RCMOS – Multidisciplinary Scientific Journal of Knowledge.
ISSN: 2675-9128. São Paulo-SP.
Year IV, v.1, n.1, jan./ jul. 2024. | submission: 2024-09-30 | accepted: 2024-10-02 | publication: 2024-10-04

SEVERE SKIN REACTIONS: A COMPREHENSIVE OVERVIEW OF STEVENS-JOHNSON SYNDROME, ITS ETIOLOGY, PATHOPHYSIOLOGY AND THERAPEUTIC APPROACHES *SEVERE CUTANEOUS REACTIONS: A COMPREHENSIVE OVERVIEW OF STEVENS-JOHNSON SYN-DROME, ITS ETIOLOGY, PATHOPHYSIOLOGY, AND THERAPEUTIC APPROACHES*

Luana Gabriela Alves da Silva– Federal University of Health Sciences of Porto Alegre Taynne da Silva Viana– University Center of Belo Horizonte
Julia Silva Santos– Belo Horizonte University Center

SUMMARY
Stevens-Johnson syndrome (SJS) is a rare and serious condition characterized by epidermal detachment and lesions in the mucous membranes, mainly in the mouth, eyes and genitals. Often triggered by adverse reactions to medications such as antibiotics and anticonvulsants, SJS can also be caused by viral infections and, rarely, neoplasia. SJS forms a spectrum with Toxic Epidermal Necrolysis (TEN), differing in the extent of the affected skin: in SJS, less than 10% of the body surface is affected, while in TEN the involvement exceeds 30%. Although rare, with an incidence of 1.2 to 6 cases per million people, SJS has high mortality and morbidity, with complications such as serious infections and permanent damage to the skin and mucous membranes. Early diagnosis is crucial, based on characteristic lesions and history of recent medication use. In some cases, a biopsy is necessary to confirm the diagnosis. Treatment involves a multidisciplinary approach, with intensive care, immediate withdrawal of the offending drug, and immune modulation with corticosteroids or intravenous immunoglobulin. Although new therapies, such as cyclosporine and special wound dressings, are being explored, there is still a need for consensus on the ideal protocol, as well as advances in personalized diagnosis and treatment.

Keywords: Stevens-Johnson syndrome. Hypersensitivity. Dermatological emergency.

ABSTRACT
Stevens-Johnson Syndrome (SJS) is a rare and severe condition characterized by epidermal detachment and mucosal lesions, primarily affecting the mouth, eyes, and genitals. Often triggered by adverse drug reactions, such as antibiotics and anticonvulsants, SJS can also be caused by viral infections and, rarely, neoplasms. SJS forms a spectrum with Toxic Epidermal Necrolysis (TEN), differing in the extent of skin involvement: in SJS, less than 10% of the body surface is affected, while in TEN, the involvement exceeds 30%. Although rare, with an incidence of 1.2 to 6 cases per million people, SJS carries high morbidity and mortality, leading to complications such as severe infections and permanent damage to the skin and mucous membranes. Early diagnosis is crucial, based on characteristic lesions and a recent history of medication use. In some cases, a biopsy is necessary to confirm the diagnosis. Treatment involves a multidisciplinary approach, including intensive care, immediate discontinuation of the causative drug, and immune modulation with corticosteroids or intravenous immunoglobulin. While new therapies, such as cyclosporine and special wound dressings, are being explored, there is still a need for consensus on the ideal treatment protocol, as well as advances in personalized diagnosis and treatment.
Keywords: Stevens-Johnson Syndrome. Hypersensitivity. Dermatological Emergency

1. INTRODUCTION

Stevens-Johnson syndrome (SJS) is a rare and severe hypersensitivity reaction characterized by extensive skin lesions and mucosal involvement, often resulting in significant systemic complications and high mortality. Originally described in 1922 by Stevens and Johnson, it was initially diagnosed as a severe form of erythema multiforme, a dermatological condition first identified in 1866 by Ferdinand Von Hebra. However, with advances in research, a distinction was established between erythema multiforme major and SJS, consolidating it as a unique and extremely serious pathology (PRADO et al., 2024).

SJS, together with Toxic Epidermal Necrolysis (TEN), forms a spectrum of skin diseases severe, differing mainly in the extent of the involvement of the body surface: while SJS affects less than 10% of the skin, TEN can affect more than 30%, leading to a higher risk of death. Both, however, share similar clinical characteristics, such as high fever, skin blisters, epidermal desquamation and painful lesions in mucous membranes, especially in the mouth, eyes and genitals (SILVA et al., 2018).

Studies indicate that the main cause of these syndromes is hypersensitivity to medications, with 50 to 80% of SJS cases being related to drug use (VIEIRA, 2016). Although rare, with an incidence of 1.2 to 6 per million people per year in Brazil, SJS represents a significant clinical challenge due to its high mortality rate and the long-term complications it can generate, such as vision loss and severe damage to the skin and mucous membranes.

Thus, the management of SJS requires a multidisciplinary and urgent approach, with immediate interruption of the underlying cause and intensive clinical support to minimize systemic damage and promote recovery. The severity of the condition and its devastating impact on patients' quality of life make further investigations and advances in the diagnosis and treatment of this complex disease essential.

2. MATERIAL AND METHOD

This study is a Bibliographic Review carried out from August to October 2024. Literature searches were performed in the PubMed and SciELO databases using the following Health Sciences Descriptors (DeCS): (Stevens-Johnson Syndrome) AND (Hypersensitivity) AND (Dermatological Emergency). The inclusion criteria were: articles in Portuguese, English, Spanish and French, available in full. The exclusion criteria were: duplicate articles, available in abstract form, that did not directly address the studied proposal and that did not meet the other inclusion criteria. After associating the descriptors used in the researched databases, a total of 18 articles were found. After applying the inclusion and exclusion criteria, 10 articles were selected, and a total of 9 studies were used to compose the collection.

3. RESULTS AND DISCUSSION

Stevens-Johnson syndrome (SJS) is a rare and severe mucocutaneous reaction characterized by epidermal detachment and skin lesions in areas of skin and mucous membranes. Although it is an uncommon condition, with an annual incidence of approximately 1.7 cases per million people, SJS has high morbidity and mortality, especially when not diagnosed and treated early. Toxic Epidermal Necrolysis (TEN), often compared to SJS, differs in the severity and extent of epidermal involvement. In Stevens-Johnson syndrome, epidermal detachment affects less than 10% of the body surface, while in TEN this value exceeds 30%. The severity of SJS lies not only in skin destruction, but also in the involvement of multiple mucous membranes, such as the oral and ocular cavities, in addition to the potential progression to systemic complications (SILVA et al., 2018).

The development of Stevens-Johnson Syndrome is usually triggered by adverse drug reactions, mainly due to the use of antibiotics, anticonvulsants and non-steroidal anti-inflammatory drugs, which are the main causes, responsible for approximately 30% to 50% of cases (VIEIRA, 2016). After a few days or weeks of using the medications mentioned above, some individuals may initiate a dysregulated immune cascade, which results in the destruction of keratinocytes and the separation between the epidermis and the dermis. Early recognition of signs and immediate removal of the causative agent are essential to reduce disease progression, minimize morbidity, and improve patient prognosis. SJS, which is more common in women and adults, is an extremely urgent medical condition, requiring intensive hospital care and multidisciplinary support (PRADO et al., 2024)

The etiology of SJS is strongly related to a dysregulated immune response, triggered by medications or, less frequently, by viral infections, vaccines and neoplasms. Genetic predisposition plays an important role in the development of the disease, with certain HLA (Hypertensive Antigen) alleles being associated with the development of the disease.

Human Leukocyte) appear to increase the risk of adverse reactions. The presence of specific genetic factors results in an abnormal interaction between the immune system and drugs, leading to the inadequate activation of CD8+ T cells, which are responsible for initiating the process of keratinocyte apoptosis (SANTOS et al., 2018). The widespread apoptosis of these cells compromises skin integrity, facilitating fluid loss and invasion by pathogens. This process is exacerbated by the release of granzymes and perforins, proteins that increase cell membrane permeability, promoting skin necrosis. The characteristic tissue destruction is what differentiates SJS from other less serious dermatological conditions, such as erythema multiforme. Simultaneously, uncontrolled activation of the immune system aggravates the condition, leading to a continuous cycle of inflammation and necrosis. Furthermore, continuous tissue damage creates an environment conducive to secondary infections, further complicating the clinical picture (VIEIRA et al., 2021).

Clinically, Stevens-Johnson Syndrome initially presents with nonspecific symptoms, such as fever, malaise, headache, rhinitis and myalgias, which can be easily confused with common viral conditions. These symptoms are followed, within a few days, by characteristic skin lesions, which include purpuric macules, atypical target lesions and disseminated blisters. The blisters tend to evolve into areas of epidermal detachment, exposing large areas of denuded skin, which contributes to intense pain and an increased risk of infection. The mucous membranes are also frequently affected, especially those of the oral cavity, where the rupture of blisters results in painful ulcers covered by fibrinopurulent exudate (VIEIRA et al., 2021).

The diagnosis of Stevens-Johnson syndrome is primarily clinical, based on the characteristics of the skin and mucosal lesions, as well as the recent history of drug exposure. However, diagnostic confirmation often requires skin biopsy, which demonstrates keratinocyte necrosis and cleavage at the dermoepidermal junction, confirming the observed tissue destruction. The differential diagnosis includes a number of other serious dermatoses, such as pemphigus vulgaris, staphylococcal scalded skin syndrome, and lichen planus, all of which share some clinical features with SJS but have different underlying mechanisms (NETO et al., 2019).

Furthermore, identification of the offending drug is a crucial part of diagnosis and management. Drug challenge tests are rarely used due to the high risk of severe recurrent reactions. Therefore, a detailed medical history and cautious elimination of medications are essential to reduce the risk of future attacks. More advanced diagnostic tools, such as the detection of immunological biomarkers, are still under development but may in the future help predict which patients are at greatest risk (ROVIELLO et al., 2019).

Treatment of SJS involves a multidisciplinary approach, with the main focus on immediate withdrawal of the causative medication and clinical stabilization of the patient. Initial interventions include intensive care in burn units, due to the extensive nature of the skin lesions, in addition to fluid replacement and strict pain control. Anticoagulants are often administered to prevent thromboembolic complications, and care of oral and ocular lesions is also essential to avoid long-term sequelae. Topical solutions of anesthetics and antibiotics help control pain and prevent secondary infections in the mucous membranes and skin (ROVIELLO et al., 2019).

Systemic pharmacologic therapies, such as intravenous immunoglobulin and corticosteroids, have been used to modulate the immune response and limit disease progression. Although cyclosporine has also shown benefit in some studies, there is still no widely accepted therapeutic protocol.
due to the rarity of SJS and the variability in response to treatments. In addition, the use of dressings
of silver hydroalginate on skin lesions has shown effectiveness in accelerating healing, although
its high cost may limit its availability in some regions (SILVA et al., 2018).

FINAL CONSIDERATIONS

Stevens-Johnson syndrome (SJS) is a serious and challenging medical condition with high morbidity and mortality, especially when not treated early. The main characteristic of SJS is epidermal detachment in less than 10% of the body surface and involvement of the mucous membranes,

which differentiates it from Toxic Epidermal Necrolysis (TEN). Early diagnosis, combined with immediate interruption of the triggering agent, is essential for a better prognosis and reduction of disease progression, which can result in systemic complications and increase the risk of serious infections (COELHO et al., 2021).

The etiology of SJS is predominantly related to adverse drug reactions, especially antibiotics, anticonvulsants, and nonsteroidal anti-inflammatory drugs. The dysregulated immune mechanism that results in keratinocyte destruction and skin detachment is largely influenced by genetic factors, such as specific HLA alleles. These genetic factors predispose certain individuals to an exaggerated immune response to drugs, resulting in epidermal necrosis and increased skin permeability. This immunological complexity makes SJS a difficult disease to predict and treat, highlighting the need for a greater understanding of pharmacogenetics in the management of the syndrome (ROVIELLO et al., 2019).

The diagnosis of SJS is fundamentally clinical, based on the observation of the characteristics of the skin and mucosal lesions, as well as the history of recent medication use. However, confirmation often requires a skin biopsy, which can demonstrate the histological changes characteristic of the disease. Differential diagnosis with other serious dermatoses is crucial to avoid errors in clinical management. In addition, accurate identification of the triggering agent is extremely important, since re-exposure to the medication can trigger new reactions, worsening the patient's clinical condition (VIEIRA et al., 2016).

The treatment of SJS is complex and requires a multidisciplinary approach involving intensive care and comprehensive clinical support. Immediate removal of the causative agent, management of skin lesions, and modulation of the immune response with immunoglobulins or corticosteroids are essential steps in treatment. Although new therapeutic approaches, such as cyclosporine and specialized dressings for lesions, are being explored, there is still a lack of consensus on the ideal protocol (ROVIELLO et al., 2019). The development of new diagnostic tools and personalized therapies based on genetics may be an important advance in the future to improve clinical outcomes in patients with SJS.

REFERENCES

COELHO, Amanda Batista et al. Stevens-Johnson Syndrome: a dermatological disease or a pharmacodermia?**Brazilian Journal of Health Review**, v. 4, no. 4, p. 15115-15125, 2021.

NETO, Humberto Codagnoni et al. Stevens-Johnson syndrome associated with phenytoin in the postoperative period of cerebral intraparenchymal hemorrhage: case report.**Fag Journal Of Health (FJH)**, v. 1, no. 4, p. 169- 184, 2019.

PRADO, Anna Clara Alves Martins et al. STEVENS-JOHNSON SYNDROME: CLINICAL MANIFESTATIONS AND SURGICAL IMPLICATIONS.**Ibero-American Journal of Humanities, Sciences and Education**, v. 10, no. 9, p. 1048-1057, 2024.

ROVIELLO, Cristina Ferreira et al. Manifestations and treatment of toxic epidermal necrolysis and Stevens-Johnson syndrome.**Journal Health NPEPS**, v. 4, no. 1, p. 319-329, 2019.

SANTOS, VM et al. Stevens-Johnson syndrome - case report. Journal of Medicine and Health of Brasília, v.7, n.3, p. 329-38, 2018.

SILVA, GS et al. Case report and literature review of Stevens-Johnson syndrome associated with an episode of chickenpox. Arquivos Catarinenses de Medicina, v.47, n.3, p. 226-234, Oct 2018. Available at: http://www.acm.org.br/acm/seer/index.ph/arquivos/article/view/464. Accessed on: September 12, 2024.

VIEIRA, Natália Abreu Silva et al. Stevens-Johnson syndrome: integrative review.**Sustinere Magazine**, v. 9, no. 1, p. 96-107, 2021.

VIEIRA, KKF Stevens-Johnson syndrome and toxic epidermal necrolysis: dermatological emergency.

Report
case study and literature review. Federal University of Roraima. 2016.