

STEVENS-JOHNSON SYNDROME: REPORT ON A CASE WITH A STRANGE COMPLAINT OF ALLERGY TO BUS

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SUMMARY – Stevens-Johnson syndrome is an uncommon inflammatory skin disorder in which immune mechanisms, cytotoxic reactions, and delayed hypersensitivity seem to be involved. Herein, an unusual case with strange complaint of “bus allergy” is presented, suffering from severe generalized itching and skin lesions, followed by ulcers in his mouth and genitalia. The diagnosis of Stevens-Johnson syndrome was made and appropriate treatment was advised. However, detailed medical history revealed a completely different cause of his allergic reactions, as he had occasionally used dimenhydrinate because of motion sickness in his history. Therefore, adverse drug reaction to dimenhydrinate was considered as the main underlying cause of the disease. In conclusion, thorough medical history should be taken to make a definitive diagnosis and identify the underlying disease, since accurate diagnosis and appropriate treatment can prevent further complications.

Key words: *Hypersensitivity – drug effects; Drug toxicity; Stevens-Johnson syndrome*

Introduction

Allergic reaction is a hypersensitivity disorder of the immune system, which manifests as uncontrolled or disturbed immune reactions to a dosage of foreign antigens. There has been an increased incidence and prevalence of allergic diseases during the last decades, which could be due to some environmental factors in addition to the genetic factors¹.

Stevens-Johnson syndrome (SJS) is an uncommon acute inflammatory skin disorder due to allergic reaction or infection in which mucous membranes such as oral, genital, and conjunctival mucosa can also be frequently involved. Although the mechanism of the disease has not yet been completely understood, immune mechanisms, cytotoxic reactions, and delayed hypersensitivity could be involved².

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Herein, we report a case with a strange complaint of “bus allergy”, followed by SJS, which turned out to have a completely different cause of his allergic reactions.

Case Report

A 17-year-old boy living in Tehran, capital of Iran, usually took several trips every year to his hometown, a northern city in Iran located about 200 km far from Tehran. He was referred to our center with a chief complaint of “bus allergy”!

He was born to non-consanguine parents. He lived with his parents and his 14-year-old sister. His father and sister had seasonal allergy to pollens in spring, but he did not report any type of allergic reactions or serious medical disease.

His problems started two years before, when he took a bus from Tehran to his hometown, when he experienced severe generalized itching and redness of his body within a few hours. As he described, his lesions

were of a typical wheal and flare type associated with dermatographism, which suggested urticaria. It is important to note that he had no systemic manifestations or angioedema, and those symptoms relieved within 2 days, but on his trip back to Tehran, he experienced the same condition again, which was self-limited. The same condition happened for the third time, when he went to another trip to a different city and on his way back. However, he explained that this condition did not happen in local buses he took inside the city.

The last time, he had such reactions when he was going from Tehran to his hometown. At the end of this trip, when he was still in the bus, he experienced severe generalized itching and skin lesions, which were followed by ulcers in his mouth and genitalia within a few days. Therefore, he was referred to our center for further investigations. Laboratory data showed leukocytosis (WBC=14,000/mm³) and eosinophilia (eosinophils=920/mm³). Serum IgE level (tested by ELISA) was 420 IU/mL. Patch tests for common allergens and mold were negative.

On physical examination, we found predominantly central distribution of dusky-red, purpuric, and livid maculae on his face and body, some of which suggested atypical flat target lesions. Some of the lesions on his face and trunk showed confluence. Purulent conjunctivitis, stomatitis, gingival ulcers, and genital ulcers were also detected. There was no obvious skin detachment, but Nikolsky's sign on the necrotic and erythematous maculae was positive, which was approximately in less than 10% of his body surface. These manifestations suggested SJS, which was subsequently confirmed by skin biopsy.

A detailed medical history led to an interesting point: he explained that he had a history of motion sickness and had used dimenhydrinate every time he was going to have a trip to other cities in order to avoid this complaint. Therefore, adverse drug reaction to dimenhydrinate was considered as the main underlying cause of the disease in this patient.

Since the patient was not very ill, only supportive care was prescribed, while systemic corticosteroid (prednisolone 50 mg/day) was also started and tapered in a week, which resulted in complete symptom relief. The patient was advised to discontinue use of dimenhydrinate on his future trips. He did not experience such a condition during 1-year follow-up.

Discussion

Adverse drug reactions (ADRs) can frequently occur in the general population. ADRs are the most common iatrogenic complication recorded in 5% to 15% of all drug administrations. The complicating factors are numerous types of clinical manifestations and various mechanisms by which different drugs can cause ADRs³.

Different immune and non-immune pathways are known to be responsible for drug reactions. The non-immune effects of drugs, which make the majority of the causes (75%-80%) are usually predictable, while the remaining 20%-25% of ADRs are thought to be predictable and can happen either through an immune or non-immune route⁴. Among all ADRs, the immune pathway accounts for only 5%-10%, which include the actual IgE mediated drug hypersensitivities as a subgroup^{5,6}.

Stevens-Johnson syndrome could be triggered by preceding medication, especially non-steroidal anti-inflammatory agents, antibiotics, and anticonvulsants². However, antihistamine combinations are not at the top of the list for immediate allergic reactions⁷. Dimenhydrinate is a commonly used over-the-counter (OTC) antihistamine preparation⁸, used for rhinitis, nausea and motion sickness, dizziness, and anxiety⁷. It is a combination of two major components: diphenhydramine, which is an ethanamine as the antihistaminic element, and 8-chlorotheophylline, which is derived from xanthine to reduce the diphenhydramine induced sedation⁷. Dimenhydrinate allergic reactions, like in other antihistamine combinations, are very uncommon, but the most frequent type of reported allergic reactions to this drug are contact photoallergic dermatitis⁶ and fixed drug eruptions^{7,9,10}, with a noticeable number of cases involved. Cases of urticaria¹¹ and anaphylactic reaction^{7,8} due to dimenhydrinate allergy have also been reported.

As stated in a very recent report, updated on September 12, 2012, 868 individuals reported to have side effects when taking dimenhydrinate¹². Among them, 23 (2.65%) subjects had SJS, of which eight, surprisingly, happened in the year 2007. This study also showed that all of the cases had been using dimenhydrinate for less than 1 month at the time of experiencing SJS. It should be noted that although SJS mostly happens in children and adolescents, only

about 13.8% of those with SJS due to dimenhydrinate were aged between 10 and 19 years. In all of these cases, similar to our case, SJS was not severe, and this is an acceptable prognostic factor for those physicians who might experience the management of a SJS case on dimenhydrinate.

An important point in drug reactions is that sometimes a minor component of the drug is the actual culprit, as in the reported anaphylactic case of allergy to the theophylline fraction of dimenhydrinate⁸. Also, allergies to the artificial color or additive basis of the pills from a specific pharmaceutical industry should be considered.

On patch testing for dimenhydrinate allergy, it was shown that in the cases with allergy to the diphenhydramine component of the drug, this allergic reaction was isolated to diphenhydramine¹³ and no cross reaction⁹ between this allergy and other ethanolamine preparations was found. This means that in case of IgE mediated allergic reactions to diphenhydramine or dimenhydrinate, it is safe to use other antihistaminic drugs to reduce the allergic symptoms in such patients.

In the patient presented, important was the misdiagnosis made for his allergic reactions, which was only a result of inadequate history taking. Taking drug history is an unavoidable part of every medical history, which can be very important for the diagnosis and later-on needed medications. Proper history taking along with due attention paid to every particular part of the history can easily lead to a correct diagnosis, less paraclinical cost, and our principal goal in medicine, which is helping the patients who need our help.

In this report, we presented a case of allergic reaction in the form of urticaria and SJS, as different manifestations of adverse drug reactions to dimenhydrinate. Although allergic reactions to antihistamine combinations are rare, it is important to have in mind that perhaps the drugs, which are expected to reduce allergic symptoms, may be allergy causing elements themselves. Our duty is to prevent the predictable reactions by taking a concise but inclusive history of any type of previous hypersensitivities in our patients.

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Sažetak

STEVENS-JOHNSONOV SINDROM: PRIKAZ SLUČAJA NEUOBIČAJENE ALERGIJE NA AUTOBUS

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Stevens-Johnsonov sindrom je rijetka upalna bolest kože gdje se pretpostavlja da su uključeni imuni mehanizmi, citotoksične reakcije i odgođena preosjetljivost. Ovdje se prikazuje neuobičajen slučaj čudne "alergije na autobus" u bolesnika s teškim generaliziranim svrbežom i oštećenjima kože, nakon čega su nastali ulkusi u njegovim ustima i genitalijama. Kod bolesnika je dijagnosticiran Stevens-Johnsonov sindrom i preporučeno je odgovarajuće liječenje. Međutim, detaljna anamneza otkrila je potpuno drugi uzrok njegovih alergijskih reakcija, jer je povremeno uzimao dimenhidrat zbog bolesti pokreta u anamnezi. Stoga je zaključeno da je štetna reakcija na dimenhidrat bila glavni osnovni uzrok bolesti. Postavljanje konačne dijagnoze i utvrđivanje osnovne bolesti zahtijeva detaljno uzimanje anamneze, jer točna dijagnoza i primjereno liječenje mogu spriječiti daljnje komplikacije.

Ključne riječi: *Preosjetljivost – učinak lijekova; Toksičnost lijekova; Stevens-Johnsonov sindrom*