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CASE REPORT ON LOSARTAN INDUCED STEVENS JOHNSON SYNDROME

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ABSTRACT

Steven-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN) is one of the dermatologic conditions that can be potentially fatal. Steven-Johnson syndrome is an infrequent and a severe form of erythema multiform (EM). It is considered to be a less severe form of toxic epidermal necrolysis (TEN). SJS is most commonly triggered by medications, characterized by extensive necrosis and detachment of the epidermis. SJS can be differentiated from other skin conditions on three clinical criteria, (i) the pattern of individual skin lesions, (ii) distribution of lesions, and (iii) extent of epidermal detachment. Losartan belongs to a group of drugs called angiotensin II receptor antagonists. It keeps blood vessels from narrowing, which lowers blood pressure and improves blood flow. Losartan is used to treat high blood pressure (hypertension). It is also used to lower the risk of stroke in certain people with heart disease. SJS by use of Antihypertensive Drug (Losartan) is rare.

KEYWORDS: Stevens-Johnson Syndrome, Losartan, Cutaneous Reaction.

INTRODUCTION

Cutaneous eruption is one of the most common forms of adverse drug reaction manifestations. Stevens– Johnson syndrome (SJS) is one such manifestation which is an acute inflammatory and reactive disorder with skin and severe mucous membrane changes. Often patients have associated constitutional symptoms, including fever. This syndrome can be precipitated either by infection or medication. SJS may present as a nonspecific febrile

illness leading to malaise, headache, cough, rhinorrhea with polymorphic lesions of the skin and mucous membrane characterized by acute blisters and erosions.

Losartan Hydrochloride is among the most extensively used Angiotensin II Receptor Blockers (ARBs) antihypertensive agent. It is being considered relatively safe, adverse reactions including cutaneous hypersensitivity reactions have not been reported much.

Very few cases of EM or SJS have been reported with the ingestion of Losartan. We can only find one case report of Losartan-induced Stevens-Johnson syndrome.[1] Hence, we present a rare case of SJS occurred due to the ingestion of Losartan.

CASE REPORT

A 48 year old female, known case of Hypertension - On T. Losartan + Hydrochlorothiazide 1-0-0, came to the emergency department with complaints of raised erythematous skin lesions over face trunk and limbs since 4 days. It was insidious in onset and gradually progressive in nature. She also c/o difficulty in swallowing. Patient attributes it to anti-hypertensive medication (Losartan + Hydrochlorothiazide) that were prescribed for her from a local hospital 1 week back. Initially the lesions appeared over lips that later spread to face, neck, trunk and extremities. At the time of admission all her vitals were found to be normal; Blood Pressure: 110/80mmHg, Pulse Rate: 80/min, Temperature: 97.6 F and her FBS was found to be high (171 mg/dL). All her blood investigations were normal except elevated ESR (52 mm/hr) and transaminases [AST (SGOT): Serum 79 U/L (10 - 40), ALT (SGPT): Serum 134 U/L (10 - 40)]. She was treated with oral anti histamines, topical antibiotics, emollients and other supportive medications. At the time of discharge, she was symptomatically better, hemodynamically stable and mild erythema was present over face and skin lesions were resolving.

DISCUSSION

Cutaneous adverse drug reactions (CADRs) are very commonly encountered problem in the Dermatology department. Steven-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN) is one of the dermatologic conditions that can be potentially fatal. Steven-Johnson syndrome is an infrequent and a severe form of erythema multiform (EM). It is considered to be a less severe form of toxic epidermal necrolysis (TEN).[2]

"A new eruptive fever with stomatitis and ophthalmia" was described as a severe variant of EM and was termed by Steven and Johnson in 1922.[3]

Stevens-Johnson syndrome (SJS) is a rare, severe mucocutaneous reactions, most commonly triggered by medications, characterized by extensive necrosis and detachment of the epidermis. Often, it begins with flu-like symptoms, followed by a painful red or purplish rash that spreads and blisters. Then the top layer of the affected skin dies, sheds and then heals.

SJS can be differentiated from other skin conditions on three clinical criteria, (i) the pattern of individual skin lesions, (ii) distribution of lesions, and (iii) extent of epidermal detachment.

Losartan belongs to a group of drugs called angiotensin II receptor antagonists. It keeps blood vessels from narrowing, which lowers blood pressure and improves blood flow.

Losartan is used to treat high blood pressure (hypertension). It is also used to lower the risk of stroke in certain people with heart disease.

Losartan is used to slow long-term kidney damage in people with type 2 diabetes who also have high blood pressure.

The incidence of SJS has been estimated to be around 1–6/1,000,000 persons per year with a mortality rate of 1–5% which rises up to 30% in TEN. Multiple drugs have been identified to cause SJS and TEN, antibiotics (sulfonamides) being the most common.[4]

The most important clinical signs and symptoms of SJS are the following:

- prodromal signs: 2-3 days of malaise, rash, fever, cough, arthralgia, myalgia, rhinitis, headache, anorexia, and nausea and vomiting, with or without diarrhea
- conjunctivitis, usually occurring 1-3 days before the skin lesions appear
- intense erythema, progressing rapidly to epidermolysis and ceasing in 2-3 days
- blisters
- mucous membrane erosion
- hemorrhagic crusting of the lips
- epidermal detachment
- positive Nikolsky sign
- target-like lesions
- extreme pain

- dehydration, which may lead to hypovolemic shock and death
- mimicking of the staphylococcal scalded skin syndrome (similar appearance, but blisters rise nearer the skin's surface)

Stevens-Johnson etiology is mainly a reaction to medication. More than 80% of cases of SJS are drug related. Several drugs have been identified during the last decade as a triggering cause:

- NSAIDs, especially ibuprofen (2003)
- anticonvulsants (phenytoin, valproic acid, phenobarbital, carbamazepine)
- antibiotics (sulphonamides, aminopenicillins, quinolones, cephalosporins, tetracyclines, imidazole antifungal agents (1995)
- allopurinol
- corticosteroids.[5]

The first step in the management was an immediate withdrawal of the offending agent followed by supportive care. Garcia-Doval *et al*., report that earlier the drug is withdrawn, better the prognosis while exposure to drugs with longer half-lives increases the risk of death. Supportive care must include the management of fluid and electrolyte requirements.[6]

Routine antibiotics are not indicated unless there is the evidence of infection as fever may be part of the disease process. Debridement of necrotic skin should not be performed before disease activity ceases. However, in our case, there were lesions on axilla, abdomen, thighs and trunk region in the healing phase, so debridement was not a necessary step. Topical antiseptics (0.5% silver nitrate or 0.05% chlorhexidine) are used to paint, bathe, or dress the patients. Dressings may be gauzes with petrolatum, silver nitrate, povidone-iodine, and hydrogels. Some authors use biologic skin covers after epidermal stripping cadaveric allografts, cultured human allogeneic or autologous epidermal sheets. In our case, gentian violet application for lips and skin lesions were advocated.

Dramatic improvement in both SJS-TEN has been reported with the use of intravenous immunoglobulin, 0.2–0.75 g/kg body weight. Alternative systemic treatment methods for the acute phase of SJS-TEN include hemodialysis, plasmapheresis, cyclophosphamide, and cyclosporine.[7]

Use of corticosteroid in the management of SJS is controversial. According to some, their use can lead to delayed wound healing, increased chances of infection, masking of early signs of sepsis, gastrointestinal bleeding, and increased mortality. If steroids are to be used, it should be initiated during initial stage and rapidly tapered off.[8,9] Antibiotics with intravenous corticosteroid shown a remarkable improvement in a similar case.[10] Hence, we prescribed tablet predinsolone 30 mg three times daily daily for 7 days. Further tapered to 20 mg twice daily for next 7 days. Gradually, 10 mg and 5 mg for consecutive 7 days. His condition improved no sequelae were found during 35–40 days of follow-up.

CONCLUSION

SJS by use of Antihypertensive Drug (Losartan) is rare. A careful history of use of offending drugs with clinical examination for skin and mucous membrane involvement should raise high suspicion for the disease. Although the recovery in our case was satisfactory, a long-term follow-up is warranted to look into complications and appropriate management.

CONFLICTS OF INTEREST

The authors have obtained the necessary patient consent forms where the patients have given their approval for participation in the investigation, followed by representation in the concerned article. The patients do understand that the authors will ensure that their identities won't be revealed.

REFERENCES

1. Bonnici H, Bygum A. Losartan-induced Stevens-Johnson syndrome in a geriatric patient.
2. Ugeskr Laeger, 2007 Mar 26; 169(13): 1233-4.
3. Khawaja A, Shahab A, Hussain SA. Acetaminophen induced Steven Johnson syndrome-toxic epidermal necrolysis overlap. J Pak Med Assoc., 2012; 62: 524–7. [PubMed] [Google Scholar]
4. Ramineni HB, Eluri P, Vipparla K, Suryadevara V. Phenobarbital induced Stevens-Johnson syndrome: A case report. Int J Res Med Sci., 2015; 3: 492–3. [Google Scholar]
5. French LE. Toxic epidermal necrolysis and Stevens Johnson syndrome: Our current understanding. Allergol Int., 2006; 55: 9–16. [PubMed] [Google Scholar]
6. Castana. *et.al*;, Stevens-Johnson Syndrome: a Case Report. D. Alexakis Ann Burns Fire Disasters, 2009 Sep 30; 22(3): 147–151.
7. Garcia-Doval I, LeCleach L, Bocquet H, Otero XL, Roujeau JC. Toxic epidermal necrolysis and Stevens-Johnson syndrome: Does early withdrawal of causative drugs

decrease the risk of death? Arch Dermatol, 2000; 136: 323–7. [PubMed] [Google Scholar]

8. Roujeau JC, Kelly JP, Naldi L, Rzany B, Stern RS, Anderson T, et al. Medication use and the risk of Stevens-Johnson syndrome or toxic epidermal necrolysis. N Engl J Med., 1995; 333: 1600–7. [PubMed] [Google Scholar]
9. Budania RJ, Dakhale GN, Sontakke SD, Patnaik PS. Fatal Stevens-Johnson syndrome induced by phenytoin: A case report. Int J Basic Clin Pharmacol, 2013; 2: 843–5. [Google Scholar]
10. Patterson R, Grammer LC, Greenberger PA, Lawrence ID, Zeiss CR, Detjen PF, et al. Stevens-Johnson syndrome (SJS): Effectiveness of corticosteroids in management and recurrent SJS. Allergy Proc., 1992; 13: 89–95. [PubMed] [Google Scholar]
11. Biswal S, Sahoo SS. Paracetamol induced Stevens-Johnson syndrome – Toxic epidermal necrolysis overlap syndrome. Int J Dermatol, 2014; 53: 1042–4. [PubMed] [Google Scholar]