

TEACHING FILES (GRAND ROUNDS)

DESQUAMATING RASH WITH HEPATITIS

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KEYWORDS

ARTICLE HISTORY

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Clinical Problem:

A seven-year-old female child presented with fever for 3 days, oral ulcers and rash all over the body for one day. She was on sodium valproate at 20 mg/kg/day since a month in view of focal seizures. Baseline liver function tests (LFT) were normal prior to starting valproate. On admission, child had generalized exfoliating rash (Figure 1), jaundice and shock (blood pressure of 76/50 mm of Hg) requiring fluid resuscitation. She was treated with zinc, local paraffin application and glycerin mouth wash for oral ulcers. Sodium valproate was withdrawn and levetiracetam was started. Complete blood count revealed hemoglobin of 9.7 gm/dl, total leucocyte counts 10,000 cells/cumm (50% polymorphs, 40% lymphocytes and 6% eosinophils), platelet count 450,000 cells/cumm. Liver function tests (LFTs) were deranged (Table 1). Pancreatic function tests were also deranged with serum amylase of 162 IU/L and serum lipase of 448 IU/L. Ultrasound abdomen revealed hepatomegaly with increased gall bladder thickness. Serum creatinine was 0.4 mg/dl. IgM for dengue and scrub typhus, hepatitis A IgM, Hepatitis E IgM, malaria antigen test, HIV Elisa were negative. Prothrombin time was 17 sec and INR was 1.8 which were corrected after Vitamin K injection.

Figure 1. Desquamating rash



What is the cause of rash and hepatitis in this child?

Discussion:

Sodium valproate induced Steven-Johnson syndrome (SJS). The antiepileptics phenytoin, carbamazepine, phenobarbitone, and primidone can cause hypersensitivity reactions. It is rarely reported by sodium valproate.¹ The common side effects of sodium valproate include anorexia, nausea, vomiting, sedation, ataxia, tremor, alopecia, stimulation of appetite, elevation of hepatic transaminases, and rarely fulminant hepatitis.² In a study done on 245 people admitted with Toxic Epidermal Necrolysis (TEN) or SJS and 1147 people admitted for other reasons, drugs used before the onset of symptoms was studied and the crude relative risk for SJS or TEN was

Table 1. Trend of liver function test

Liver parameters	Day 1	Day 3	Day 5	Day 7
Bilirubin (mg/dl)	3.2	0.4	0.6	0.4
ALT (IU/L)	537	410	212	119
AST (IU/L)	732	480	300	142

Note: ALT - Alanine aminotransferase, AST - Aspartate aminotransferase

found to be as follows: carbamazepine 90, phenytoin 53, phenobarbitone 45 and sodium valproate 25.³ SJS is a type IV hypersensitivity reaction in which a drug or its metabolite initiates autoimmune reactions by stimulating cytotoxic T cells and T helper cells.⁴ Valproic acid is known to inhibit mitochondrial respiration resulting in mitochondrial dysfunction, oxidative stress, and increased cell death. Microvesicular hepatosteatosis is a peculiar feature

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of valparin induced hepatitis and is suggestive of mitochondrial involvement especially the β -oxidation.⁵ The clinical features of SJS include fever, signs of upper respiratory tract involvement and initially conjunctivitis later on followed by the detachment of mucous membranes (oropharyngeal, conjunctival, anogenital and nasal). There is involvement of more than one mucous membrane. Cutaneous lesions may be in form in the form of dusky erythematous macules, purpura or target lesions associated with pain and burning sensation. The cutaneous involvement is symmetrical and involves trunk and limbs over 2–3 days. Also, there blister formation and shear pressure over the skin may lead to epidermal detachment also known as pseudo-Nikolsky's sign.⁶ The management of SJS involves multidisciplinary approach. Prompt withdrawal of the inciting agent, early initiation of oral or parenteral corticosteroids prednisolone 1-2 mg/kg/day for 7-10 days, and providing other supportive measures as topical pain anesthetics, antiseptics, eye care to prevent scar form the basis of treatment and prevention of complications. Intravenous immunoglobulin has some role in amelioration of symptoms in SJS however not much role has been established.⁶

Compliance with ethical standards

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Conflict of Interest: None

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