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Incidence and pattern of Thrombocy to penia in cardiac surgery patients

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Allopurinol Induced Stevens-Johnson Syndrome: A Case Report

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Introduction

Adverse cutaneous reactions to drugs are freqilent, affecting 2 to 3 percent of hospitalised patients[1]. Stevens-Johnson syndrome is a rare, life-threatening drug-induced cutaneous reaction[2]. 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 implicated[4].
Although sonic drugs are clearly more often responsible than others, all drugs, especially those introduced within one month of the reaction, should be considered suspect[3]. A limited number of drugs including sulfonamides, anticonvulsant agents, and allopurinol are consistently associated with this syndrome; whether nonsteroida! anti-inflammatory drugs (NSAIDs), analgesic agents, and nonsulfonamide antibiotics are associated with it is controversial[2]. 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 allopurino induced Stevens Johnson syndrome presenting after drug usage for 3 weeks.

Case ReportReport

A 65-year old lady with no known co-morbids 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 symblepheron/synech iae 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 (NSA I Ds) like Loxoprofen Na, Naproxen, Diclofenac, lbuprofen and Azapropazone. All these were discontinued 4 weeks prior to presentation, and allopurinol 300 rng 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 necrolysis [3]. 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 cni 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 ciythematous base, the skin peels off in >3 cm sheets, the Nikolskv'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 (1 0-30%)[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 epidernial cells[9,10]. However, both type III (immune— complex) and type IV (cell-mediated) hypersensitivity reactions have been implicated in the pathogenesis[11].

Patients often have underlying diseases A role for infection as a colactor has been postulated. but re is little supporting evidence. Conditions that alter immunologic function, including systemic lupus erythematosus may increase risk[13]. 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 insu liii 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 dermaoiogic conSuJtatlOfls should also be considered[3], Pain control, fluid replacement, aseptic handling, and avoidance of any adhesive material are important[3]. 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 promising[3].

Allopurinol a potent inhibitor of the synthesis of uric acid, is the drug most commonly prescribed for the treatment of primary and secondary hyperuricem ia 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 ol diuretics (especially thiazides) may be predisposing factors. Less common hut more severe cutaneous intolerance reactions to allopurinol may occur, including exfoliative erythroderma, the Stevens-Johnson syndrome, and the most severe reaction, toxic epidermal necrolysis[14]. 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 asymptonlatic hyperuricaem Ia. The benefits of treatment with aliopurinol appear questionable in patients with asymptomatic hyperuricern Ia and do not justify the risks associated with long-term administration[14], It should be prescribed with care, especially in patients with chronic renal failure who

may be prone to severe allopurino hypersensitivity reactions[15].
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 countries[16]. 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 al lopurino Hinduced Stevens-John son 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 multisvstern ic disease, or impaired renal function.

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