CARBAMAZEPINE INDUCED STEVENS-JOHNSON SYNDROME- A CASE REPORT

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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- N₄₈L₄₂M₂E₆. Other laboratory investigations were normal and included haemoglobin- 11.6 g/dL, blood group and Rh type-B positive, platelet count- 2.4/μL, serum creatinine- 1 mg/dL, random blood sugar- 85 mg/dL, electrolytes- sodium - 141 mmol/L, potassium - 4.1 mmol/L, chloride - 117 mEq/L, HIV-I/HIV-II antibodies- negative, 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 granulysin are thought to be responsible for the disseminated keratinocyte apoptosis in SJS/TEN.^[2] 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

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Figure 2. Erythematous Macules on Back

Figure 3. Oral Erosions and Haemorrhagic Crusting on Lips

DISCUSSION OF MANAGEMENT

The carbamazepine treatment was stopped immediately. The patient was administered Inj. dexamethasone (IV 0.5 mg twice daily) and Inj. pantoprazole (IV 40 mg once daily) for first 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.^[3] 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

- [1] Kumar A, Kansal D, Chaudhary UK, et al. Carbamazepine-induced Stevens Johnson syndrome: a case series of three case reports. *IJBCP* 2015;4(4):797-801.
- [2] Harr T, French LE. Toxic epidermal necrolysis and Stevens-Johnson syndrome. *Orphanet journal of rare diseases* 2010;5:39.
- [3] Allanore LV, Roujeau JC. Epidermal necrolysis (Stevens johnson syndrome and toxic epidermal necrolysis). In: Goldsmith LA, Katz SI, Gilchrist BA, et al. (eds). *Fitzpatrick's dermatology in general medicine*. 8th edn. United States of America. The McGraw-Hill Companies, Inc 2012:439-48.
- [4] Patel PP, Gandhi AM, Desai CK, et al. An analysis of drug induced Stevens-Johnson syndrome. *The Indian journal of medical research* 2012;136(6):1051-3.
- [5] Patel TK, Thakkar SH, Sharma DC. Cutaneous adverse drug reactions in Indian population: a systematic review. *Indian dermatology online journal* 2014;5(6):76-86.
- [6] Lochareernkul C, Loplumlert J, Limotai C, et al. Carbamazepine and phenytoin induced Stevens-Johnson syndrome is associated with HLA-B* 1502 allele in Thai population. *Epilepsia* 2008;49(12):2087-91.
- [7] Hu FY, Wu XT, An DM, et al. Phenytoin-induced Stevens-Johnson syndrome with negative HLA-B* 1502 allele in mainland China: two cases. *Seizure* 2011;20(5):431-2.
- [8] Kandil AO, Dvorak T, Mignano J, et al. Multifocal Stevens-Johnson syndrome after concurrent phenytoin and cranial and thoracic radiation treatment, a case report. *Radiation Oncology* 2010;5:49.
- [9] Czajkowski R, Weiss-Rostkowska V, Wankiewicz A, et al. Stevens-Johnson syndrome induced by carbamazepine. *Acta poloniae pharmaceutica* 2007;64(1):89-92.