Ref: Ro Med J. 2023;70(4)
DOI: 10.37897/RMJ.2023.4.1

Stevens-Johnson syndrome following the use of phenytoin: A case report

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ABSTRACT

Background. This paper reports a case where the patient developed Stevens - Johnson syndrome (SJS) following the use of phenytoin.

Case description. The case was an 85-year-old male admitted to the 9-Dey Hospital in Torbat-Heydariyeh city, Iran with a diagnosis of cardiovascular accident (CVA). On Day 2 of hospitalization, phenytoin medication was started to control the patient's seizures. On Day 10, the patient developed a 39.2°C fever and also a generalized rash starting from the upper limbs and spreading to the whole body. The dermatologist diagnosed SJS and recommended replacing phenytoin with an alternative drug for seizure control. From Day 15 onwards, his rashes started to decrease and almost entirely disappeared a week later.

Conclusion. Considering the range and severity of the adverse effects of SJS, physicians need to be familiar with the symptoms of these reactions so that the drug can be replaced as soon as such symptoms emerge.

Keywords: Stevens - Johnson syndrome, disorder, phenytoin

INTRODUCTION

First described in 1922 by the pediatricians Stevens and Johnson [1], Stevens - Johnson syndrome (SJS) is a rare disorder caused by the hypersensitivity of the immune system, which has an annual incidence of 1 to 7 cases per 100,000,000 people worldwide [2]. SJS and its more severe form called Toxic Epidermal Necrolysis (TEN) are dermatological medical emergencies characterized by rapidly progressive skin necrosis, mostly caused by acute reactions to certain drugs. While rare, these unexpected reactions have notable morbidity and mortality rates [3].

It has been reported that the risk of SJS and TEN arises following the use of antibiotics (sulfonamides), anticonvulsants (phenytoin, carbamazepine, and lamotrigine), and nonsteroidal anti-inflammatory drugs. Being a severe manifestation of an idiosyncratic immune reaction to certain drugs, SJS/TEN is more likely to occur in people infected with the human immunodeficiency virus (HIV), for whom the incidence rate is about 1 in 1,000 [4]. Overall, more than 100 types of drugs are known to cause SJS/TEN, but there are reports of the higher impact of certain drugs (such as sulfonamide antibiotics and anticonvulsants) in the occurrence of this condition [5].

Anticonvulsants are generally associated with a risk of severe cutaneous reactions like SJS. Among these drugs, phenytoin is one of the most common causes of this syndrome [6]. Such cases are important because roughly 0.3-7% of all deaths among hospitalized patients are caused by adverse drug reactions (ADR). The leading causes of drug-induced SJS are believed to be antimicrobials (37.27%), followed by anticonvulsants (35.73%) and non-steroidal anti-inflammatory drugs (15.93%) [7]. Considering the rarity of this syndrome and the importance of its timely diagnosis and treatment, this paper reports a case of SJS following the use of phenytoin.

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Article History:
Received: 8 December 2023
Accepted: 29 December 2023

CASE REPORT

The case was a 85-year-old male admitted on February 15, 2020, to the ICU of the 9-Dey Hospital in the city of Torbat Heydariyeh (Iran) with a diagnosis of left CVA. The patient had a history of UTI and had fever, diarrhea, and abdominal pain from two days prior, although he had no diarrhea at the time of admission. On admission, the patient had right-sided hemiparesis, had open eyes, could not speak, obey, or recognize family members, was not aware of time, had focal seizures in the jaw area, had no symptoms of respiratory disease, had a spo2 of 93-95%, was extubated and had a Foley catheter. On the 10th day, a CV line was inserted under a guide in the right jugular vein. Spiral CT of the brain was normal, only showing slight dilatation in the ventricles and cisterns, indicating senile changes. The lung CT gave no indication of COVID-19, only showing effusion in the basal pleura on both sides along with the consolidation of the lower part of the lung, which the consulted surgical specialist decided does not merit chest tube insertion. Ultrasound of the kidney and urinary tract reported a longitudinal diameter of 116mm for the right kidney and 108 mm for the left kidney, and normal results in terms of kidney parenchyma thickness, kidney stones, hydronephrosis, and kidney cyst.

On the 2nd day of admission (Day 2), the patient developed fever (39.5° Celsius) and seizures, for which phenytoin injection (125 mg three times a day) was prescribed, following consultation with an infectious disease specialist, along with ciprofloxacin (400 mg) and ceftriaxone (1g twice a day). Also, lung CT and U/A, U/C tests were requested. A cardiologist was also consulted to examine the possibility of endocarditis. The consulted cardiologist ruled out this possibility as the patient had an EF of 55%.

On Day 4, LP was performed on the patient, and the HSV sample indicated herpes encephalitis, for which the patient was given acyclovir (750 mg three times a day).

On Day 6, the patient experienced loss of consciousness (GCS=6-7) and O2sat drop (82-85%) and was therefore intubated and connected to a ventilator in the SIMV mode.

On Day 6, the patient also exhibited an increase in creatinine up to about 5 mg/dL, and the infectious disease specialist was consulted again to decide whether to use non-nephrotoxic antibiotics. The consulted specialist recommended continuing with the previous antibiotics and using acyclovir at a daily dose of 350 mg if GFR<10 or 750 mg if 10<GFR<20 for 14 to 21 days.

From Day 7 up to Day 10, seizures and fever were under control, GCS was 7-8, and the patient remained intubated and under ventilator in the SIMV mode. On Day 10, the patient developed a generalized rash starting from the upper limbs and spreading to the whole body, and his fever returned (39.2° Celsius). The antibiotics and phenytoin were paused to decide how to proceed after consultation with infectious disease and dermatology specialists.

The patient had no history of allergy or poisoning. Differential diagnoses of this disease including Staphylococcal scalded skin syndrome, chemical burns, toxic shock syndrome, and measles were considered and staphylococcal culture tests, specific antibody titers, history taking. Sampling of damaged skin and clinical examination were reviewed and rejected.

The consulted infectious disease specialist recommended using antibiotics based on the results of the culture test and antibiogram. The consulted dermatologist diagnosed SJS and recommended using topical triamcinolone lotion and replacing phenytoin with an alternative drug for seizure control. Accordingly, phe-

FIGURE 1. Day 10: the patient developed generalized rashes and a 39.2°C fever; antibiotics and phenytoin were paused and infectious and dermatology specialists were consulted

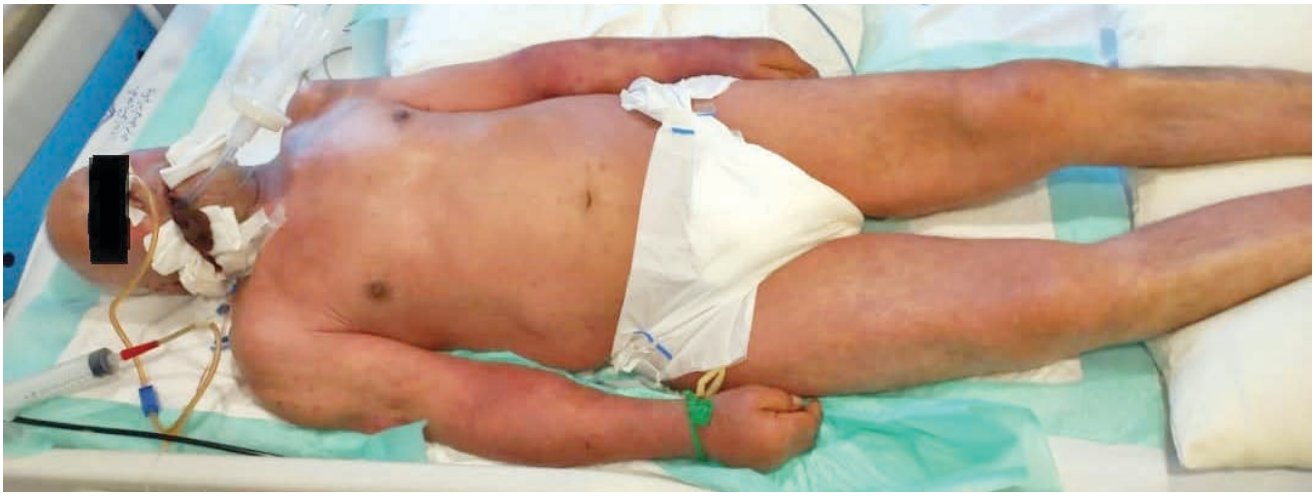

FIGURE 2. Day 10 to Day 15: the patient's rashes started to decrease and eventually disappeared

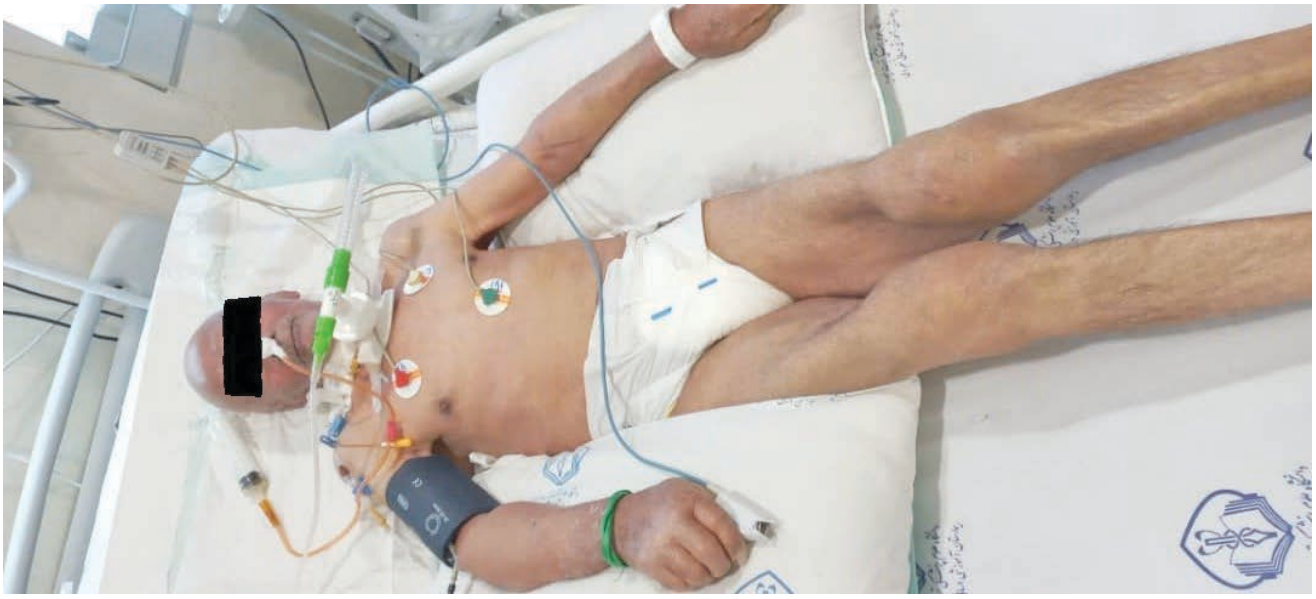

FIGURE 3. Day 23: the patient was tracheostomized and achieved spontaneous breathing under T-Piece with GCS=9

nytoin was replaced with Lobel (500 mg twice a day).

From Day 10 to Day 15, after discontinuing Phenytoin and starting Levebel and topical Triamcinolone lotion the patient's rashes started to decrease and eventually disappeared.

On Day 16, because of resistance to extubation, the patient was tracheostomized and connected to a ventilator in the SIMV mode.

From Day 20 onwards, the patient's respiratory secretions decreased and the ventilation was switched to the CPAP mode. On Day 23, the patient was separated from the ventilator and achieved spontaneous breathing under T-Piece with GCS=9.

DISCUSSION

Stevens-Johnson syndrome (SJS) and its more extensive form called Toxic Epidermal Necrolysis (TEN) are severe drug reactions that involve the skin and mucous membranes [8]. These reactions emerge suddenly usually with symptoms such as fever, sore throat, and fatigue appearing a few days before the appearance of skin lesions [3]. According to some studies, the incidence of SJS and TEN is about 2 per 1,000,000 people and their risk increases with age [9]. The mortality rate has been estimated to be less than 10% for SJS and more than 40% for TEN, with sepsis being the primary cause of death in most cases [10].

In the present study, the patient had a seizure on the second day of admission, and phenytoin was started for the patient. From the 10th day, the patient developed generalized rashes that spread to the whole body, and after infectious consultation, skin consultation and paraclinical procedures and clinical examinations, the diagnosis of Steven Johnson syndrome was given to the patient.

Also, in this study, the causes of Steven Johnson syndrome were investigated and in various studies, most of the cases are attributed to drug causes. Considering the severe complications and even death that may occur as a result of these drug reactions, identifying the most common drugs that cause the above reactions are of particular importance [11].

According to existing reports, the most common causes of these reactions are antimicrobial drugs such as penicillin, nonsteroidal anti-inflammatory drugs such as ibuprofen, and anticonvulsants such as phenytoin [12]. Among the 132 reported cases of drug-induced Steven Johnson syndrome registered in the ADR Center, the drug phenytoin was responsible for 10 of the cases. Among them, one person has also died [13]. In this regard, in a case report of phenytoin-induced SJS in a 60-year-old man, Inamdar et al. described phenytoin as the drug that most commonly causes SJS and TEN [4]. Also, in a study by Alirezaei et al. on the incidence of SJS and TEN in hospitalized patients, the medications that most commonly cause such reactions were found to be anticonvulsants and nonsteroidal anti-inflammatory drugs, in that order [14]. In a report paper published by Prabhu et al., on a 28-year-old woman with a history of hepatitis and left pleural effusion, SJS was caused by phenytoin and aggravated by cefepime [15]. In our case, however, while phenytoin was identified as the cause of reactions, antibiotic drugs did not aggravate the reactions. Also, while Pannu et al., reported that phenytoin-induced SJS caused bronchiolitis [16] and Kodliwadmath et al. stated that it caused myocarditis in a 43-year-old man, [17] our case developed no specific complication after SJS.

CONCLUSION

As in many other reports, the SJS reported in this paper was caused by phenytoin. Considering the range and severity of the effects of SJS and TEN, which include extensive skin damage, infection, and lung problems, physicians and other medical staff need to be familiar with the symptoms of these reactions and receive training on the side effects of anticonvulsants so that the drug can be switched as soon as such symptoms emerge, before it causes serious skin injuries and other adverse effects. Necessary information to the general public for non-use Anticonvulsant drugs should be provided without a doctor's prescription.

Acknowledgment:
This article is the result of a research project with the ethics committee code IR.THUMS.REC.1400.021. Therefore, we would like to thank and appreciate all the relevant authorities and the patient's family for agreeing to the implementation of this research project.

Conflict of interest:
The authors declare that there is no conflict of interest associated with this study.

Financial support: none declared

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