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A Case Report on Amoxicillin Induced Stevens- Johnson Syndrome

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Abstract

Stevens-Johnson syndrome (SJS) is a very rare, potentially lethal skin reaction usually resulting from drug reaction. SJS is characterized especially by extensive erosive lesions of the skin and mucous membrane (i.e. the mouth, nose, esophagus, anus and genitalia), detachment of epidermis and acute skin blisters. We report the case of a 13-year old female who presented an erythematous rash with flaccid blisters all over the face, mucous membranes and various parts of body, developing a week after course of oral amoxicillin 500mg twice daily. The physical examination showed a generalized erythematous rash with flaccid blisters filled with liquid involving large areas of the body. This case report addresses the fact that severe hypersensitivity reactions may rarely occur with amoxicillin, which can be potentially dangerous and life threatening. It also intends to raise awareness about early detection and management of severe adverse drug reactions (ADR) for better treatment and recovery.

Keywords

amoxicillin; Stevens-Johnson syndrome; drug eruption; rash; blisters

Introduction

Stevens - Johnson syndrome (SJS) is a rare, life threatening condition usually associated with medicines use rather than other etiologic factors. It is a severe forms of exfoliative dermatitis, characterized by extensive epidermal erythema and blistering, which leads to necrosis and detachment of the epidermis. It can also cause mucosal lesions. The more usual culprits are antimicrobials like sulfonamide followed by nonsteroidal anti-inflammatory drugs (NSAIDs), anticonvulsant drugs, and anti-gout drugs. SJS is more commonly seen in children who are susceptible to viral infections. Mortality is higher in the elderly [1].

Recovery after Stevens-Johnson syndrome can take weeks to months, depending on the severity of the condition. Laboratory tests cannot determine the drug causing SJS. Diagnosis depends on the history of the patient's medication intake and the relative risk of drugs that may induce SJS. Re-challenge to establish the causality of a drug and ADR is not indicated since it can elicit a new episode of SJS [2].

Case Report

A 13-year old female with an erythematous and bullous eruption was admitted to the

emergency ward. Her condition was severe, involving an epidermal detachment observed of more then 10% of the body surface area. Extensive sloughing of the epidermal area was also noted. Further history revealed that she had been diagnosed with otitis media recently and had been prescribed amoxicillin 500mg twice daily for a week. Physical examination also showed that eye, mouth and pharyngeal mucosae were affected by erosive lesions (Image 1). Lesions began symmetrically on the face and the upper part of the torso and extended rapidly, with maximal progression to the extremities in 2-3 days.

Laboratory investigation showed the following: white blood cell count of 13.3 * 10^9/ L (normal range: 4-10*10^9) with no eosinophilia. Liver enzymes were within normal range: aspartate aminotransferase was 37 IU/L (normal range: 3-40 IU/L); alanine aminotransferase was 33 IU/L (normal range 3-45 IU/L). Serum urea level was found to be 11 mmol/l. Haemoglobin level decreased to 10.5 gm%. Platelet count was slightly increased to 528,000 platelets per microliter (mcL).C-reactive protein was 12mg/dl. Viral and bacterial infections including tests for Epstein Barr Virus (EBV). Cytomegalovirus (CMV) and Mycoplasma pneumonia were negative.

The presumptive cause was amoxicillin. The drug was immediately withdrawn. Empirical therapy with intravenous acyclovir 20mg/kg q8hr was started but was discontinued after results of herpes culture proved negative. Good hygiene and use of non-adhesive dressings for genital areas were used for healing of mucosal erosions. Keno Oral Paste 0.1 % (triamcinolone acetonide) local corticosteroid, intravenous antibiotic meropenem 500 mg BD, antihistamine pheniramine maleate 22.75 mg BD, bronchodilator theophylline 84.7 mg plus etophylline 25.3 mg combination BD and intravenous fluids i.e. normal saline were administered as supportive therapy. Intensive supportive therapy was started with intravenous corticosteroids like dexamethasone 8mg plus methylprednisolone 1mg/kg/day with favorable results. The flaccid blisters began to decrease progressively and the condition improved after discontinuation of amoxicillin. Cyclosporine was administered in the dose of 3 mg/kg body weight in three divided dosage for 07 days and then tapered over another 07 days. She was subsequently discharged well, after six weeks of rehabilitation (Image 2).

Discussion

SJS is one of the dermatological conditions that can be potentially fatal. In SJS, the extent of total skin surface involvement is less than 10%; more than 30% skin involvement is termed as toxic epidermal necrolysis (TEN), while 10-30% is designated SJS/TEN overlap syndrome. Both conditions are typically associated with vesicles and blisters. In severe cases, there is extensive necrosis of the epidermis and mucous membranes. Although the exact etiology of SJS/TEN is not fully understood, it is believed to be an immune-mediated hypersensitivity reaction in which cytotoxic T-lymphocytes play a role in its pathogenesis [3].

Tissue damage in SJS is thought to be caused by keratinocyte cell death from massive, accelerated apoptosis. Several pathways can induce apoptosis. Cytotoxic T cells that express the skin-homing receptor, cutaneous lymphocyte-associated antigen (CLA), are seen early in the development of cutaneous lesions. Cytotoxic T cells and macrophages seem to play an important role in the extensive epithelial necrosis and sub epithelial detachment. Various cytokines (TNF-α, interferon-γ, IL-6 and 18 and the Fas ligand) may also contribute to epidermal cell death as well as to some of the constitutional symptoms. Some believe that apoptosis is principally mediated by the Fas/FasL apoptotic pathway, while

others suggest the role of other cytokines as primary mediators (TNF-α, perforin, granzyme B, and interferon gamma) [4,5].

In clinical practice, these reactions are usually manifestations of a drug-induced hypersensitivity. The etiological factors of SJS can range from viral infections to various pharmacological agents. The commonly associated drugs are antimicrobials (sulfonamide and other nonsulfonamide antibiotics such as aminopenicillins, cephalosporins, and quinolones), anticonvulsants (carbamazepine, phenytoin, phenobarbitone, and valproic acid), NSAIDs of the oxicam type, and allopurinol [6,7].

The penicillin antibiotics can cause hypersensitivity reactions such as rash and erythema on the skin. Patel et al [8] reported that penicillin's are one of the antimicrobials frequently causing severe cutaneous adverse drug reactions (CADRs) in the Indian population. To date, few cases of amoxicillin-induced SJS/TEN have been reported [6,9]. These adverse events are usually minimized by early withdrawal of the suspected offending agent (amoxicillin in this case).

We report the case of a 13-year old female who presented with an erythematous rash with flaccid blisters all over the face, mucous membranes and various parts of body. Extensive debridement of nonviable epidermis followed by immediate covering with biologic dressings was performed. Though the etiology includes immune medicated reactions, amoxicillin might have caused a hypersensitivity reaction which progressed to fluid filled lesions within a few days. Amoxicillin had been prescribed as per body surface area and body weight of the patient to treat otitis media. Though there is no clear evidence for dose related adverse events of amoxicillin, the idiosyncratic delayed hypersensitivity profile worsened the condition.

The role of systemic corticosteroids in SJS is controversial. It was not until 1976 that Rasmussen published a retrospective study suggesting that the “treatment of SJS with corticosteroids may be associated with significant side effects and prolonged recovery.” Specifically, the study indicated that patients receiving systemic corticosteroids (compared to supportive care) had a longer hospital stay and more complications than those who were not treated with corticosteroids. Subsequent articles supported the concerns reported by Rasmussen et al [10]. Ginsburg published a retrospective study that found that both rates of infection and complications were greater in patients with SJS when treated with corticosteroids [11].

Patterson et al prospectively evaluated 67 patients, finding that systemic corticosteroid use in SJS demonstrated an improved outcome with no increase in complications and found SJS to be a corticosteroid-responsive condition with a hastened recovery through its use. The article concludes “that managing physicians believed corticosteroids were not only essential for management, but possibly essential for survival in many cases [12].” In SJS, corticosteroids suppress the immunological functions of the damaging effects of cytotoxic T lymphocytes and the macrophages [13].

Consideration was given for symptomatic treatment. Careful monitoring of fluid balance with strict input and output charts was done. Re-epithelialization took place for more than 3 weeks and disabling non-pruritic lesions remained. In addition to this corticosteroid treatment, cyclosporine for 2 weeks and counseling was given to the patient's parents resulting in full recovery of the patient.

Conclusion

There is a possible association between the adverse effect (SJS) and amoxicillin. Although these CADRs are predominantly mild in nature, they can at times be, severe in manifestation. In developing countries like India, where infectious diseases are widely prevalent, the frequent use of amoxicillin and the subsequent ADRs cannot be avoided. Thus, as soon as the offending drug causing ADR is identified, immediate withdrawl of the drug is mandatory along with other symptomatic treatment given simultaneously.

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Figures

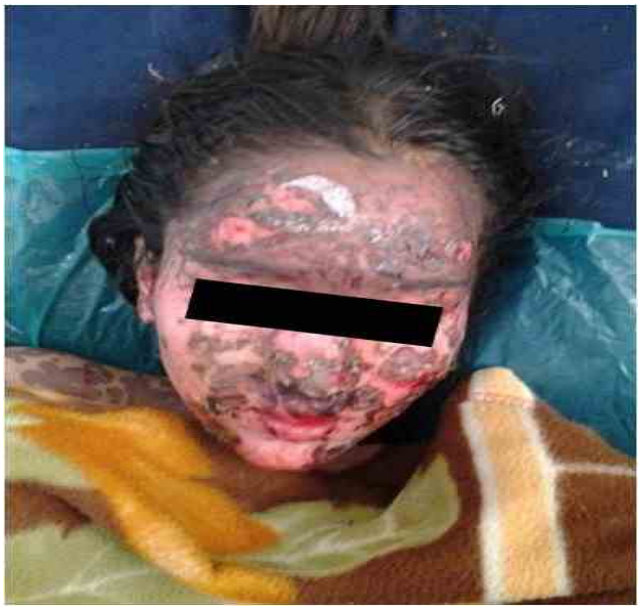

Figure 1: Erythematous and Bullous rash

Figure 2: Recovery of erythematous and bullous rash

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