

Case Report

Stevens-Johnson syndrome: a case report of possible cephalosporin-induced cutaneous adverse reaction

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Abstract

A severe medical condition known as Stevens-Johnson syndrome (SJS) is marked by a cutaneous and mucosal reaction from the use of specific medications. The prodromal illness is followed by severe mucocutaneous symptoms in this immune-mediated disease. We describe the clinical history of a 55-year-old Caucasian woman who was exposed to cephalosporins.

In resource-constrained countries and hospitals where cutaneous biopsy is not readily available, it is not easy to diagnose Steven Johnson Syndrome. This is particularly true in countries where the incidence of infectious diseases such as scarlet fever and measles is high and the early symptoms of SJS can be mistaken for these conditions. We used the Naranjo scale to confirm the probable association of the drug with the syndrome. Physicians while writing prescriptions for their patients need to warn them of potential side effects and they should keep in mind conditions like Stevens-Johnson syndrome. This case report highlights the need for improved knowledge and understanding of SJS among healthcare practitioners in resource-limited communities where the prevalence of infectious diseases is high.

Key words: Stevens-Johnson syndrome; cephalosporins; scarlet fever; severe cutaneous adverse reaction; Naranjo scale.

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Introduction

We report a very interesting case of Stevens-Johnson syndrome (SJS) which is a rare severe cutaneous adverse reaction (SCAR) belonging to type IV hypersensitivity disorders. This is an immune-mediated condition characterized by the detachment of the epidermis and mucous membrane. This hypersensitivity reaction is recognized as a dysregulation of cellular immunity [1]. The SJS is categorized into three different forms: a mild form, called Erythema Multiforme (EM) (where < 10% total body surface area (TBSA) is affected), the main form (between 10 and 30%), and the severe form, called toxic epidermal necrolysis (TEN) (skin involvement of > 30%).

This syndrome was initially described in 1922. Alan Lyell provided an early description of TEN in 1956 [2]. The incidence of SJS/TEN is roughly 4-6 cases per million person/year [3]. While the incidence of SJS in developing countries is not well documented, it is believed to be higher compared to developed ones. Healthcare practitioners in resource-limited

communities face a problem due to a lack of knowledge regarding SJS, which can result in delayed or incorrect diagnoses and management of the disease. This is especially true in regions where the prevalence of infectious diseases like measles and scarlet fever is high, thus the early signs of SJS might be confused with aforementioned diseases ongoing with exanthems.

Recent studies in the United States reported mortality rates of 4.8% for SJS, 19.4%, and 14.8% for SJS/TEN overlap and TEN respectively [4]. Approximately 50% of cases of SJS and 80–90% of cases of TEN are drug-induced [5]. However, sometimes immunodeficiency syndrome in patients increases the risk of diseases. *Mycoplasma pneumonia* is likely the second most common cause, particularly in children, though this is somewhat controversial.

The exact pathogenesis of SJS/TEN is not known; however, it appears that through an unknown mechanism, cytotoxic T cells and natural killers begin to attack keratinocytes and cause massive apoptosis [6]. Many drugs have been identified as a triggering cause

for SJS/TEN among which cephalosporins are at a higher position [7].

Nikolsky's sign is pathognomonic for SJS/TEN, when lateral pressure is applied to an intact blister's border, the normal epidermis is forced out of place, causing the blister to spread [8].

We used the Naranjo scale to rule out the association of SJS with the exposed drug. To standardize the evaluation of causality for all adverse drug reactions, the Naranjo ADR probability scale was created. The scale was not intended for use in ordinary clinical practice, but rather in controlled trials and registration studies of novel drugs [9]. It is simple to apply and widely used.

The purpose of this case report is to increase awareness among clinicians, especially in developing countries regarding drug-induced-SJS, which can mimic other infectious diseases like scarlet fever whose treatment and management cardinaly are different and could worsen a patient's condition. To the best of our knowledge, this is an unusual occurrence and could be

the first reported case of drug-related SJS that has been mimicked as scarlet fever.

Case presentation

A 55-year-old female who was euglycemic and normotensive was admitted to the “National Center of Infectious Diseases” of Armenia with a positive streptococcal throat smear and rash. She had a generalized painful skin macular rash all over the body, tonsillitis with resolved pus, tongue affection (hyperemic and swollen) i.e., strawberry tongue, and encrusted lips. Nikolsky's sign was positive which indicated necrolysis.

The disease started a week ago when she had only a sore throat and fever for which she had taken ibuprofen orally. When her condition did not improve, her family physician prescribed Cefixime after revealing a positive streptococcal culture from a throat swab test. According to her, two days after taking her oral medication, she developed a rash that was non-pruritic and painless which initially started from the trunk and soon spread all over the body. Less than 10% skin detachment of body surface area was initially affected. The patient was recommended for hospitalization in an infectious diseases hospital, due to suspicion of scarlet fever with streptococcal throat, small spotted rash, and strawberry tongue.

On admission to our hospital, her vitals were: Blood pressure 118/70 mm Hg, heart rate 91 beats/min, and oxygen saturation 100%. Empirical therapy with Cephalosporin (Ceftriaxone) was continued in the hospital against streptococcal infection along with fluconazole for prevention of fungal infections. CBC Profile was normal except for white blood cell count which was slightly elevated to 15000 cells per microliter. Serum Na, 131 mEq/L; K, 4.6 mEq/L; total protein, 5.7 g/dL; albumin, 2.6 g/dL, Procalcitonin, 0.194 ng/mL. Her liver enzymes and serum creatinine were normal. Tests for human immunodeficiency virus (HIV), hepatitis A, B, and C viruses, herpes simplex virus, Epstein–Barr virus, influenza A, and mycoplasma pneumoniae were negative. The patient didn't receive any vaccination or other therapies prior to the current episode of illness. The rash worsened on the 3rd day of hospitalization. Oral mucosa was involved with painful hemorrhagic erosion (Figure 1).

Dermatological consultation was initiated and rejected scarlet fever after which the probable diagnosis of SJS was made. All drugs were discontinued immediately and steroid therapy was initiated with Prednisolone (1.0 mg/kg/day). After a day of stopping the drugs, her clinical symptoms started to improve.

Figure 1. Skin rash covering face and neck along with mucosal involvement.



The patient was clinically diagnosed with Steven Johnson Syndrome and transferred to a dermatological clinic. Unfortunately, after the discharge of the patient, her follow-up couldn't be maintained.

Discussion

Stevens-Johnson syndrome is a rare but serious skin reaction that is usually caused by taking certain medicines. It needs to be treated immediately in the hospital. In a study by Sethuraman *et al.* penicillins, cephalosporins, and fluoroquinolones were the most common drugs causing SJS [7]. Here we have described a case of a female adult patient with possible Cephalosporins induced Stevens-Johnson syndrome.

Stevens-Johnson syndrome can start with flu-like symptoms, such as a high temperature, sore throat, cough, and joint pain. In our patient's case, the initial presentation was only a sore throat and fever with confirmed results of streptococcal tonsillitis. The features did not improve even after intake of NSAIDs for 3 days and then on the third day, broad-spectrum cephalosporin antibiotics (PANCEF) were prescribed to the patient by a family physician. After getting swab sample test results which confirmed streptococcal tonsillitis, Cefixime against tonsillitis was prescribed (Cefixime and Ofloxacin). Cases of streptococcal tonsillitis have been reported earlier and are the most common bacterial cause of pharyngitis for which antibiotics are indicated [10]. In our case, along with taking antibiotics, the rash appeared on the whole body, which caused confusion to consider the case as scarlet fever based on sore throat and rash [11], with fever and strawberry tongue. Cephalosporin was continued in the hospital, keeping in mind the presence of bacterial infection. Cephalosporins are useful against skin infection, resistant bacteria, meningitis, and other infections. Due to consideration of scarlet fever and

continuing cephalosporin, the patient's condition worsened even more. On dermatological consultation, scarlet fever was rejected and finally, SJS was highlighted as a probable diagnosis of the condition.

To identify the drug, the Naranjo Scale also known as ADR (Adverse Drug Reaction) Probability Scale was used [9]. The score for the Naranjo scale in our case was five (Table 1). The drug comes under probable cause according to the Naranjo Scale and can be confirmed by withdrawing the drug.

The first step in the treatment is to identify the offending drug and stop using it. Others are pathogenetic and symptomatic, with particular emphasis on airway and hemodynamic stability, wound care, and pain relief measures [12]. Therefore, on an urgent basis, all drugs were stopped and Prednisolone (1.0 mg/kg/day) was prescribed. When her condition started improving and no new rashes could be seen, a clinical diagnosis of Steven Johnson Syndrome was made. Ceftriaxone was the culprit for SJS in our patient.

It may be difficult to diagnose and effectively manage SJS in some developing countries due to inadequate availability of medical care and diagnostic equipment. Treatment delays and less favorable results may result from this.

In terms of the financial cost of healthcare as well as the effects on patients and their families, SJS can have a major burden in developing nations like Armenia. High rates of hospitalization, admission to the intensive care unit, and protracted recuperation times are all related to SJS. The cost of maintaining SJS can be a considerable financial burden for both patients and healthcare systems in underdeveloped regions with scarce healthcare resources.

This case report highlights the importance of misdiagnosis of this disease (SJS) and further worsening the conditions, as there are no fixed specific

Table 1. Adverse Drug Reaction Probability Scale.

S. No	Question	Yes	No	Do Not Know	Score
1.	Are there previous conclusive reports on this reaction?	+1	0	0	Yes
2.	Did the adverse event appear after the suspected drug was administered?	+2	-1	0	Yes
3.	Did the adverse event improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	Yes
4.	Did the adverse event reappear when the drug was readministered?	+2	-1	0	0
5.	Are there alternative causes that could on their own have caused the reaction?	-1	+2	0	0
6.	Did the reaction reappear when a placebo was given?	-1	+1	0	0
7.	Was the drug detected in blood or other fluids in concentrations known to be toxic?	+1	0	0	0
8.	Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	Yes
9.	Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	No
10.	Was the adverse event confirmed by any objective evidence?	+1	0	0	0
		Total Score: 5			

labs or imaging that will clinch the diagnosis [13]. Physicians must therefore consider Stevens-Johnson syndrome as a potential complication of treatment, especially when the use of medication is questionable. Patient history, mainly drug history, and recognizing the rash type (clinical diagnosis) will mainly help in the diagnosis of SJS. The diagnosis can be made earlier if physicians keep in mind the following pattern: painful rapidly progressing targetoid rash, mucosal involvement, and drug of notoriety recently started [13]. One important thing in our case that is missed by physicians is skin biopsy [14] because of limited access, which is important in diagnosis. This case report also educates us in treating SJS patients by eliminating and stopping offending drugs even when we have confirmed bacterial infection which requires antibacterial treatment in case of doubts about SJS.

Conclusions

Considering the fact that scarlet fever is a typical pediatric infectious disease, the appearance of rash in adult patients with streptococcal tonsillitis and receiving antibacterial agents should warn physicians regarding allergic reactions, especially SJS and TEN. The stoppage of all potential culprit drugs has paramount importance in the treatment of SJS. Since there is limited literature on this case, clinicians should keep in mind the possible complications of drugs while prescribing them.

Consent

The informed consent form was obtained from the patient for publishing the case.

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