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Allopurinol Induced Stevens-Johnson Syndrome: A Case Report

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Introduction

Adverse cutaneous reactions to drugs are frequent, affecting 2 to 3 percent of hospitalised patients¹. Stevens-Johnson syndrome is a rare, life-threatening drug-induced cutaneous reaction². Epidermal necrosis causes erosions of the mucous membranes, extensive detachment of the epidermis, and severe constitutional symptoms^{2,3}. Drugs are an important cause of Stevens-Johnson syndrome, but infections or a combination of drugs and infections has also been implicated⁴. Although some drugs are clearly more often responsible than others, all drugs, especially those introduced within one month of the reaction, should be considered suspect³. A limited number of drugs including sulfonamides, anticonvulsant agents, and allopurinol are consistently associated with this syndrome; whether nonsteroidal anti-inflammatory drugs (NSAIDs), analgesic agents, and nonsulfonamide antibiotics are associated with it is controversial². Allopurinol, which is most often administered for long periods, is frequently cited as a cause of Stevens-Johnson syndrome^{2,3}. The risk is not constant over time. We report a case of allopurinol induced Stevens Johnson syndrome presenting after drug usage for 3 weeks.

Case Report

A 65-year old lady with no known co-morbidities except joint pains since 4 months presented to the Emergency Room (ER) of The Aga Khan University Hospital (AKUH) complaining of a maculopapular rash, high grade fever of 38.8°C, loose motions since one week, and vomiting since the morning of presentation. A provisional diagnosis of drug-induced reaction, or viral infection was made. Her skin lesions were irregular erythematous and purpuric macules; later they became papular, followed by development of blisters and weeping lesions and eventually extensive desquamation. The distribution of the rash was widespread involving the face, eyelids, oropharynx and trunk. At least 36% of the body surface area was involved. The conjunctiva were congested and oedematous but there was no corneal erosion or symblepharon/synechia formation. Painful ulcers were present on the lips and the palate. The lesions first erupted on the mucous membranes and then extended all over the body. The cutaneous lesions emerged dramatically all together.

During her hospital stay the blisters ruptured with raw ulceration and there was extensive skin denudation. Crusting developed on the lips. However, the skin did not peel off in >3 cm sheets. lesions. No prior history of such a reaction was reported. Her past medical history was unremarkable except for joint pains for the last 3 months for which she had been on several non-steroidal anti-inflammatory drugs (NSAIDs) like Loxoprofen Na, Naproxen, Diclofenac, Ibuprofen and Azapropazone. All these were discontinued 4 weeks prior to presentation, and allopurinol 300 mg BID was started only three weeks back, as her serum uric acid level had been discovered to be high.

The hospital management was conservative, and she was taken care of in isolation. She was treated with systemic prednisolone 60 mg/ day, tapered off in 15 days. Cutaneous lesions were taken care of with topical therapy and local anaesthetic creams. Topical antibiotics like Sofra-Tulle dressings were applied on the wounds. Adequate hydration and nutrition were ensured with intravenous fluids and a high protein diet.

Discussion

Stevens-Johnson syndrome is a rare but severe blistering mucocutaneous disease with a high rate of

morbidity and mortality^{3,5-7} Mortality rates are below 5 percent for Stevens-Johnson syndrome but about 30 percent for toxic epidermal necrolysis³. The typical interval from beginning of drug therapy to onset of reaction is 1-3 weeks, but is shorter with rechallenge^{2,5,6}.

In Stevens-Johnson syndrome, the individual lesions are <3 cm in diameter, there is involvement of at least 2 mucous membranes, >10% of the body area is involved and there may be typical or atypical target lesions. Toxic epidermal necrolysis is characterized by bullae and/or erosions over 20% of body area on an erythematous base, the skin peels off in >3 cm sheets, the Nikolsky's sign is positive, there are frequent areas of confluent erythema, and the fever is higher (>38° C)⁸. Lesions of the respiratory tract and gastrointestinal tract are present in nearly all cases of toxic epidermal necrolysis, but infrequently in Stevens-Johnson syndrome (10-30%)^{3,5,7}.

The exact etiology is not confirmed. The recurrence of Stevens-Johnson syndrome within 48 hours of rechallenge, (although the initial reaction occurs about 14 days after treatment is begun), argues against a direct toxic effect and is more consistent with immunologic mechanisms^{3,6}. The immunopathologic pattern of early lesions suggests a cell-mediated cytotoxic reaction against epidermal cells^{9,10}.

However, both type III (immune— complex) and type IV (cell-mediated) hypersensitivity reactions have been implicated in the pathogenesis¹¹.

Patients often have underlying diseases. A role for infection as a cofactor has been postulated, but there is little supporting evidence. Conditions that alter immunologic function, including systemic lupus erythematosus may increase risk¹³. A genetic predisposition is thought to exist.

The complications are similar to those of extensive thermal burns. Massive transepidermal fluid losses, often with associated electrolyte imbalance may occur. Prerenal azotemia is common. A hypercatabolic state sometimes with insulin resistance, and diffuse interstitial pneumonitis leading to the adult respiratory distress syndrome are possible sequelae. Ocular complications may include persistent photophobia, burning eyes, visual impairment and even blindness.

The main principles of therapy are the same as for thermal burns, including aggressive fluid replacement, nutritional support, environmental temperature control, and antibiotics as indicated^{3,12}. Termination of nonessential drug therapy, local supportive care and ophthalmologic and dermatologic consultation should also be considered³. Pain control, fluid replacement, aseptic handling, and avoidance of any adhesive material are important³. Treatment with antihistamines, antibiotics for secondary infections, corticosteroids and mucous membrane regimen are recommended.

Therapies that reduce morbidity associated with skin loss or accelerate regrowth of the skin are most promising³.

Allopurinol, a potent inhibitor of the synthesis of uric acid, is the drug most commonly prescribed for the treatment of primary and secondary hyperuricemia. Generally the drug is well tolerated, although 2% of patients develop a mildly pruritic rash. If allopurinol is administered together with ampicillin or in renal insufficiency this incidence may increase to 20%¹⁴. Impaired renal function and concomitant intake of diuretics (especially thiazides) may be predisposing factors. Less common but more severe cutaneous intolerance reactions to allopurinol may occur, including exfoliative erythroderma, the Stevens-Johnson syndrome, and the most severe reaction, toxic epidermal necrolysis¹⁴. These are often associated with multisystemic disease such as immune complex vasculitis, eosinophilia hepatitis, and progressive renal failure (allopurinol hypersensitivity syndrome)¹⁴.

In view of the severe intolerance reactions that may result, the attitude towards prescription of allopurinol ought to be reconsidered. It is often prescribed widely and indiscriminately even for asymptomatic hyperuricemia. The benefits of treatment with allopurinol appear questionable in patients with asymptomatic hyperuricemia and do not justify the risks associated with long-term administration¹⁴. It should be prescribed with care, especially in patients with chronic renal failure who

may be prone to severe allopurinol hypersensitivity reactions¹⁵.

This case is illustrative of the considerable morbidity associated with irrational and indiscriminate drug usage. The problem is compounded by the fact that drugs that have a high incidence of side effects or significant risk of fatal idiosyncrasy are commonly sold over the counter, especially in developing countries¹⁶. Patients who develop Stevens-Johnson syndrome are in a precarious condition, and their management entails a great deal of vigilance. Fortunately, in this case appropriate surveillance led to considerable recovery, and the patient was discharged with strict instructions to avoid any possible precipitant drugs, and in particular allopurinol, the agent implicated in her recent predicament. Several case reports and studies substantiate the definite association between allopurinol usage and the development of Stevens Johnson syndrome^{15,17-20}. However, no cases of allopurinol induced Stevens-Johnson syndrome are cited in local literature. To our knowledge, our report describes the first such case in the indigenous setting. It is imperative that this possible consequence be kept in mind whilst prescribing this medicine, especially in individuals who are immunocompromised due to multisystemic disease, or impaired renal function.

References

1. Bigby M, Jick S, Jick H, et al. Drug-induced cutaneous reactions: a report from the Boston Collaborative Drug Surveillance Program on 15,438 consecutive inpatients. 1975 to 1982. *JAMA*, 1986;256:3358-63.
2. Roujeau JC, Kelly JP, Naldi U, et al. Medication use and the risk of Stevens-Johnson syndrome or Toxic Epidermal Necrolysis. *N. Eng. J. Med* 1995;333:1600-07.
3. Roujeau JC, Stem RS. Severe cutaneous adverse reactions to drugs. *N. Engl. J. Med.*, 1994;331:1272-85.
4. Yetiv J7., Bianchini JR, Owen JA Jr. Etiologic factors of the Stevens-Johnson syndrome. *South Med J.* 1980;73:599-602.
5. Chan HL, Stem RS, Ainetti KA, et al. The incidence of Erythema Multiforme, Stevens—Johnson Syndrome, and Toxic Epidermal Necrolysis: A population-based study with particular reference to reactions caused by drugs among outpatients. *Arch. Dermatol.*, 1990; 26:43-47.
6. Revuz J, Penso D, Roujeau JC, et al. Toxic epidermal necrolysis: clinical findings and prognosis factors in 87 patients. *Arch. Dermatol* 1987;123:1160-65.
7. Schopf E, Siuhmer A, Rzany B, et al. Toxic epidermal Necrolysis and Stevens-Johnson syndrome: an epidemiologic study from West Germany. *Arch. Dermatol.*, 1991;127:839-12.
8. Roujeau JC, Guillaume JC, Fabre JR. Toxic Epidermal Necrolysis (Leid Syndrome); Incidence and drug etiology in France. 1981-1985. *Arch. Dermatol.*, 1990;126:37-42.
9. Merot Y, Gravelle F, Guillen FJ, et al. Lymphocyte subsets and Langerhans cells in toxic epidermal necrolysis: report of a case. *Arch Dermatol* 1986;122:455-58.
10. Correia O, Delgado L, Ramos JP, et al. Cutaneous T-cell recruitment in toxic epidermal necrolysis: further evidence of CD8 lymphocyte involvement. *Arch. Dermatol.*, 1993;129:466-68.
11. Stampien TM, Schwartz RA. Erythema multiforme. *Amer. Fam. Phys.*, 1992;46:1171-76.
12. Lehrner KA, Kirsner RS, Tallman PG, et al. Treatment of the cutaneous involvement in Stevens-Johnson syndrome and toxic epidermal necrolysis with silver nitrate impregnated dressings. *Arch. Dermatology*, 1998; 34:877-79.
13. Patterson R, Dykewicz MS, Gonzales A, et al. Erythema multiforme and Stevens-Johnson syndrome. Descriptive and therapeutic controversy. *Chest*, 1990;98:331-36.
14. Aubock J, Fritsch P. Asymptomatic hyperuricaemia and allopurinol induced toxic epidermal necrolysis. *Br. Med. J.*, 1985;290:1969-70.
15. Pennell DJ, Nunan T, O'Doherty MJ, et al. Fatal Stevens—Johnson syndrome in a patient on captopril and allopurinol. *Lancet*, 1984;1:463.

16. Trisha G. Drug prescription and Self-Medication in India: An Exploratory Survey. Soc. Sci. and Med 1987;25:307-18.
17. Gonzalez U, Reyes F, Kershenovich J, et al. Hypersensitivity syndrome caused by allopurinol A case of massive hepatic necrosis. Rev. Invest. Chin., 995:47:409-13.
15. Huang RY, Liu-IIB, Wong CK. Stevens-Johnson syndrome:a review of 42 cases. Cluing I tiia I Hsuch Tsa Chieh Taipei, 1993;51:225-30.
19. Arellano F, Sacristan JA. Attopurinol hytsersensilivity syndrome: a review Ann. Pharmacother., 1993;27:337-43.
20. Stratigos JD, Bartsokas SK, Capetanikas J. Further experiences of toxic epidermal necrolysis incriminating allopurinol, pyrazolone and derivatives. Br. J. Dermatol., 1972:86:564-67.