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Phenytoin Induced Toxic Epidermal Necrolysis Syndrome

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Abstract **Case Report**

Steven johnson syndrome (SJS) and Toxic epidermal necrolysis (TENS) are rare but potentially fatal cutaneous hypersensitivity reactions most often triggered idiosyncratically in response to drugs or viral infections. We report a case of TENS syndrome secondary to phenytoin treated with cyclosporine. Various medications have been used previously for its treatment including intravenous immunoglobulin, steroids, cyclosporine, cyclophosphamide, TNF antagonists, pentoxiphylline but overall cyclosporine has shown superior efficacy.

Keywords: Steven johnson syndrome, toxic epidermal necrolysis syndrome, phenytoin, cyclosporine.

INTRODUCTION

Stevens Johnson syndrome (SJS) and toxic epidermal necrolysis (TENS) are rare manifestations of cutaneous hypersensitivity reaction which develop in response to drugs or some viral infections like herpes [1]. The syndrome is preceded by a prodromal phase of flu like non-specific symptoms which evolve over 1-3 weeks to cutaneous manifestations in the form of macular eruptions over the trunk, face and upper limb [2]. Involvement of mucous membrane is seen in 90% of cases. Diagnosis is made on clinical suspicion and confirmed by biopsy. Prognosis depends upon the age of patient, associated comorbidities and percentage of area involved. SJS and TEN are two variants of the same condition differing only in the percentage of skin detachment. Usually in SJS body surface area (BSA) involvement is <10%, in SJS-TEN overlap BSA involvement is between 10-30% and >30% BSA detachment is seen in TEN [3]. Commonly implicated drugs are anti-epileptics, antibiotics like sulphonamides, isoniazid, NSAIDS. Sepsis is the most common complication of SJS/TENS and a major cause of mortality in these patients.

CASE REPORT

A 54 year old gentleman presented to the emergency department with history of fever with maculopapular rash all over the body, lip erosions and crusting since 2 days. He was recently diagnosed 2 weeks back as having superior saggital venous sinus thrombosis with right cortical venous bleed and had been started on tablet dabigatran for anticoagulation and tablet phenytoin for seizure prevention. He was a known case of hypertension and was on tablet telmisartan 80 mg OD. No history of any other comorbidity. On admission he was febrile -Temp 101 F, Pulse- 110/ min, Blood pressure 120/70 mm hg, respiratory rate – 18/min, oxygen saturation 98 % at room air. Systemic examination was unremarkable. Generalized erythematous maculopapular lesions were present all over the body, associated with erosions and crusting over lips and scrotum. Oral ulcerations over buccal mucosa and conjunctival congestion with exudative discharge were present. Chest xray, ultrasonography of abdomen and pelvis and 2d echocardiogram were normal. Liver enzymes were deranged, rest of routine blood tests, coagulation profile, serological markers for HIV, HBsag, HCV were normal. SCORTEN Score [4] was 2. Fluorescein dye stain test was done for both eyes. Ophthalmology and dermatology opinion was taken. Naranjo ADR probability score was 8. Patient was diagnosed as having phenytoin induced toxic epidermal necrolysis with drug induced liver injury, admitted in intensive care unit and started on intravenous steroids, antibiotics, antihistaminic and oral cyclosporine. Phenytoin and was stopped and patient was started on injectable levetiracetam. Central line was inserted and hydration maintained as per CVP. Cyclosporine was started at 5 mg/kg/day with gradual tapering over 3 weeks. Skin biopsy was suggestive of fibro collagenous tissue with

mixed inflammatory cell infiltrate comprising predominantly of lymphocytes, few macrophages, eosinophils and fibroblasts. Amniotic membrane grafting was done for both eyes. The Patient improved over 3 weeks with complete healing of skin lesions and was discharged on tab levetiracetam and tab dabigatran and remained asymptomatic at follow-up.

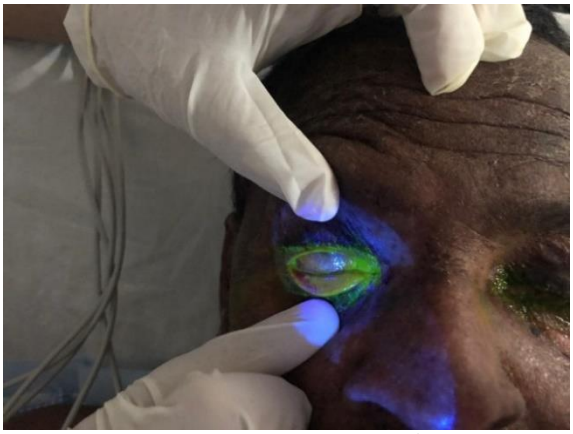

Fig-1 : Fluorescein dye staining of eyes

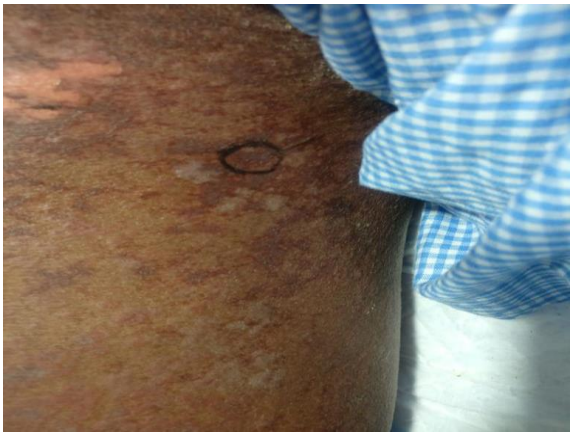

Fig-2 : Maculopapular rash over trunk

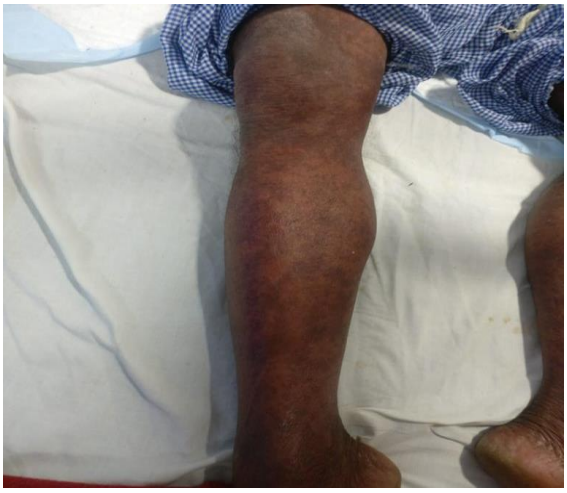

Fig-3: Rash over Lower limbs

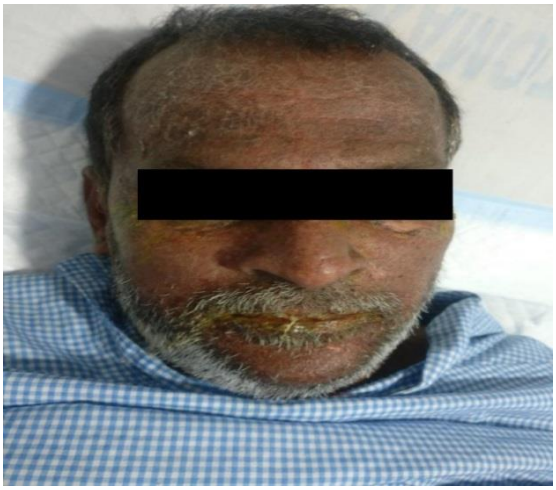

Fig-4: Lip erosions with crusting

	Day 1	**Day 3**	**Day 10**
Hb	14.2	11.7	11.2
TLC	5190 (P-66, L-32, M-2, E-0)	4550	5970
Platelet	1.57	1.62	3.04
Bili(T)	1.01	1.09	0.97
Bili(D)	0.25	0.45	0.28
SGOT	501	62	25
SGPT	409	167	52
AlkPo4	103	247	203
Total Protein	6.0	5.72	5.22
Albumin	3.2	2.66	2.23
BUN	22.4	15	19.2
Creatinine	1.29	0.71	0.70
Na/K	124/4.7	132/4.5	136/3.5
PT/INR	13.1/1.12	12.2/1.04	12.8/1.09
Blood/Urine/Skin lesion swab Culture/Sensitivity	Sterile		

DISCUSSION

SJS and TEN are a type IV hypersensitivity reaction with an approximate incidence of 1-2/million/year [5]. SJS is associated with a mortality rate of 1-5% which increases to 25-35% in case of TEN. Risk of developing SJS after starting anticonvulsants is maximum in the first 8 weeks of therapy and it occurs idiosyncratically. Among antiepileptics, those with aromatic structure and longer half-lives are more commonly involved in the development of SJS. Important differentials include drug induced pemphigous, viral exanthems, phototoxic eruption, paraneoplastic pemphigus, linear IgA bullous dermatosis. SJS/TEN develops due to immune dysfunction due to some genetic defect triggered by altered drug metabolism and its interaction with the immune components. CD8+ cytotoxic T Lymphocytes are primarily involved in this type IV hypersensitivity reaction. Cytotoxic molecules-FasL and granulysin are thought to be responsible for the disseminated keratinocyte apoptosis in SJS/TEN. Dabigatran also has been associated with drug induced exanthema [6], DRESS (drug rash, eosinophilia, systemic symtoms) syndrome and leukocytoclastic vasculitis [7]. Although there are no previous documented cases in literature of dabigatran causing SJS/TENS, the theoretic possibility remains.

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