



Amoxicillin and clavulanic acid-induced Stevens-Johnson Syndrome in a dialysis patient

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Article History:

Received on: 05 Oct 2020
Revised on: 07 Nov 2020
Accepted on: 12 Nov 2020

Keywords:

Amoxicillin,
Adverse reaction,
Clavulanic Acid,
Hypersensitivity,
Steven Johnson
Syndrome

ABSTRACT

A 48-year-old male patient with chronic kidney disease on haemodialysis came with complaints of worsening fever comprising maculopapular rashes and was diagnosed with Stevens-Johnson Syndrome- Toxic Epidermal Necrolysis (SJS-TEN) with sepsis (probably catheter-associated). The patient developed rashes with skin eruptions over the abdomen, trunk, around hands, face with redness and swelling on both legs following intake of Augmentin (containing amoxicillin and clavulanic acid). His management was done with IV steroids, antibiotics and supportive treatment. Stevens-Johnson syndrome (SJS) is an immune-mediated delayed hypersensitivity reaction with a severe form of cutaneous reactions involving areas of the face, genitals and mucous membrane of GI tract and respiratory tract. These manifestations occur as a result of certain drugs or due to any infection. In 95 % of the reported cases, drugs, including penicillin, was found to be a cause. In this case, report the patient had SJS with TEN comprising >30% of body surface area (BSA).



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ISSN: 0975-7538

DOI: <https://doi.org/10.26452/ijrps.v11i4.3921>

Production and Hosted by

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INTRODUCTION

The SJS-TEN is an immune-mediated reaction of the skin and mucous membrane, leading to tissue necrosis and detachment (Fritsch and Sidoroff, 2000) where pathogenesis includes activation of cytotoxic T lymphocytes (Harr and French, 2010; French, 2006). As per studies and reported cases, > 100 drugs were found to cause SJS (Schöpf, 1991;

Roujeau and Stern, 1994) including antibacterial, anticonvulsants, non-steroidal anti-inflammatory drugs (NSAIDs), and oxide inhibitors (Zaidi, 2017). Augmentin induced SJS is a rarely seen reaction comprising to <1%. Here we are detailing an atypical case of Augmentin induced SJS.

CASE HISTORY

A 48-year-old male patient with Chronic Kidney Disease (stage V-D) on maintenance haemodialysis presented to our hospital with complaints of worsening fever and maculopapular rashes lasting five days. He was apparently alright five days back when he developed fever, intermittent, with chills and rigours following a history of drug ingestion of Augmentin (containing amoxicillin and clavulanic acid) 625mg 1-1-1 for one week, which he took for three days and started developing rashes with skin eruptions all over the body and worsening fever. The eruptions comprised of erythematous, fluid-filled lesions over abdomen, trunk, around hands

and face, had swelled with redness on both legs and diarrhoea during that period. He was then admitted at a local hospital where they discontinued Augmentin and was started on Meropenem and Vancomycin suspecting sepsis associated with CLABSI (Central line-associated bloodstream infection). The patients' fever and rashes worsened and even showed worsening despite the broad-spectrum antibiotics. Hence, the patient referred to our hospital, a tertiary care teaching facility. On general examination, he had erythematous macular rashes throughout the body with erosions around the mouth.

On careful history attaining, we noticed an initial temporal association between Augmentin intake and the onset of rash with fever, and later the worsening of lesions with a subsequent intake of broad-spectrum antibiotics along with mucosal involvement, suggestive of Steven Johnson Syndrome. Given a Dermatology consultation, they reaffirmed the diagnosis as Augmentin induced SJS. All broad-spectrum antibiotics were discontinued and started on IV steroids with the topical antibiotic application. As he had elevated inflammatory markers, procalcitonin of 1.87 with fever and insitu central line, empiric Vancomycin was continued. Clinically he showed significant improvement with management mentioned above and became afebrile, lesions subsided, erythema reduced and started exfoliating over arms and scalp for one week. Blood culture at the time of hospital admission was negative, and Vancomycin discontinued. Intravenous Hydrocortisone was converted to oral Wysolone and tapered and stopped for one week. The patient's condition improved and was cautioned against the usage of the betalactam antibiotics in the future.

DISCUSSION

The history of SJS occurred in 1922 when two scientists described two paediatric patients admitted with fever and skin eruption separated by normal tissue, conjunctivitis, inflamed mucous membranes, and one of them had a total loss of vision (Bohigian, 2015). SJS is a type IV(subtype C) delayed hypersensitivity reaction which begins within eight weeks (usually 4 to 30 days) following the exposure to the causative drug (Harr and French, 2010) and has a treatment duration of 2-4 weeks. The minor form of SJS involves < 10% BSA, overlapping TEN is 10-30% of BSA and TEN is detachment more than 30% of BSA. Clinical features include fever, headache, cough, sore throat followed by lesions and blistering of mucous membrane affecting deeper layers of skin and can be easily misdiagnosed and treated with

antibiotics. SJS and TEN were formerly thought to be different medical conditions, but are now regarded as part of a disease spectrum, where SJS is least severe and TEN at the more end (Hart and Frerichs, 2015).

Causative drugs include antibiotics especially sulfa drugs, penicillins, carbamazepine (Das et al., 2016), NSAIDS(Non-steroidal anti-inflammatory drugs) (except Aspirin), yet in 25% of cases, no drug can be identified. Reported incidence comprises 2-6 cases per million per year. It can be differentiated from other skin conditions on three clinical criteria, (1) pattern of individual lesions, (2) distributions of each lesion, (3) and epidermal detachment. A significant cause of decease amid hospitalized patients include ADR (0.3% - 7 %) varying from mild rashes to severe reactions, including SJS-TEN (Patel et al., 2012). In our case, the patient consumed amoxicillin-clavulanic acid combination that caused SJS with TEN involving >30% of BSA, which is uncommon(<1%). Patch test and intra dermal testing(IDT) are contraindicated in the phase of acute drug reaction (Phillips et al., 2019). Diagnosis includes a detailed history attaining process to identify a most likely causative drug initiated within the last eight week, and early identification and discontinuation play a significant role in the management of SJS (Dugan, 2013). Corticosteroids and IV immunoglobulin with fluid replenishment for electrolyte imbalances are also given.

CONCLUSION

Augmentin (containing amoxicillin and clavulanic acid) is a commonly used penicillin group of antibiotics and can cause delayed severe hypersensitivity reactions which are rare yet, severe and fatal. Considering the low sensitivity of patch test, clinicians should be aware of these ADR and should consider drug fever and SJS as a differential of sepsis. Prompt reporting of ADRs is important to avoid noncompliance to treatment, to promote rational use of drugs and to prevent serious fatalities.

Conflict of Interest

The authors declare that there is no conflict of interest for this study.

Funding Support

The authors declare that there is no funding support for this study.

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