment scale. It revealed that sodium valproate was the probable cause (overall score 8) of Stevens Johnson Syndrome. Assessment using Modified Schumock and Thornton Scale revealed that the adverse drug reaction was definitely preventable. Similar adverse drug reaction induced by sodium valproate therapy was reported.[8] The SCORTEN criteria score was 1 and the risk of dying from SJS was>3.2%.

A systematic review of treatment of SJS in children recommended early cessation of the causative drug and diligent supportive therapy along with either intravenous immunoglobulin (IVIg) or corticosteroids. Patients treated with dressing and support treatments alone without a steroid have longer hospitalization, remission, and are more prone to complications and death .[9] Early use of short term dexamethasone therapy seems beneficial. Short term dexamethasone therapy (1.5 mg/kg/day) on three consecutive days at an early stage of the reaction may reduce mortality without affecting the healing time.[10]

The patient was not prescribed steroid here. Symptomatic treatment was initiated and maintained throughout the treatment. Antihistamine, pheniramine maleate was prescribed to control allergic reactions.

Syrup iron folic acid was prescribed to treat anemia. Liquid paraffin lotion was prescribed for external application to soothen the skin. Soframycin (Framycetin sulphate) ointment was also prescribed to prevent potential infection. The condition of patient was not improved with the treatment and she was referred to a dermatologist for further action.

CONCLUSION

Prescribers should be more cautious while prescribing medicines for special populations like pediatrics. The parents should be made aware of the common and serious adverse drug reactions their children may encounter, how to detect them and what management strategy they should follow. Recommendations regarding periodical liver function tests while using sodium valproate were advised to rule out hepatotoxicity at an early stage.

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