CARBAMAZEPINE INDUCED STEVENS-JOHNSON SYNDROME- A CASE REPORT

Amulya F. Yaraguppi1, Ramesh H2

1Postgraduate Student, Department of Pharmacology, Karnataka Institute of Medical Sciences, Hubballi, Karnataka. 2Associate Professor, Department of Pharmacology, Karnataka Institute of Medical Sciences, Hubballi, Karnataka.


PRESENTATION OF CASE
A 33-year-old woman with generalised dermatitis was admitted to Dermatology Department, KIMS, Hubballi. She had an eight-day history of generalised pruritus that initially started in eyes and later on spread all over the body. There was five-day history of skin rash which started on face and later on spread to chest, back, upper limbs, lower limbs, palms and soles. The patient had three-day history of fever, oral pain and dysphagia. Past medical history was only remarkable for epilepsy diagnosed a month back. The patient was receiving carbamazepine 200 mg twice daily. Family history was not significant.

Physical examination at the time of admission revealed moderately built female, febrile with a temperature of 38.2°C. On dermatological examination, multiple erythematous, maculopapular lesions were observed on the face, chest, trunk, upper and lower limbs and the palms and soles (Figure 1 and 2). She had eroded lesions on the oral and vermilion border of lips covered with haemorrhagic crusts (Figure 3). The mucous membranes of the patient were dry, but there were no genital lesions found. On ophthalmologic examination, ulcerative blepharitis was seen. The only significant laboratory test result was increased, total leucocyte count-13,000/mm3 with differential count- Neutrophils 61%, Lymphocytes 38%, Monocytes 1%, Eosinophils 2%. Other laboratory investigations were normal and included haemoglobin-11.6 g/dL, blood group and Rh type- O+ve. HBsAg negative, CT scan of brain- no significant abnormality seen.

Differential Diagnosis
The differential diagnosis include, Stevens-Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN) or drug-induced pemphigus foliaceus. SJS involves less than 10% of the area, and TEN involves more than 30% of epidermal detachment. The haemorrhagic-erosive lesions are present on at least one mucosal surface.[1]

Clinical Diagnosis
SJS and TEN are rare, but lethal manifestations of a type IV hypersensitivity reaction.[2] SJS is usually associated with anticonvulsants including carbamazepine, lamotrigine, phenobarbital, phenytoin and valproic acid.[3] Risk of developing SJS after anticonvulsants is maximum in the first 2 months of therapy. Among antiepileptics, those with aromatic structure and long half lives are commonly involved in the precipitation of SJS. In addition, there is a high degree of cross reactivity among the antiepileptics.[4] A study has shown that the risk of developing cutaneous adverse drug reaction is high in females.[5] In this female patient, mucocutaneous symptoms specific for SJS appeared one month after initiating treatment with carbamazepine. The onset of lesions within 1 month of taking carbamazepine and involving less than 10% of the body surface covered with atypical target lesions with oral involvement seen in this patient makes SJS more likely.

Pathological Discussion
Mechanism of SJS is uncertain, but has been linked to immune dysfunction. It is presumed that owing to some genetic defect, there is altered metabolism of drug and its interaction with the immune components, which provokes the catastrophic reaction. CD8+ cytotoxic T-lymphocytes are believed to initiate this type IV hypersensitivity reaction. Cytotoxic molecules-FasL and granzyme are thought to be responsible for the disseminated keratinocyte apoptosis in SJS/TEN.[6] In fact the HLAB*1502 allele has been linked with carbamazepine induced SJS in Thai population.[6] Lack of such findings in Caucasians along with the findings of recent studies showing the roles of alleles other than HLAB*1502 even in the Han Chinese have exempted the allele from becoming the universal marker.[7] Additionally, carbamazepine being a strong inducer of CYP450, is linked to induction of oxidative stress and generation of reactive oxygen species.[8] This may be an additive pathogenetic mechanism.

Mucous membrane involvement is observed in approximately 90% of cases and can precede or follow the skin eruption. In our patient, the skin and mucosal lesions appeared simultaneously and were limited to buccal mucosa and vermilion border of the lips. No genital lesions were found. Approximately, 80% of SJS patients have conjunctival lesions.[3]

Figure 1. Haemorrhagic Lesions over Face, Upper Trunk and Upper Extremities
DISCUSSION OF MANAGEMENT
The carbamazepine treatment was stopped immediately. The patient was administered Inj. decamethasone (IV 0.5 mg twice daily) and Inj. pantoprazole (IV 40 mg once daily) for 9 days and later Tab. Prednisone (40 mg once daily) tapered during 3 weeks and Tab. pantoprazole (40 mg once daily). The patient also received Inj. ceftriaxone (IV 1000 mg twice daily), Tab. cetirizine (10 mg twice daily), benzocaine gel (20% w/w) topically, chlorhexidine mouthwash solution and calamine lotion. Carbamazepine was replaced with Tab. levetiracetam (500 mg twice daily) after neurologist referral. Management was mainly supportive with attention to fluid balance, nutritional status and pain relief. Other treatment included systemic antibiotic, antimicrobial dressings. During the hospitalisation, temperature normalised and after therapy all symptoms and skin lesions resolved progressively. The skin lesions healed without scarring but with hyperpigmentation, during 3 weeks and the patient left the hospital in a good general state.

Management of SJS with corticosteroids is still controversial. Some studies found that such therapy could prevent the extension of the disease when administered during the early phase, especially as intravenous pulses for a few days. Other studies concluded that steroids did not stop the progression of the disease and were even associated with increased mortality and adverse effects, particularly sepsis.[9]

Our patient did receive corticosteroids and prophylactic systemic antibiotics.

Carbamazepine that was initially used as an antiepileptic is now also used with increased frequency for different indications including chronic pain, trigeminal neuralgia and herpetic neuralgias.[1] Some authors suggest that genetic searching for HLA-B*1502 and patch tests (1% and 10% carbamazepine in petrolatum) could detect high-risk patients of SJS or TEN development.[9]

FINAL DIAGNOSIS
Carbamazepine induced Stevens-Johnson syndrome.

REFERENCES