Scholars Journal of Medical Case Reports
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Anesthesiology and Intensive Care

Stevens Johnson Syndrome Triggered by Carbamazepine

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DOI: 10.36347/sjmcr.2022.v10i06.026 | **Received:** 28.05.2022 | **Accepted:** 21.06.2022 | **Published:** 25.06.2022

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Abstract **Case Report**

Stevens Johnson syndrome is one of the most severe types of cutaneous adverse reactions to drugs. We report a case of Stevens Johnson syndrome in a child after carbamazepine application. Based on data from the literature we discuss mechanisms of pathogenesis, the role of Ag HLA-B*1502, clinical manifestation and management in these severe life-threatening diseases.

Keywords: carbamazepine - stevens Johnson syndrome.

INTRODUCTION

Carbamazepine is an antiepileptic indicated in tonic clonic seizures, for neuropathic pain, and in the prevention of recurrence of bipolar disorders, but he may be responsible of stevens johnson syndrome.

Stevens Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are both acute life-threatening dermatoses characterized by extensive epidermal sloughing at the dermoepidermal junction resulting from keratinocyte apoptosis [1]. We present a patient with epilepsy who developed SJS triggered by carbamazepine.

CASE PRESENTATION

The 9 years old boy, no history of drug allergies in the past, followed in neurology for epilepsy (partial tonic clonic seizures) initially treated with sodium valproate, stopped because of his inefficiency and replaced by the carbamazepine: 100mg/day then gradually increased after 2 weeks to 400 mg/day.

After 3 weeks of post-initiation of carbamazepine, the patient had a fever, multiple skin lesions, cheilitis and conjunctivitis. He was admitted to our department from the intensive care unit. His general state was severe at the begining of treatment, with Spo2 of 98%, a blood pressure recording of 90/50 mmHg and a regular pulse of 110 beats/min.In dermatological examination, multiple erythematous lesions with blisters and large desquamation were observed (Figure 2).

He has eroded lesions on the lips covered with hamorragic crusts, severe oedema of lips and eyelids and conjonctival injection, with difficulty opening her eyes (Figure 1).

Routine laboratory assessments showed normal blood counts without hypereosinophilia. Renal function, hepatic enzyme levels, and serum electrolyte levels were all within normal and serological test was negative for HIV. The carbamazepine treatment was replaced with phenobrabital. Determination of HLA antigen B*1502 is not available.

Our management was a mainly supportive, with attention to fluid challenge, nutritionnal status and pain relief. He was receiving Hydrocortisone Sodium Succinate intravenously during 10 days 3 x 100 mg tapered systematically and after, 30 mg of prednisone with gradual reduction of dosages until stopping after 3 weeks. He received other treatment included ceftriaxone ,topical antimicrobial dressing, antiseptic mouth wash, and tetracycline eye ointment.

All symptoms and skin lesions resolved progressively within 3 weeks, and the patient left our department in a good general state.

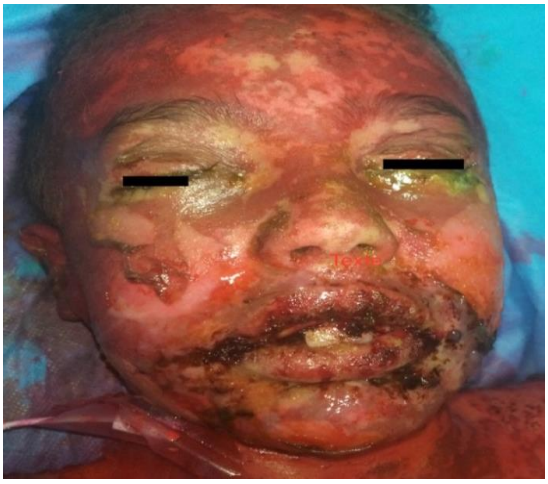

Figure 1: Mucous membrane involement in SJS with erosions and haemorragic crusts on lips

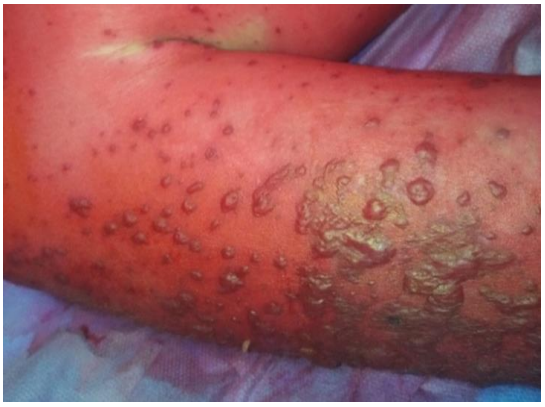

Figure 2: Erythematous macules with blisters in the upper limbs typical for SJS

DISCUSSION

Stevens-Johnson syndrome (SJS) is a serious mucocutaneous reaction induced by immune complex mediated hypersensitivity reaction. Anti-epileptic drugs are one of the commonest causes of Stevens- Johnson syndrome. Incidence of Carbamazepine induced SJS is around 14–20 per 100,000 [2, 3]. In our case latency periods was 3 weeks. median latency period (interquartile range) for the development of SJS with carbamazepine is 15 days (12–20) [4]. latency periods of 4 weeks have also been reported [5]. Carbamazepine-induced SJS has long been though of as an idiosyncratic, dose independent, unpredictable adverse event specific to an individual [6]; however, current evidence indicates that carbamazepine-induced SJS/TEN is a predictable, specific, delayed hypersensitivity immune reaction involving human leukocyte antigen (HLA) alleles specific for carbamazepine and other drugs in defined populations [7]. HLA-B*15:02 and HLA-B*31:01 have been associated with carbamazepine induced SJS in Asian (Han Chinese, Thai, Indian and Malaysian) and Caucasian (and Japanese) populations, respectively [8, 9]. However, we were not able to genotype our patient for HLA alleles, therefore we cannot confirm the involvement of the phenotype- specific characteristics of the patient that might have contributed to the development of SJS.

In differential diagnosis, Drug rash with eosinophilia and systemic symptoms (DRESS) should be considered, he is defined as a multisystemic disorder resulting from reaction to certain drugs, especially anticonvulsants, but also sulfonamides, minocycline, allopurinol and others. The diagnosis of DRESS involves 3 criteria: drug-induced skin eruption, eosinophilia > 1.5 Â~ 109/l or atypical lymphocytes, and at least 1 of such systemic abnormalities as hepatitis, nephropathy, lung disease, myocardial involvement, or enlarged lymph nodes. Skin lesions could be oedematous and convert to blisters. Nikolsky's sign could be positive.The patient often has fever and malaise [10].

The most important differential diagnosis, especially in children and younger adults, is staphylococcal scalded skin syndrome (SSSS). Patients suffer from widespread skin erosions or display multiple vesicles. Nikolsky's sign is positive but these patients never develop mucous membrane lesions [11].

The therapeutic management of patients with SJS requires multidisciplinary management; which remains contreversial especially for the use of systemic corticosteroids. These drugs are the mainstay in some units but other investigators consider systemic corticosteroids to provoke prolonged wound healing and increased risk of infection, hiding early signs of sepsis, severe gastrointestinal bleeding and increased mortality [12, 13]. In contrast, a favourable influence of high doses of systemic steroids tapering over 7-10 days during the course of disease was observed by several authors [14, 15].

The risk of infection is high, but no prophylactic antibiotic therapy is indicated. Empirical antibiotic use is generally avoided and reserved for infection confirmed by a positive culture [16]. Cyclosporine: 3mg/kg/day for 2 weeks and Cyclophosphamide is also proposed by some authors in an initial dose of 300 mg per day [17]. intravenous immunoglobulin used in cases of SJS and TEN as a substance significantly decreasing mortality rates in patients [18]. Topical therapy is essential to reduce loss of fluid and electrolytes and to prevent infections [18]. We use mild topical antiseptic solutions, such as chlorhexidine and silver nitrate. If biological compounds are not available, synthetic and semisynthetic bandages should be applied. It is important to keep the wounds wet to prevent progression of necrosis. Changes of dressings have to be performed under aseptic conditions once daily and a microbial test for wound infection should be performed at least three times per week from various body parts [17]. Eye care plays a crucial role in the management of SJS/TEN patients, since ocular involvement may lead to

severe complications and long-term consequences ranging from visual impairment to synechia formation and complete blindness. The most common late complication is severe dry eyes [19]. Topical antibiotics should not be empirically administered unless there are clinical signs of concomitant ocular infection [19].

CONCLUSIONS

Stevens–Johnson syndrome (SJS) triggered by carbamazepine is one of the most severe types of cutaneous adverse reactions to drugs. Patients with a positive Ag HLA-B* 1502 have a high risk of SJS.Early diagnosis, supportive care and careful monitoring for complications are very important for the good management in SJS.

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