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Case Study

Losartan-H Induced Steven Johnson's Syndrome – A Case Report

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ABSTRACT

Steven Johnson's Syndrome (SJS) is a life-threatening mucocutaneous reaction characterized by skin detachment and blistering. SJS is most commonly triggered by medications, characterized by extensive necrosis and detachment of the epidermis. This case report delves into a rare adverse drug reaction involving Losartan, an angiotensin II receptor antagonist, and hydrochlorothiazide which is a diuretic commonly used for hypertension. A 72-year-old female developed Steven Johnson Syndrome (SJS) after administration of a Losartan-Hydrochlorothiazide combination., the patient's past medication history showed that she was on Tab. Amlodipine 5mg for a long period and developed pedal edema for this reason they visited the nearby clinic. Later, Tab. Amlodipine 5 mg was changed to Tab. Repace H (Losartan 50 mg + Hydrochlorothiazide 12.5 mg). During the initiation of Tab. Repace H, due to an increase in itching, redness, blistering, and breathing difficulty, was then hospitalized at a tertiary care hospital, where Tab. Losartan H was withdrawn, and treated symptomatically. Management involved a multidrug approach, including intravenous corticosteroids, antibiotics, and topical antimicrobials. The incidence of Losartan-induced SJS is rare, with an estimated annual occurrence of 1-6 per million persons.
This case underscores the importance of vigilance in prescribing antihypertensive medications, especially in older individuals, as SJS can be potentially life-threatening. The study challenges previous assertions about drugs with low SJS risk, highlighting the need for ongoing research and clinician awareness.

INTRODUCTION

Adverse drug reaction (ADR) is a major contributor to morbidity and mortality. According to estimates, ADRs account for 2.9%–5.6% of all hospital admissions, and 35% of hospitalized patients encounter an ADR during their stay.

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Steven Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are severe and life-threatening mucocutaneous reactions characterized by blisters and skin detachment. Usually affecting the skin and mucous membranes, Steven Johnson Syndrome (SJS) is an uncommon but severe type of immune complex-mediated hypersensitivity reaction to medications. Even though the precise cause of SJS is unknown; Antibacterials (Sulfonamides), Anticonvulsants (Phenytoin, Phenobarbital, and Carbamazepine), Analgesics, Oxide inhibitors (Allopurinol), and Nonsteroidal anti-inflammatory drugs (Oxicam derivatives) are linked to 95% of cases of occurance. Non-drug causes include viral infections, bacterial and fungal infections, acute graft-versus-host reactions, hepatitis, and acquired immunodeficiency syndrome(1). Losartan is an angiotensin-II receptor antagonist with an antihypertensive activity. Losartan is the first orally available angiotensin-receptor antagonist without agonist properties. The recommended dose is 12.5 to 25 mg initially; the target dose is 100 mg once daily. It is applied majorly in the treatment of heart failure and hypertension. It is also used to address renal issues in patients with type 2 diabetes. It also lowers the risk of stroke in patients with high blood pressure and cardiac hypertrophy(2). Hydrochlorothiazide is a diuretic used to alleviate swelling brought on by fluid accumulation and hypertension. Additional applications include the management of renal tubular acidosis and diabetic insipidus, as well as the reduction of kidney stone risk in individuals with elevated urine calcium levels. When taken orally, hydrochlorothiazide can be used in combination with other blood pressure drugs as a single pill for maximum efficacy. A thiazide drug called hydrochlorothiazide causes natriuresis by preventing sodium and chloride ions from being reabsorbed from the kidney's distal convoluted tubules. This first causes a decrease in blood volume and an increase in urine volume. It is thought to lower the resistance of peripheral vessels(3). Losartan-induced Steven Johnson Syndrome is normally very rare. It is estimated that the annual incidence of SJS is 1–6,000,000 persons, with a death rate of 1-4%, increasing to 30% in TEN(4).

CASE STUDY

A 72-year-old female, with a known case of hypertension was taking Tab. Losartan 50 mg + Hydrochlorothiazide 12.5 mg OD, and admitted to the Department of General Medicine. She had complaints of fever, dysuria, and erythema. The major symptoms observed include; severe peeling skin of the mouth, genital area, palm, and sole. She also had itchy rashes all over the; body, cheeks, inside the mouth, and buccal mucosa for 3 days. It was insidious in onset and gradually progressive in nature. The patient was conscious, oriented, and febrile, Blood Pressure was found to be 110/60mmHg, Pulse rate was 99 beats/min, and SPO2 was 95% on room air. Her Urine culture revealed the presence of Klebsiella pneumoniae. The blood culture of the patient showed no specific growth. The patient's medication history revealed the patient was on the medication Amlodipine 5 mg BD for hypertension. Since the Patient developed uncontrollable blood pressure and pedal oedema, she consulted a nearby local hospital and the doctor changed the drug from Amlodipine 5mg to losartan H. A day after taking losartan H, the patient developed fever, itching, and redness in the palm and sole and was admitted to a tertiary care hospital. Where she experienced breathing difficulty and dysuria on admission. The patient confirmed that she was still on Tab. losartan H. The Dermatologist later confirmed it as a case of Steven Johnson Syndrome (SJS), prompting it as a cause for the withdrawal of losartan H. The

physician advised to administer Enalapril 5 mg if blood pressure exceeds 140/90 mmHg. The patient's condition improved by treatment involving Inj. Methylprednisolone 40 mg, Inj. Deriphyllin, Tab. Montek LC (Montelukast + Levocetirizine), Tab Lanol ER (Paracetamol Extended Release) 650 mg, Inj.Cefglobe (Cefperazone + Sulbactam) 1.5 gm, Syrup Mucaine gel and topical medications involving T-bact ointment, Mometasone furoate and Fusidic acid cream, Liquid paraffin, Metronidazole gel, Moisturex soft cream. At the time of discharge, her skin lesions were healing, she had mild erythema over her face, and her symptoms had improve

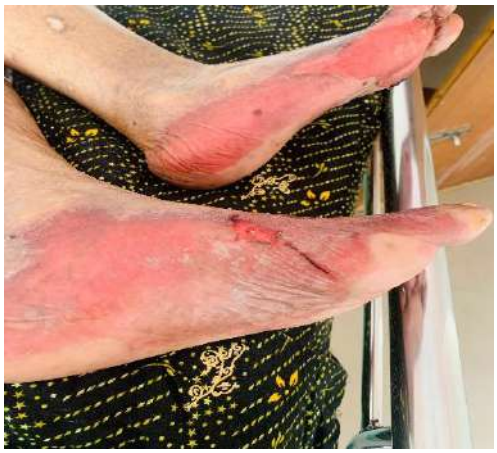

Fig 1: Skin blistering and rednessat the toes at the time of admission.

Fig 2: Skin blistering on the lips and redness on the hand at the time of admission

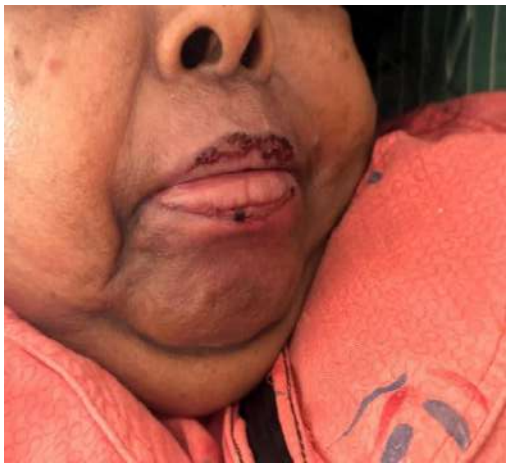

Fig 3: Skin lesions healed on the lips after treatment.

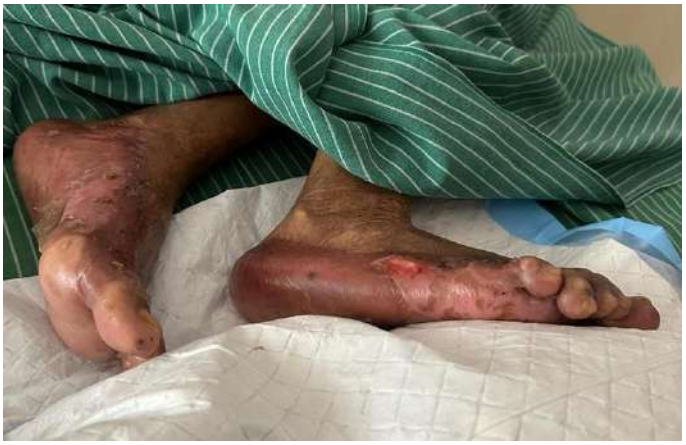

Fig 4: Skin lesions healed on the toes after treatment.

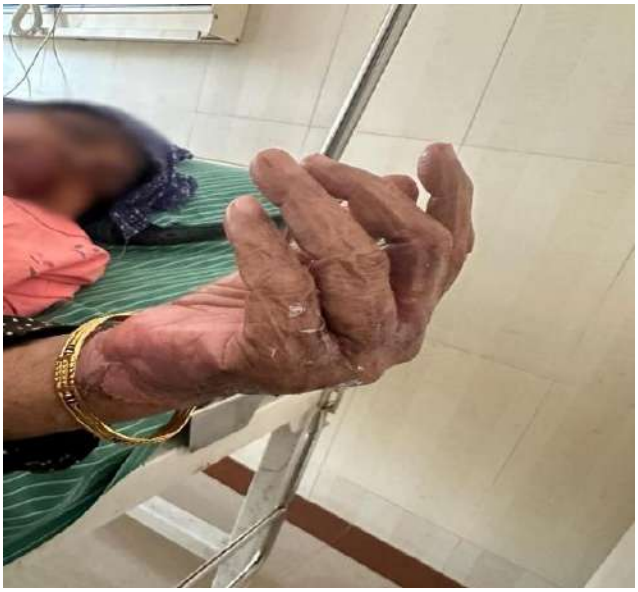

Fig 5: Skin lesions healed on the hands after treatment.

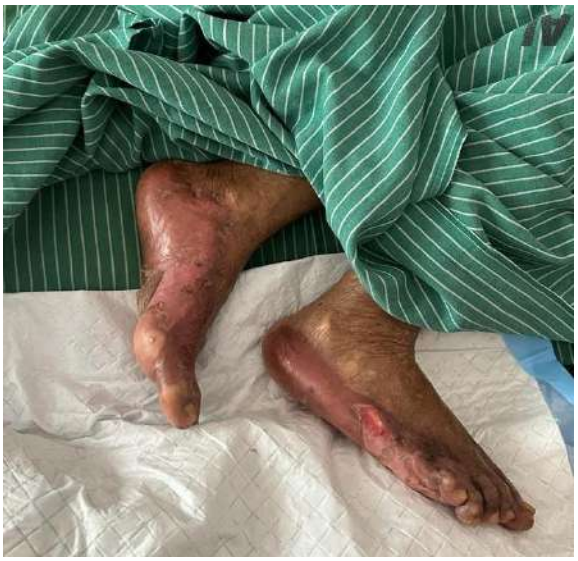

Fig 6: Occurance of peeling and appearance of new skin on the toes after treatment

DISCUSSION

In this documented case, a 72-year-old female patient was admitted with complaints of fever,

erythema, and severe peeling of skin on the mouth, genital area, palm, and sole. Itchy rashes over the body, cheeks, inside mouth, and buccal mucosa for 3 days. From the patient reconciliation, it was found that the patient was on Tab. losartan H for the past 4 days. It was later diagnosed as Tab. losartan-H induced Steven Johnsons Syndrome by the physician, as the patient developed rashes after the introduction of this medication. The FDA has approved losartan for the treatment of several illnesses, including diabetic nephropathy and hypertension. ARBs have a reputation for being Reno-protective in those with type 2 diabetes. Losartan prevents angiotensin II-induced cardiac remodeling in hypertension with left ventricular hypertrophy(5). Hydrochlorothiazide belongs to a class of medications called diuretics also known as water pills. It is used alone or in combination with other medications to treat high blood pressure. The recommended dose for treating fluid retention is 25 to 100 milligrams daily as a single or divided dose and the recommended dose for treating hypertension is 12.5 - 50 milligrams per oral once daily(6). Steven Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are blistering eruptions that are rare but severe and life-threatening. They are considered to be variants of the same disorder and are often discussed together as SJS/TEN. Onset occurs within 7 to 14 days after drug exposure. Patients are presented with generalized tender/ painful bullous formation over the body with fever, headache, and respiratory symptoms leading to rapid clinical deterioration. Lesions show rapid confluence and spread, resulting in extensive epidermal detachment and sloughing. This may result in marked fluid loss, hypotension, electrolyte imbalances, and secondary infections(7). The incidence of SJS, SJS/TEN-overlap, and TEN combined between 1991 and 1995 was estimated to be 1.53-1.89 per one million people annually based on a population-based registry in Germany. According to Maja Mockenhaupt's research, 40% of patients older than 40 also had a higher risk of developing SJS, which is consistent with the 72-year-old patient in our instance(8). A similar case report of SJS was reported by Gikku Mariyam Varghese et.al in which the management of treatment was an immediate withdrawal of the offending agent followed by supportive care. Our study also supports it. Garcia-Doval et al., reports that; earlier the drug is withdrawn, the better the prognosis, while exposure to drugs with longer half-lives increases the risk of death. The management of SJS with corticosteroids is controversial. If steroids are to be taken, they should be started in the early stages and evenly tapered. Corticosteroids with antibiotics have shown an appreciable improvement in a similar case. In this case, Inj methyl prednisone 40 mg IV BD was given for 7 days and was further tapered to 20 mg BD for 5 days. Gradually 10 mg and 5 mg for consecutive 5 days. It is necessary to monitor for infection, and if a clinical suspicion develops, anti-infective medicine should be begun empirically until culture and sensitivity results are obtained. Antibiotic Inj. Cefglobe (Cefperazone + Sulbactam) 1.5 gm, IV BD for 7 days was given here to the patient. Erythema and lesions were calmed down upon the use of topical antimicrobials such as Metrogyl DC (Metronidazole) ointment, candid ointment, liquid paraffin, Moisturex soft cream, Momate cream, T-bact ointment, DK gel for genitals. Mucositis was healed with syrup Mucain gel. Causality assessment for the ADR was done by using Naranjo adverse reaction probability scale and the score was found to be 8, this indicates that the reaction was probable. Maja Mockenhaupt's study, reports that drugs with the least risk for SJS/TEN are Beta-blockers, ACE-inhibitors, Calcium channel blockers, Thiazide diuretics (with Sulfonamide structure), Sulfonylurea anti-diabetics (with Sulfonamide structure), Insulin and

NSAIDs (propionic acid type i.e., ibuprofen) but our study contradicts with his statement.

CONCLUSION

This case report, reports the fact that severe hypersensitivity reactions can occur with Losartan - Hydrochlorothiazide combination which is a rare adverse drug reaction. SJS can be a possibly dangerous and life-threatening condition. A thorough history of drug use along with a physical examination showing signs of skin and mucous membrane involvement should raise serious suspicions about the illness. Therefore, clinicians must be more cautious while prescribing drugs which belongs to these classes.

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