Chapter 204

Stevens-Johnson syndrome in a patient with epilepsy and Parkinson's disease: Case report

https://doi.org/10.56238/devopinterscie-204

Joanilson Andrade Freire Junior
Federal University of Tocantins, Brazil
ORCID: https://orcid.org/0000-0001-6195-9539
E-mail: joanilson.junior@mail.uft.edu.br

João Vitor Vieira dos Santos
Federal University of Tocantins, Brazil
ORCID: https://orcid.org/0000-0003-4681-4088
E-mail: joao.vieira@mail.uft.edu.br

João Vitor Nunes Climaco
Federal University of Tocantins, Brazil
ORCID: https://orcid.org/0000-0002-8465-3556
E-mail: joao.nunes@mail.uft.edu.br

Ana Caroline Gonçalves de Sá Novaes
Federal University of Tocantins, Brazil
ORCID: https://orcid.org/0000-0002-3350-5676
E-mail: ana.novaes@mail.uft.edu.br

Zuleika Santiago de Medeiros Carneiro
Federal University of Tocantins, Brazil
ORCID: https://orcid.org/0000-0002-7533-2224
E-mail: zuleika.carneiro@mail.uft.edu.br

Virgílio Ribeiro Guedes
Federal University of Tocantins, Brazil
ORCID: https://orcid.org/0000-0001-9484-5095
E-mail: vrguedes@uft.edu.br

Nilo Fernandes da Costa
Federal University of Tocantins, Brazil
ORCID: https://orcid.org/0000-0002-0586-4305
E-mail: nfc@uft.edu.br

ABSTRACT
Steven-Johnson Syndrome commonly occurs as an idiosyncratic reaction to systemic medications such as antibiotics, antiepileptics, and nonsteroidal anti-inflammatory drugs. It can also be triggered by non-pharmacological causes. It is a pathology with a significant impact on public health due to the high mortality rate. The clinical picture presents nonspecific symptoms, such as fever, odynophagia, and itchy eyes. However, it is characterized by initial erythematous and livid macules, which involve the skin of the pre-sternal trunk and face and may affect the palms of the hands and soles of the feet. Diagnosis of the syndrome requires the collection of a complete clinical history, with special attention to drug exposure, thorough physical examination of the skin lesions, determination of the affected skin area, evaluation of mucosal involvement, and complementary tests, such as skin biopsy for histopathological study. Prognosis is related to the rapid identification of the causative drug and its discontinuation, not related to the dose or type of drug. A case of Stevens-Johnson Syndrome is reported in a 70-year-old patient with epilepsy and Parkinson's disease, in northern Brazil, emphasizing the clinical characteristics and the adopted treatment.

Keywords: Pharmacodermia, Rash, Erythema multiforme.

1 INTRODUCTION

Erythema multiforme was first described by Ferdinand Von Hebra in 1866 and at that time was considered a relatively benign condition. In 1950, the condition was divided into two categories: erythema multiforme minor (Von Hebra) and erythema multiforme major, which became known as Stevens-Johnson Syndrome (SJS). In 1993, Bastuji and Roujeau proposed that erythema multiforme major and Stevens-Johnson syndrome were distinct diseases and that the term “erythema multiforme” should only be used to refer to patients with target lesions or edematous papules, with or without lesions. mucous membranes; SJS,

in turn, should refer to the syndrome characterized by mucosal erosions, small blisters, and erythematous or purpuric lesions different from the classic targets (Bulisani et al., 2006), (Grünwald et al, 2020).

Currently, erythema multiforme can be classified into the following clinical situations: Erythema Multiforme Minor, Erythema Multiforme Major, SJS, and Toxic Epidermal Necrolysis – TEN. SJS and TEN are also known together as a single entity called Epidermal Necrolysis (EN). SJS/TEN most commonly occurs as an idiosyncratic reaction to systemic medications such as antibiotics, antiepileptics, nonsteroidal anti-inflammatory drugs, and allopurinol. SJS/TEN can also occur secondary to viral infections, vaccinations, and other non-pharmacological triggers (Shanbhag et al., 2020), (Cai et al., 2019).

Cutaneous manifestations are usually preceded by nonspecific symptoms, such as fever, discomfort when swallowing, and itchy eyes. Erythematous and livid macules typify the morphology of early skin lesions. The first sites of skin involvement include the presternal trunk region, and the face and may also involve the palms of the hands and soles of the feet. In about 90% of patients, there is the involvement of the mucosa of the mouth, genital, and/or gastrointestinal tract, visible as erythema and erosions. Other frequent presentations at the beginning of the pathology are ophthalmic, and this varies from acute conjunctivitis, erythema, eyelid edema, ocular secretions and crusts, corneal erosion, formation of conjunctival membrane or pseudomembrane and, in severe cases, ulcerations, cicatricial lesions, shortening of the fornix and symblepharon. However, the late complications of SJS/TEN cannot be predicted by the severity of the acute ocular manifestations (Fakoya et al., 2018).

The treatment modality used in patient management depends on the etiology of the disease. SSJ has a significant impact on public health due to the high mortality rate, which varies from 20 to 25%. In Brazil, the incidence of SJS is between 1.2 and 6 per million/year and of TEN from 0.4 to 1.2 per million per year, occurring mainly in adult men (Rocha et al., 2018).

Given the above, the present study aims to report a case of Stevens-Johnson Syndrome, in northern Brazil, emphasizing the clinical characteristics and the treatment adopted, to contribute to the medical literature on cases of pharmacopeias. For this purpose, data were collected from the medical records, with the patient's authorization and acceptance to participate in the study and the General Hospital of Palmas, exclusively for scientific purposes. In addition, the images were captured during hospitalization, with prior authorization from the patient. The elaboration of this project is justified by the scarcity of detailed case reports on SJS available in scientific databases, as well as the importance of discussing the therapeutic approach adopted in the care of patients with this syndrome.

2 METHODOLOGY

This is a case report, approached descriptively and qualitatively, where according to Pereira et al. (2018), is characterized as research that directly collects data related to the study through access to medical records and examinations provided, with the researcher being the primary instrument. The study was approved by the Research Ethics Committee (opinion number: 5,597,114). The Free and Informed Consent

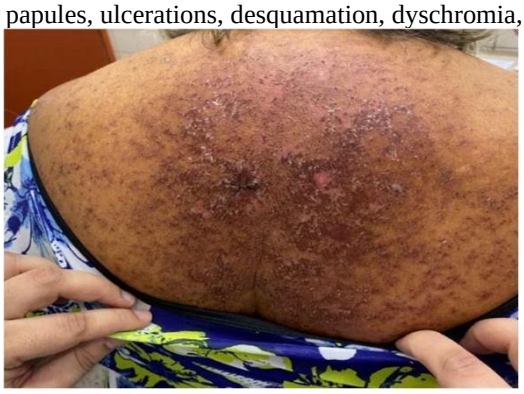
Term was elaborated on and signed by the involved parties for participation in the research and the ethical principles of the Declaration of Helsinki were respected.

3 RESULTS AND DISCUSSION

Female patient, 70 years old, retired, seen at Hospital Oswaldo Cruz (HOC) in 2021. She had had exanthematic papules all over her body for 10 days, which evolved with itching and pain, intensified with increasing ambient temperature. She manifested: inappetence, unchecked fever, conjunctival hyperemia, dizziness, nausea, syncope, sporadic hypomnesia, odynophagia, epigastralgia, dyspnea, dysuria, intense polyarthralgia and paresis of the lower limbs. 20 days after the appointment, she had two episodes of syncope; given this, lamotrigine and oxcarbazepine were prescribed by a neurosurgeon.

Patient with a pathological history of epilepsy, Parkinson's disease, and systemic arterial hypertension. In use of medications: lamotrigine, oxcarbazepine, levodopa, Benserazid, losartan and acetylsalicylic acid. At the HOC, they suspended all medications in use and transferred the patient to the Hospital Geral de Palmas (HGP) with a diagnostic hypothesis of SJS. At the HGP, the patient, on physical examination, presented: a regular general condition, eucardic, eupneic, normotensive, anicteric, cyanotic, afebrile, lucid, and oriented in time and space. On dermatological examination: papular rash on all limbs, face, and anterior and posterior trunk, with a positive Nikolsky sign (Figure 1). Eyes: erythema, enanthema, and tearing (Figure 2). Lips and tongue: edema and vesicles of serious content. Palpable cervical lymph nodes on the right side and edematous right lower limb. The requested laboratory tests showed hyponatremia and elevation of inflammatory markers. The diagnostic hypotheses were: SJS, Guillain-barré syndrome, and arboviruses.

Figure 1: Back: macules, papules, ulcerations, desquamation, dyschromia, forming a plaque lesion.



Source: The author himself

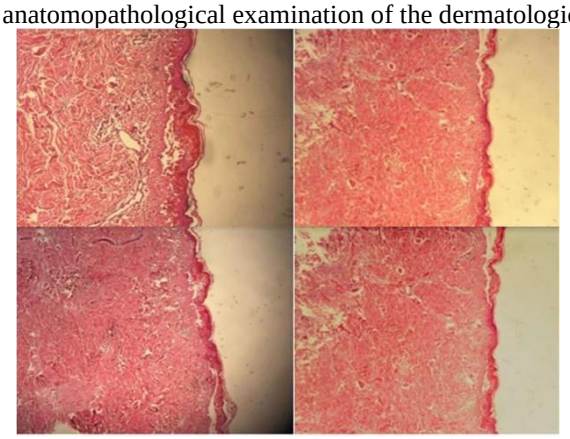
Figure 2: Left eye: erythema, enanthema, and serous discharge.

Source: The author himself

The approach was multidisciplinary, including dermatology, infectology, psychiatry, internal medicine, nursing, and nutrition. On the advice of dermatology, the case was managed as pharmacodermia and the prescription consisted of vigorous hydration, oral diet for SAH, analgesics, antiemetics, antacids, antithrombolytics, antihistamines, corticotherapy, antihypertensives, general care and replacement of the antiepileptic drugs lamotrigine and oxcarbazepine by valproate of sodium and valproic acid. Serologies for arboviruses were requested and dermatological material was collected for biopsy.

On the fourth day of hospitalization, the patient's dermatological condition improved, the laboratory tests showed no significant alterations, and after initiating the use of sodium valproate and valproic acid, there were no epileptic seizures. The anatomopathological result of the biopsy was released on the tenth day of hospitalization, with the conclusion of interface dermatosis with a perivascular pattern with numerous intra-epidermal apoptotic keratinocytes (Figure 3). In a note, the pathologist described that erythema multiforme was a possibility, requiring correlation with clinical aspects. Due to the good evolution of the condition, the patient was discharged from the hospital on the tenth day and instructed to return to the unit after fifteen days for medical follow-up.

Figure 3: anatomopathological examination of the dermatological biopsy



Source: The author himself

To detail the classification of the phenotypes of this syndrome, the following types are cited: SJS, with epidermal detachment <10% body surface area plus generalized purpuric macules or flat atypical targets; SJS–NET overlap, 10–30% detachment plus disseminated purpuric macules; TEN with spots,

detachment > 30% more disseminated macules; NET without stains, the same type of detachment but without stains. (Creamer et al., 2016). Since the case presented presents characteristics of the SSJ-NET overlay type.

Little is known about the pathophysiology, it is believed that these diseases are related to late hypersensitivity mediated by Th1 cells. There are also genetic factors, such as slow acetylators, who have difficulty clearing toxic drug metabolites; and an association of HLA major histocompatibility complex alleles with severe drug reactions was found. Histopathologically, death by apoptosis of keratinocytes, mediated by CD8 cells, occurs (Wong et al., 2016). During the acute stages of the most severe manifestations of these reactions, drug-responsive pro-inflammatory CD8+ T cells exhibit classic features of Th1 cytokine production and cytolysis. These T cells can be found at the site of lesions as well as systemically. (Mifsud et al., 2021).

Recommendations for diagnosing SJS/TEN require the collection of a complete clinical history, with special attention to recent drug exposure to identify the drug potentially causing the clinical condition and a thorough physical examination to assess the type of existing skin lesions, determination of the affected skin area and evaluation of mucosal involvement, in addition to complementary exams. To confirm the diagnosis and exclude another disease, it is also recommended to perform a skin biopsy for histopathological study. It is also important to highlight the participation of the dental surgeon in this diagnosis, as the oral involvement is intense and often appears in a primary form. (Santos et al., 2018), (Lopes et al., 2022).

The prognosis is related to the rapid identification of the causative drug and its discontinuation, it is not related to the dose or type of causative drug, and the main cause of death is associated with sepsis (Wong et al., 2016). In the reported case, the discontinuation of suspected drugs was performed on their first admission to the hospital, which may have positively influenced the evolution of the case, in agreement with the literature.

Regarding the diseases that the patient has, epilepsy and Parkinson's disease (PD) were previously diagnosed. This is characterized by the accumulation of Lewy bodies in the neuronal tissue, generating neurodegeneration of the nervous system. It is estimated that there are around 6.1 million people with PD worldwide (Cabreira et al., 2019), while in Brazil, estimates are around 36,000 new cases per year, with a prevalence of 200 thousand individuals with PD (Santos et al., 2021). Its diagnosis is fundamentally based on clinical symptoms, and investigations by tests can determine its cause. Regarding the treatment, it is also symptomatic, made from a dopaminergic drug, levodopa (Cabreira et al., 2019), which the patient uses.

Epilepsy, it can be said that it is defined by neuronal hyperactivity and brain circuits leading to excessive and synchronous electrical discharges, it affects 1% of the world population, and in Brazil, it is estimated that 340 thousand new cases are diagnosed per year. For diagnosis, it is necessary to identify the number and type of seizures, in addition to imaging tests and an electroencephalogram. Pharmacological treatment, on the other hand, occurs using antiepileptic drugs (Costa et al., 2020). In this case, the previous

diagnosis of epilepsy existed, and, due to episodes of syncope, a new encephalogram was performed and oxcarbazepine and lamotrigine were prescribed by the responsible neurosurgeon.

Antiepileptic drugs are commonly associated with hypersensitivity reactions to drugs that affect the skin, including SJS and TEN (Mifsud et al., 2021). SJS can be related to more than 100 drugs, including carbamazepine and lamotrigine, the development of this reaction with the use of anticonvulsants is rare, however, it is more common to occur in the first 2 months of use and must be monitored for at least 6 weeks, and it is also suggested that the reactions are dose-related. (Mockenhaupt et al., 2005). Regarding lamotrigine, it was identified that adverse skin reactions occur in 8.3% of patients using this drug, with 0.04% of patients developing SJS/TEN (Bloom et al., 2017). Oxcarbazepine is a 10-keto analog of carbamazepine, they differ in terms of metabolism, since oxcarbazepine and its metabolites are almost completely excreted in the urine, while carbamazepine has its metabolites as the cause of side effects; therefore, OXC is considered safer. OXC-induced SJS/TEN is extremely rare, with an incidence of 0.5–6/1,000,000 in 1 year in the normal population, and only a few cases are described (Beken et al., 2017). Thus, it is assumed that the cause for this adverse reaction came from the use of prescribed anticonvulsants since the predisposition of occurrence and the time of susceptibility are compatible with what is pointed out in the research. However, it is not possible to say exactly which of the drugs caused it, or if it was the result of an interaction.

In the literature, for the treatment, it is essential the early withdrawal of the drugs suspected of being the cause, admission to the intensive care unit, in addition to symptomatic care, such as airway care, temperature control, venous access away from the lesions, electrolyte replacement, skin hydration, gastric protectors, anticoagulation, eye drops, and saline solution in ocular lesions and cleaning and hydration of the skin. Drugs such as immunoglobulins, cyclosporine, cyclophosphamide, pentoxifylline, and thalidomide can also be used, in addition to daily observations and performing cultures to identify and treat infections early. There are several updates in treatments with experimental measures that demonstrate some results, such as the use of amniotic membrane derivatives to cover the body surface. (Roviello et al., 2019), (Lipový et al., 2021).

At the first visit, there was correct management with the early suspension of the suspected drugs and correct hypothesis, in addition to hydro electrolytic replacement and referral to the intensive care unit. Subsequently, there was the recommended analgesia, antiemetics, antacids, antihistamines, and corticosteroids. There was also the use of the saline solution and eye drops in the eyes, in addition to corticosteroids in the lesions and management to prevent thrombosis, in agreement with what was found in sources.

To assess the probability of death in cases of SJS/TEN, the SCORTEN score is used, which evaluates the following criteria: age over 40 years, presence of malignancy, tachycardia above 120 bpm, percentage of epidermal detachment above 10% in admission, serum urea level above 10 mmol per liter, serum glucose above 14 mmol per liter and bicarbonate below 20 mmol per liter (Bastujigarin et al., 2000).

In the reported case, the patient only fulfilled the age criterion and some data were not evaluated, so it was not possible to estimate her risk.

4 CONCLUSION

Based on the reported case, the importance of the performance of a multidisciplinary team in the thorough investigation of the clinical history together with laboratory findings associated with the origin of the erythematous macules is observed, starting the therapy in the face of the diagnostic hypothesis, aiming to inhibit the clinical worsening of the patient. Within this therapy, the suspension of the medications in use is significant, as they are possibly responsible for the reaction, in addition to the symptomatic treatment associated with hydroelectrolytic replacement, promoting a faster improvement of the patient. Therefore, the reported case becomes an instrument for discussing a relevant situation in hospitals and reiterates the need for further studies on the subject, which deserves attention due to the high incidence and the high risk of associated mortality.

REFERENCES

Beken, b., et al. (2017). Oxcarbazepine-induced stevens–johnson syndrome: a pediatric case report. Oxford medical case reports, 2017(6), omx028.

Bloom, r., & amber, k. T. (2017). Identifying the incidence of rash, stevens-johnson syndrome and toxic epidermal necrolysis in patients taking lamotrigine: a systematic review of 122 randomized controlled trials. Anais brasileiros de dermatologia, 92, 139-141.

Bulisani, a. C. P, et al. (2006). Síndrome de stevens-johnson e necrólise epidérmica tóxica em medicina intensiva. Revista brasileira de terapia intensiva, 18, 292-297.

Cabreira, v., & massano, j. (2019). Doença de parkinson: revisão clínica e atualização. Acta médica portuguesa, 32(10).

Cai, z. R.,et al. (2020). Toxic epidermal necrolysis associated with pembrolizumab. Journal of oncology pharmacy practice, 26(5), 1259-1265.

Creamer, d., et al. (2016). Uk guidelines for the management of stevens–johnson syndrome/toxic epidermal necrolysis in adults 2016. British journal of dermatology, 174(6), 1194-1227.
De oliveira costa, l. L., et al. (2020). Update on epilepsy: literature review. Rev med (são paulo), 99(2), 170-81.

Fakoya, a. O. J., et al. (2018). Stevens-johnson syndrome and toxic epidermal necrolysis; extensive review of reports of drug-induced etiologies, and possible therapeutic modalities. Open access macedonian journal of medical sciences, 6(4), 730.

Fouchard, n., et al. (2000). Scorten: a severity-of-illness score for toxic epidermal necrolysis. Journal of investigative dermatology, 115(2), 149-153.

Grünwald, p., et al. (2020). Erythema multiforme, stevens-johnson syndrome/toxic epidermal necrolysis–diagnosis and treatment. Jddg: journal der deutschen dermatologischen gesellschaft, 18(6), 547-553.

Lipový, b., et al. (2021). Case report: wound closure acceleration in a patient with toxic epidermal necrolysis using a lyophilised amniotic membrane. Frontiers in bioengineering and biotechnology, 9, 649317.

Bomfim lopes, a. C. M., et al. (2022). Síndrome de stevens johnson e necrólise epidérmica tóxica–a importância do cirurgião dentista no diagnóstico stevens johnson syndrome and toxic epidermal necrolysis-the importance of the dental surgeon in the diagnosis. Brazilian journal of health review, 5(3), 10052-10063.

Mifsud, n. A., et al. (2021). Carbamazepine induces focused t cell responses in resolved stevens-johnson syndrome and toxic epidermal necrolysis cases but does not perturb the immunopeptidome for t cell recognition. Frontiers in immunology, 12, 653710.

Mockenhaupt, m., et al. (2005). Risk of stevens–johnson syndrome and toxic epidermal necrolysis in new users of antiepileptics. Neurology, 64(7), 1134-1138.

Neto, h. C., et al. (2019). Síndrome de stevens-johnson associada a fenitoína em pós-operatório de hemorragia intraparenquimatosa cerebral: relato de caso. Fag journal of health (fjh), 1(4), 169-184.

Pereira, a. S. Et al. (2018). Metodologia da pesquisa científica. [e-book]. Santa maria. Ed. Uab/nte/ufsm. Available: https://repositorio.ufsm.br/bitstream/handle/1/15824/lic_c

Rocha, l. P. S. (2018). Relato de caso e revisão da literatura de síndrome de stevens-johnson associada a episódio de varicela. Arquivos catarinenses de medicina, 47(3), 226-234.

Roviello, c. F., et al. (2019). Manifestações e tratamento da necrólise epidérmica tóxica e da síndrome de stevens johnson/manifestations and treatment of toxic epidermic necrolysis and stevens johnson's syndrome/manifestaciones y tratamiento de la necrolisis epidérmica tóxica... Journal health npeps, 4(1), 319-329.

Santos, g. F., et al. (2022). Doença de parkinson: padrão epidemiológico de internações no brasil. Research, society and development, 11(1).

Shanbhag, s. S., et al. (2020). Multidisciplinary care in stevens-johnson syndrome. Therapeutic advances in chronic disease, 11, 2040622319894469.

Wong, a., et al. (2016). Stevens-johnson syndrome and toxic epidermal necrolysis: a review. Revista da associação médica brasileira, 62, 468-473.