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STEVEN JOHNSON SYNDROME INDUCED BY CARBAMAZEPINE IN PEDIATRIC AGE GROUP; A RARE CASE REPORT

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ABSTRACT

Introduction: Stevens–Johnson syndrome (SJS) is a type of rare severe skin disease. Drugscommonly associated with the development of SJS/TEN include cotrimoxazole, NSAIDS,anticonvulsants like carbamazepine and infections such as Mycoplasma pneumoniae and cytomegalovirus. These have high morbidity and mortality and counts among dermatological emergencies. **Case presentation:** We report an eventful case of a 11-year-old boy who suffered from carbamazepine-induced SJS/TEN. Our patient had a follow up case of intracranial space occupying lesion in right side of brain with seizures disorder. He was taking tab carbamazepin from one month before appearing of rashes. History of prodromal symptoms and exposure to carbamazepine helped in the diagnosis. Carbamazepine abstinence anda multidisciplinary approach in symptomatic management worked very well for the patient. **Clinical discussion:** Carbamazepine-induced TES/SJS, itself is life-threatening conditions, Which manifests multisystem effects and requires a multidisciplinary approach for management. Early intervention is the key. 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. Themainstay of treatment is early recognition of the rash and immediate stopping of the drug along with the symptomatic treatment. **Conclusion:** Flu-like symptoms post carbamazepine exposure should not be overlooked as they can be prodromal symptoms of SJS/TEN. A multi- disciplinary approach and early intervention prevent secondary infections and complications. Proper counseling to patients goes a long way in preventing the development of this life-threatening condition.

INTRODUCTION

Stevens–Johnson syndrome (SJS) is a type of severe skin reaction.[1] Together with toxic epidermal necrolysis (TEN) and Stevens–Johnson/toxic epidermal necrolysis (SJS/TEN), it forms a spectrum of disease.[1,2] SJS and TEN are rare severe cutaneous reactions with annual incidences of 1.2–6 and 0.4–1.2 per million people, respectively.[3,4] Epidermal necrolysis spectrum eruptions such as Stevens–Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN) are considered a continuum and share the same pathogenesis. They are only differentiated on the body surface area by epidermal detachment.[5] Epidermal detachment of < 10%, 10–30% and > 30% are designated as SJS, SJS/TEN and TEN, respectively.[5,6] The mortality rate ranges from 1 to 5% for SJS, and 25 to 35% for TEN.[5]

SJS usually begins with fever, sore throat, and fatigue, which is commonly misdiagnosed and therefore treated with antibiotics. SJS, SJS/TEN, and TEN are often heralded by fever, sore throat, cough, and burning eyes for 1 to 3 days.[7] Patients with these disorders frequently experience burning pain of their skin at the start of disease.[7] Ulcers and other lesions begin to appear in the mucous membranes, almost always in the mouth and lips, but also in the genital and anal regions. Those in the mouth are usually extremely painful and reduce the patient's ability to eat or drink. Conjunctivitis occurs in about 30% of children who develop SJS.[8] A rash of round lesions about an inch across arises on the face, trunk, arms and legs, and soles of the feet, but usually not the scalp.[9]

SJS/TEN reactions are believed to follow a type IV hypersensitivity mechanism.[10] It is also included with drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), acute generalized exanthematous pustulosis (AGEP) and toxic epidermal necrolysis in a group of conditions known severe cutaneous adverse reactions (SCARs).[11] Drugs

commonly associated with the development of SJS/TEN include cotrimoxazole, nevirapine, allopurinol, sulfasalazine, phenytoin, phenobarbital, lamotrigine, and carbamazepine[3] Other causes can include infections such as Mycoplasma pneumoniae and cytomegalovirus, or the cause may remain unknown.[2,1] Risk factors include HIV/AIDS and systemic lupus erythematosus.[1]

SJS/TEN reactions are believed to follow a type IV hypersensitivity mechanism.[10] It is also included with drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), acute generalized exanthematous pustulosis (AGEP) and toxic epidermal necrolysis in a group of conditions known severe cutaneous adverse reactions (SCARs). the pathogenesis of these diseases has not yet been established.[11] dysregulation of the immunologic reaction is thought to be one of the most important causes. the death of keratinocytes due to apoptosis is currently thought to be the major mechanism,[12] carbamazepine, which is widely used to treat seizure disorder, bipolar disorder, trigeminal neuralgia, and chronic pain, is one of most common causes of drug hypersensitivity reactions[13] the reported frequency of serious carbamazepine hypersensitivity reaction is between 1/1,000 and 1/10,000 new exposures to the drug.[14]

CASE PRESENTATION

Patient admitted on 07 december 2021 at 4pm in ESIC emergency Jajmau hospital Kanpur, with complaint of purpuric rashes, blisters, vesicles and ulcers all over the body including conjunctiva, cornea, oral mucosa and genitalia for 10 days. Child was not given any treatmentat home in last 10 days due to misconception of chicken pox. Patient having high grade fever for 5 days before onset of rashes for which he was taken treatment from private hospital andESIC Jajmau Kanpur, in the form of injection paracetamol, ceftriaxone and tab paracetamol.

Child is follow up case of intracranial space occupying lesion in right side of brain with seizures disorder. He was taking tab carbamazepin, tab frisium from one month before appearing of rashes.

There is history of slight facial puffiness with each episodes of fever in past and every time he taken paracetamol for fever.

On examination
Patient was febrile (101°F). Pallor +, Edema +, and eyes were congested, conjunctivitis, lips were edematous.

Laboratory tests shows
- Hemoglobin (Hb) - 12.5 g%
- Total leukocytes count (TLC) – 9500 cells/cumm
- Differential leukocyte count (DLC) showed eosinophilia with $N_{48}/L_{44}/M_{06}/E_{02}/B_0$
- Platelet count adequate - 150000/cumm
- CRP- 5.5 mg/dl
- S. Na^+ - 137 mEq/l
- S. K^+ - 4.75 mEq/l
- S. Cl^- - 92.1 mEq/l

Renal function test shows
- Urea – 15.8 mg/dl
- Creatinine – 0.53 mg/dl

Uric acid – 2.1 mg/dlLiver function test shows
- Bilirubin total- 0.14 mg/dl, direct- 0.10 mg/dl
- Alkaline phosphate - 220 IU
- SGOT/PT - 68 IU/122 IU
- Total protein/albumin- 5.46/2.41 g/dl.

Urine for routine and microscopic examination showed:- WBC & Epithelial cells- 0-1/hpf.

Local Examination
Mucocutaneous examination showed generalized involvement of body including face, eye, conjunctiva, trunk, upper limb, lower limb including palm, soles and scalp in form of multiple well to ill-defined discrete to confluencent erythematous purpuric macules to papular lesionsof size varying from 0.5 to 1.0 cm to 1.0 cm × 2.0 cm with diffuse blanch able erythema. Diffuse involvement of face in the form of exfoliation is shown in **Figures 1-4.**

A typical target lesion an pustular lesions present at few places. Pitting edema presents over hand and legs. Nikolsky's sign is positive. The diagnosis of STS was made, and carbamazepine stopped and patient given intravenous (IV) f luids, injection dexamethasone 12 mg in the morning and 4 mg in the evening intramuscularly, can free (clotrimazole 1% + beclomethasone 0.01% + benzocaine 1% + glycerine) mouth paint for local application, mucaine gel 2TSF thrice daily orally, tablet paracetamol 500mg SOS, injection pantoprazole 40 mg IV before meals twice daily and antibiotics. Later on patient shifted on oral T. Prednisolone, which was one tapered slowly and stopped. The patient improved and discharged after 10 days.

Figure 1 & 2: Carbamazepine induced lesions on face, eye and conjunctiva of the 11-year-old male being treated for seizures disorder.

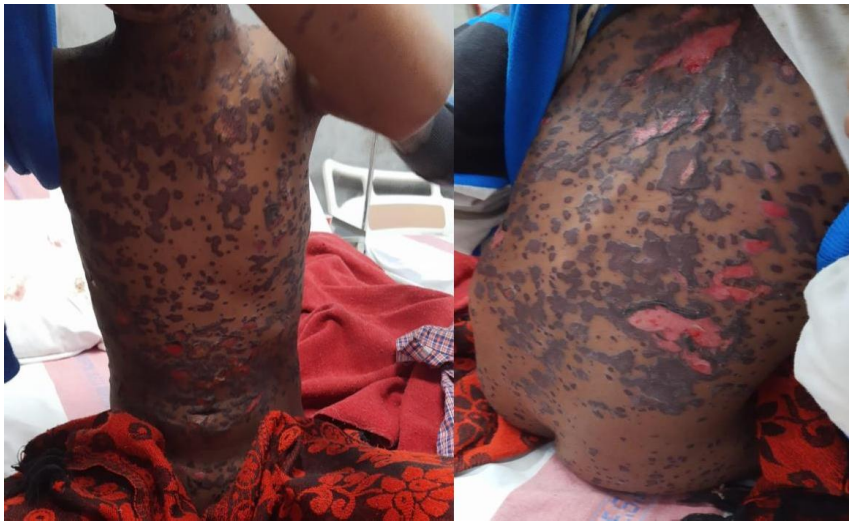

Figure 3 & 4: Carbamazepine induced lesions on chest, abdomen and back of the 11-yearold male being treated for seizures disorder.

DISCUSSION

Carbamazepine is a well-known causative agent of drug induced SJS among psychotropics.[6] There is no simple relationship between dose of carbamazepine and concentration of drug in plasma. Therapeutic concentrations are reported to be 6-12 µg/ml although considerable variations occur. Although the median latency period (interquartile range) for the development of SJS with carbamazepine is 15 days (12–20).[15] latency periods of 4 weeks have also been reported[16] Using the Algorithm of Drug causality for Epidermal Necrolysis (ALDEN) scoring system for SJS/ TEN, carbamazepine scored +6.[17]

Carbamazepine has been strongly associated with SJS. Although SJS has multiple etiologies, it is commonly triggered by viral infections (herpes simplex virus is the infectious agent more commonly involved) and neoplasias (carcinomas and lymphomas). However, the most common cause is the use of medications. Among the drugs, implicated more often are allopurinol, antibiotics, anticonvulsants and non-steroid anti-inflammatories.[18]

Carbamazepine-induced SJS has long been thought of as an idiosyncratic, dose independent, unpredictable adverse event specific to an individual.[19] **Devi et al.** conducted a 7 years study and found out that anticonvulsants were the cause implicated most in SJS especially in the first 8 weeks of treatment, and the main drug responsible (more than 80%) was carbamazepine,[20] 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.[21] The mechanism of the hypersensitivity reaction is not clear but according to **Wu et al**. There is lymphocyte and T-cell clone proliferation with the exposure to carbamazepine. The T-cell proliferation time varies from 5 min to 4 hours.[22]

The presentation is usually history of fever, along with the appearance of maculopapularrash, usually on upper body and limbs which then rapidly progresses to involve the entire body. **Yip et al.** have reported that 50 % of patients experience late ocular complications, in descending order of frequency, dry eyes, trichiasis, symblepharon, distichiasis, visual loss, entropion, ankyloblepharon, lagophthalmos, and corneal ulceration. The diagnosis is usually clinical, but skin biopsy is helpful in confirmation of diagnosis.[23]

The mainstay of treatment is early recognition of the rash and immediate stopping of the drug along with the symptomatic treatment.

CONCLUSION

Flu-like symptoms post carbamazepine exposure should not be overlooked as they can be prodromal symptoms of SJS/TEN. A multi- disciplinary approach and early intervention prevent secondary infections and complications. Carbamazepine is increasingly used for different indications, hence the careful titration of the drug and early recognition of the side effects will help in avoiding the life-threatening conditions such as SJS and other side effects associated with the drug.

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