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CASE REPORT

Oral involvement by Stevens-Johnson Syndrome associated with carbamazepine in an immunosuppressed patient: Case report

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Abstract:

Introduction: Stevens-Johnson syndrome (SJS) is caused by a delayed immune response triggered by the association of genetic and environmental factors. This reaction can be mediated mainly by some drugs. **Objective:** The purpose of this article is to report the case of a patient with SJS associated with carbamazepine. **Case report:** A man was hospitalized complaining of odynophagia, whitish plaques in the mouth and swelling of the lips. Clinical examination revealed ulcerated and erosive lesions involving the buccal mucosa, lips, tongue and hard palate. The lips were swollen and with hemorrhagic crusts. Papular and purplish-colored lesions were observed on the skin. The patient reported that the lesions started 10 days ago, coinciding with the start of carbamazepine use. The diagnosis of SJS was established based on clinical information and the patient treated with support therapy. **Conclusion:** SJS is a clinical condition that affects the oral mucosa and can be triggered by the use of carbamazepine.

Keywords: Hypersensitivity; Drug Hypersensitivity; Stevens-Johnson Syndrome; Carbamazepine; Mouth Mucosa.

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INTRODUCTION

Stevens-Johnson syndrome (SJS) has been described as a severe and potentially fatal mucocutaneous reaction. It is characterized by the appearance of blisters followed by detachment of the skin and/or mucous membranes[1]. Currently, SJS is believed to be a delayed immune response triggered mainly by patient exposure to some drugs. The main drugs with a high risk of causing SJS are: anti-infective sulfonamides, antiepileptics, non-steroidal anti-inflammatory drugs, allopurinol, nevirapine and chlormezanone[2].

Adverse drug reactions can manifest as a mild, moderate, or high-intensity reaction. However, they often require hospitalization and cause disabling and lethal sequelae[3]. Epidemiological studies show that the prevalence of SJS is rare. It varies from 1.5 - 1.8 cases per million individuals per year[4]. On the other hand, indicators of SJS prevalence in the Brazilian population are considered scarce[3].

Some authors have already reported the case of patients who developed SJS after using carbamazepine[5-7]. According to the literature, 75% of the cases already registered have a probable pharmacological origin. However, other factors may be involved, such as viral infections (HSV) and respiratory tract infections[4,8]. In addition, infections caused by bacteria, fungi and protozoa and also some tumors can trigger SJS[9-10].

Historically, SJS was reported in 1922 by Albert Mason Stevens and Frank Chambliss Johnson. These authors described the case of two patients who presented with generalized skin rashes, continuous fever, inflamed oral mucosa and severe purulent conjunctivitis[3].

SJS is characterized by the appearance of lesions on the body preceded by fever, burning eyes and dysphagia[1]. These symptoms can help in the early diagnosis, as the clinical aspect then becomes more severe with the appearance of lesions with erythematous areas, macules that become vesicles, bullae and urticaria or confluent erythema[4,8,10]. The skin involvement of the trunk, face, palms and soles of the feet is only 10%. Ninety percent of patients develop erythematous erosions on the oral, ocular, and/or genital mucosa[4,8,10].

Treatment consists of immediate removal of the hypersensitivity reaction-inducing agent and supportive therapy. The objective of this study is to report the case of an immunosuppressed patient who developed SJS associated with carbamazepine.

CASE REPORT

A 34-year–old male was admitted to the Hospital Oswaldo Cruz (Curitiba-PR/Brazil) due to odinofagia, whitish plaques in the mouth associated with swelling of the lips. During the anamneses, he reported that was infected by HIV. Furthermore, he has made regular use of antiretroviral therapy (Tenofovir + Lamivudine + Ritonavir + Atazanavir). In addition, he was a smoker (40 cigarettes / day to 22 years), occasional cocaine user, and had a previous history of syphilis.

The oral examination revealed that the patient had a good dental condition. On the other hand, he had gingival inflammation and several ulcerated and erosive lesions on the mucous membranes of the mouth. These lesions involved the buccal mucosa, lips, tongue and hard palate. The lips were swollen and covered by hemorrhagic crusts (Figure 1). Tongue lesions had a white-yellowish background that resembled a "target" appearance (Figure 1). The left cheek mucosa appeared to be more compromised, including deeper lesions and bleeding (Figures 1). Patient reported discomfort at the site of the injuries, nausea and difficulty to swallow foods.

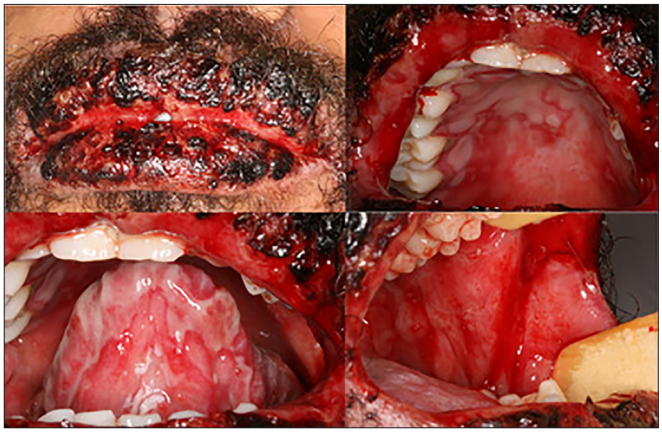

Figure 1. Oral lesions of Stevens-John syndrome involving lips, palate, tongue and buccal mucosa.

Additionally, papular and purplish-colored lesions were observed on the skin, especially on the trunk, face, palms and soles of the feet. In some regions, these lesions had a scaly appearance. Based on this information, the doctors made an initial diagnosis of Kaposi's sarcoma and herpes labialis. Thus, the patient was hospitalized and treated with dipyrone (500 mg), acyclovir (200 mg) and metochlorpramide (10 mg).

Some laboratory tests were requested to assess the general condition of the patient (Table 1). The results of laboratory tests revealed that the blood count, liver tests and blood calcium and phosphorus levels were normal. However, urea and C-reactive protein levels were elevated.

During the dental consultation, the patient reported that the lesions started approximately 10 days ago and that it coincided with the beginning of the use of carbamazepine. Then, based on the clinical information, a diagnosis of Stevens-Johnson syndrome was established. The patient was treated with benzylpenicillin, sulfatexazole + trimethoprim and fluconazole. An ointment based on vitamins A and E, fatty acids and soy lectin was used to help repair the lip vermilion lesions.

The lesions of the oral mucosa, lips and skin had fully repaired seven days later (Figure 2). Thus, the patient was discharged from the hospital and a return visit was scheduled for 15 days. The patient was well and without any skin or mouth lesions.

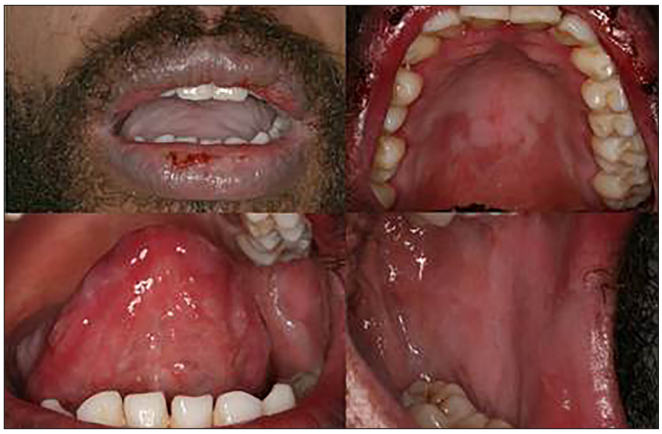

Figure 2. Repair of oral lesions caused by Stevens-Johnson syndrome after seven days of treatment.

DISCUSSION

SJS is a condition that can be misdiagnosed and can cause a delay in patient treatment. This can happen due to the various clinical signs that can mimic a mul-

Table 1. Laboratory data.

Laboratory tests	Results	Reference values
Complete Blood Count		
Erythrocytes	6.02 m / µL	4.2 - 5.9 m / µL
Hemoglobin	14.9 g / dL	14.0 - 18.0 g / dL
Hematocrit	47.5%	42 - 50%
Mean Corpuscular Volume	78.9 fL	80 - 98 f
Mean Corpuscular Hemoglobin	24.8 pg	28 - 32 pg
Mean Corpuscular Hemoglobin Concentration	31.4 g / dL	33 - 36 g / dL
Leukocytes	8.1 k / µL	0 - 5 k / µL
Basophils	1%	0 - 1%
Eosinophils	0.4%	0 - 3%
Lymphocytes	28%	30 - 45%
Monocytes	0%	0 - 6%
Mielocytes	0%	-
Metamyelocytes	0%	-
Segmented Neutrophils	56%	50 - 70%
Banded Neutrophils	56%	0 - 5%
Neutrophils	58%	50 - 70%
Reactive lymphocytes	0%	-
Platelets	217 k / µL	150 - 450 k / µL
Other tests		
Serum Glutamic Oxaloacetic Transaminase	15 U / L	10 - 40 U / L
Serum Glutamic Pyruvic Transaminase	11 U / L	10 - 40 U / L
Urea	27 mg / dL	8 - 20 mg / dL
Creatinine	1.01 mg / dL	0.70 - 1.30 mg / dL
C-reactive protein	4.89 mg / dL	≤ 0.8 mg / dL
Potassium	5 mEq / L	3.5 - 5.0 mEq / L
Sodium	138 mEq / L	136 - 145 mEq / L

titude of conditions that we commonly see in primary care, such as: upper respiratory tract infection, adverse drug reaction, conjunctivitis, viral exanthema, etc[11]. This article describes the case of an immunosuppressed patient who developed SJS associated with the use of carbamazepine.

More than 90% of SJS occurs within the first 2 months of antiepileptic drug use. Commonly, some of the drugs such as carbamazepine and phenytoin have a high incidence to cause SJS[12]. Carbamazepine is a drug commonly prescribed for the treatment of seizures, as well as in the treatment of neuropathic pain and affective disorders[13]. Studies carried out in different populations revealed that there is a strong association between the human leukocyte antigen HLA-B*1502 adverse drug reactions such as toxic epidermal necrolysis and SJS[14–16].

In this article, SJS occurred in an adult male undergoing treatment for the control of HIV infection. According to Hirapara et al.[17], male patients with HIV infection are at greater risk for SJS. On the other hand, the severity of your reaction is less in these individuals. Abacavir, a nucleoside reverse transcriptase inhibitor used to control HIV infection, has been reported to induce SJS in some patients[18]. However, the patient was not using abacavir.

The diagnosis of SJS was established based on the clinical appearance of the lesions and because the changes that appeared in the skin and mucosa coincided with the use of carbamazepine. The SJS prognosis depends on the extent of skin sloughing and development of secondary bacterial infections[19]. Therefore, the patient was treated with antimicrobials to avoid secondary infections. No corticosteroids were used to treat the patient. The treatment of SJS with corticosteroids has generated controversy, as there is a risk that this drug contributes to secondary infections (including Candida sepsis) and increases the risk of mortality[20].

SJS can also involve the eyes. When this occurs, some sequels can happen, such as: dry eyes, visual acuity, conjunctivitis, corneal erosions, and trichiasis.[1] No changes associated with SJS were observed in the patient's eyes.

Laboratory tests revealed that the patient's systemic condition was good despite HIV infection. This may reflect the patient's adherence to antiretroviral therapy. Only urea and C-reactive protein levels were elevated in relation to reference values. However, this can be attributed to tissue changes resulting from the SJS itself. Urea is produced in the liver from ammonia, resulting from protein metabolism. It dissolves in the liquids produced by organism; much of it is eliminated in urine and sweat. High levels of urea in the blood can even mean problems such as kidney failure, which is the loss of kidney function. This hypothesis was ruled out because the creatinine levels were normal. Blood urea levels in SJS patients only become a concern when they are >28 mg/dL, as it increases the risk of mortality[21]. However, there are some conditions that can also raise urea in the blood, even with the correct functioning of the kidneys, due to catabolic processes, such as: hormonal changes, strenuous activities, intensity training, infections, degenerative diseases, cancer. The elevation of C-reactive protein levels, in general, is associated with inflammatory processes[22].

Although SJS is considered a rare condition and involves the mouth and other anatomical regions, the dentist needs to be aware of the signs that can guarantee an early diagnosis. The combined treatment of the dentist with a doctor is also essential. This will ensure effective treatment and reduce the risk of patient death.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

ETHICAL APPROVAL

Data from the patient here included were treated anonymously and statement of informed consent was signed by the patient allowing the use of his dental records.

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