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NSAID (nonsteroidal anti-inflammatory drugs) Induced Stevens Johnson Syndrome in a 50-year-old woman: A case study

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ABSTRACT

Stevens-Johnson Syndrome (SJS) is a severe and rare adverse drug reaction associated with significant morbidity and mortality. Although SJS is commonly triggered by multiple drugs, non-steroidal anti-inflammatory drugs (NSAIDs), including diclofenac, have been frequently implicated. A middle-aged woman, who is 50 years old, has a prior medical record of high blood pressure, type 2 diabetes, and has recently suffered from a pulmonary embolism. She was later admitted to the intensive care unit (ICU), where she was ultimately diagnosed with Steven Johnson syndrome. Careful drug selection, close monitoring of patients with predisposing factors, and prompt identification of adverse events are crucial to prevent severe drug reactions.

1. Introduction

Stevens-Johnson Syndrome (SJS) is a rare but serious reaction of the skin and mucous membranes that can be caused by certain medications, infections, or autoimmune diseases [1]. It is estimated that the annual incidence rate of SJS in the US is around 3.4–6.1 per million population [2]. SJS is characterized by flu-like symptoms and a painful rash that spreads and blisters [3]. It can lead to severe complications, including skin infections, changes in skin color, scarring, and problems with organs such as the lungs, liver, and kidneys [4]. It can also cause long-term inflammation or vision problems in the eyes [5]. Drug-associated SJS is considered the most severe type of drug hypersensitivity reaction and can be life-threatening, with a mortality rate of up to 50% [6].

One medication that has been linked to the development of SJS is Diclofenac, which belongs to the nonsteroidal anti-inflammatory drug (NSAID) group [7]. Diclofenac is commonly used for its anti-inflammatory properties to reduce swelling, pain, or fever [8]. However, it should be avoided by individuals who have had allergic reactions to diclofenac or other NSAIDs, experienced side effects from taking NSAIDs, or have certain medical conditions such as lupus, hypertension, blood clotting disorders, Crohn's disease or ulcerative colitis, heart failure, severe liver or kidney disease, stomach ulcers, bleeding in the stomach or intestines, or are pregnant, planning to get pregnant, or breastfeeding [9].

Given the potential for serious morbidity and mortality associated with SJS, it is crucial to promptly identify and discontinue the causative medication. By understanding the risk factors and potential drug interactions, healthcare professionals can minimize the likelihood of developing SJS and improve patient outcomes. In particular, individuals with lupus should be cautious when considering the use of diclofenac, as it may exacerbate their existing skin problems and increase the risk of developing SJS. The work has been reported in line with the SCARE 2020 Criteria [10].

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2. Presentation of case

A 50-year-old woman with a medical history of hypertension, type 2 diabetes, and recent development of pulmonary embolism was admitted to the ICU. The patient's condition required aggressive treatment, including heparin at a dose of 1000 units per hour. Additionally, a course of antibiotics, including meropenem and metronidazole, was initiated to target potential infections.

To manage the patient's pain, the physician prescribed diclofenac suppositories. Two days after the initiation of diclofenac treatment, the patient's general status began deteriorating, presenting respiratory distress and inadequate ventilation. Consequently, she required intubation and initiation of mechanical ventilation.

Following intubation, the patient's skin started peeling and erythematous lesions were observed throughout her body. Dermatology consultation was requested, and the patient was diagnosed with SJS triggered by diclofenac usage (Fig. 1.).

Upon the diagnosis of SJS, diclofenac was immediately discontinued. Supportive measures were initiated, including meticulous wound care, strict infection control, fluid resuscitation, nutritional support, and pain management. The patient was also started on systemic corticosteroids to modulate the immune response.

The patient's condition gradually stabilized and showed signs of improvement. Widespread skin detachment was managed, and replacement of damaged tissues occurred. Supportive therapy lasted for several weeks, emphasizing strict monitoring of vital signs, fluid and electrolyte balance, prevention of secondary infections, and pain control. Despite all efforts, the patient succumbed to respiratory failure and severe infection.

3. Discussion

SJS is a severe and potentially life-threatening hypersensitivity reaction that can be triggered by various medications [7]. In this case study, we present a 50-year-old woman who developed SJS after using a diclofenac suppository. The aim of this discussion is to explore the possible underlying mechanisms, highlight the importance of prompt recognition and management, and discuss the implications of this case.

The development of SJS in our patient following diclofenac suppository use raises concerns about the potential for this medication to induce severe adverse reactions [8]. Diclofenac is a NSAID commonly used for its analgesic and anti-inflammatory properties [9]. Although SJS is a rare adverse event associated with diclofenac use, previous reports have suggested a potential link between the drug and the syndrome.

It is important to note that SJS is a multifactorial condition that can be triggered by various factors, including genetic predisposition, viral infections, and medication use [11]. In our case, the temporal relationship between the initiation of diclofenac and the development of SJS suggests a possible drug-induced reaction. However, further investigations, such as patch testing or genetic studies, would be necessary to confirm the causal relationship.

The pathogenesis of SJS involves a complex interplay between the immune system and the drug or its metabolites [12]. It is hypothesized that certain drugs, including diclofenac binding to endogenous proteins and triggering an immune response. This immune response leads to the destruction of epidermal cells, resulting in the characteristic skin manifestations seen in SJS [13]. The severity of the reaction can vary, with SJS being the milder form and toxic epidermal necrolysis (TEN) representing the more severe end of the spectrum [14].

Prompt recognition and management of SJS are crucial to prevent further complications and improve patient outcomes [15]. In our case, the patient presented with fever, mucosal involvement, and a characteristic skin rash, which prompted the diagnosis of SJS. Immediate discontinuation of diclofenac, supportive care, and consultation with a dermatologist were essential in managing the patient's condition. Early recognition and appropriate management can help reduce morbidity and mortality associated with SJS [16].

The implications of this case study highlight the need for healthcare professionals to be aware of the potential risk of SJS associated with diclofenac use. Patient education regarding the signs and symptoms of SJS and the importance of seeking medical attention in case of any adverse reactions is crucial. Furthermore, healthcare providers should consider alternative treatment options or exercise caution when prescribing diclofenac to patients with a history of hypersensitivity reactions.

Educating patients about COVID-19 and potential drug reactions is crucial for nurses in ensuring the well-being of those under their care [17–23]. By providing clear and concise information, nurses empower patients to make informed decisions about their health. In the context of COVID-19, this education can include guidance on preventive measures, symptom recognition, and vaccination information [24–29]. Additionally, informing patients about potential drug reactions helps in managing their medications effectively and reduces the risk of adverse effects [3–31]. Through education, nurses play a pivotal role in promoting patient safety, enabling individuals to actively participate in their own healthcare, and fostering a sense of trust and confidence in the healthcare system [32].

4. Conclusion

This case highlights the importance of vigilance when prescribing medications, especially in patients with multiple comorbidities. Diclofenac, although widely used for its analgesic effects, carries the risk of severe adverse effects such as Stevens-Johnson syndrome. It is crucial that healthcare professionals recognize these potential complications and exercise caution when prescribing diclofenac.

By understanding and identifying the risks associated with



Fig. 1. Stevens-Johnson Syndrome.

diclofenac, healthcare providers can minimize adverse outcomes and ensure patient safety. Promoting awareness about medication side effects, particularly in vulnerable populations, is vital for optimizing patient care and reducing preventable morbidity and mortality.

Ethical approval

The ethics committee of Urmia University of Medical Sciences approved the study (Ethical code: IR.UMSU.REC.1402.348).

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None.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

CRediT authorship contribution statement

Pariya Mohsennezhad: Formal analysis, Data curation. Raheleh Pourbahram: Writing – review & editing. Elaheh Salamat: Supervision. Naser Parizad: Formal analysis, Supervision, Validation, Visualization. Yousef Mohammadpour: Project administration. Samaneh Bazbandi: Funding acquisition. Navid Faraji: Writing – original draft, Validation. Rasoul Goli: Data curation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

No data was used for the research described in the article.

References

- R. Frantz, S. Huang, A. Are, K. Motaparthi, Stevens–Johnson syndrome and toxic epidermal necrolysis: a review of diagnosis and management, Medicina 57 (9) (2021) 895. Aug 28.
- [2] S.S. Shanbhag, J. Chodosh, C. Fathy, J. Goverman, C. Mitchell, H.N. Saeed, Multidisciplinary care in Stevens-Johnson syndrome, Ther. Adv. Chronic Dis. (2020). Apr;11:2040622319894469.
- [3] N.J. Maloney, V. Ravi, K. Cheng, D.Q. Bach, S. Worswick, Stevens-Johnson syndrome and toxic epidermal necrolysis-like reactions to checkpoint inhibitors: a systematic review, Int. J. Dermatol. 59 (6) (2020) e183–e188 (Jun).
- [4] M.O. Elboraey, E.E. Essa, Stevens-Johnson syndrome post second dose of Pfizer COVID-19 vaccine: a case report, Oral. Surg., Oral. Med., Oral. Pathol. Oral. Radiol. 132 (4) (2021) e139–e142. Oct 1.
- [5] D. Zimmerman, N.H. Dang, Stevens–Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN) immunologic reactions, Oncol. Crit. Care (2020) 267–280.
- [6] P. Mansouri, R. Chalangari, K. Martits-Chalangari, N. Mozafari, Stevens-Johnson syndrome due to COVID-19 vaccination, Clin. Case Rep. 9 (11) (2021) e05099 (Nov).
- [7] M.P. Kumar, T.S. Kumar, D. Girirajsekhar, NSAID induced Stevens Johnson Syndrome or tumor epidermal necrolysis, Indian J. Pharm. Pract. 15 (3) (2022).
- [8] Q.H. Shao, X.D. Yin, N. Zeng, Z.X. Zhou, X.Y. Mao, Y. Zhu, B. Zhao, Z.L. Li, Stevens-Johnson Syndrome following non-steroidal anti-inflammatory drugs: a real-world analysis of post-marketing surveillance data, Front. Pediatr. 10 (2022) 896867. May 6.
- [9] M. Mockenhaupt, J.P. Kelly, D. Kaufman, R.S. Stern, SCAR Study Group. The risk of Stevens-Johnson syndrome and toxic epidermal necrolysis associated with nonsteroidal antiinflammatory drugs: a multinational perspective, J. Rheumatol. 30 (10) (2003) 2234–2240. Oct 1.

- [10] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, A. Kerwan, A. Thoma, et al., The SCARE 2020 guideline: updating consensus Surgical CAse REport (SCARE) guidelines, Dec 1, Int. J. Surg. 84 (2020) 226–230, https://doi.org/10.1016/j. ijsu.2020.10.034.
- [11] L. Cheng, Current pharmacogenetic perspective on Stevens-Johnson syndrome and toxic epidermal necrolysis, Front. Pharmacol. 12 (2021) 588063. Apr 26.
- [12] A. Jacobsen, B. Olabi, A. Langley, J. Beecker, E. Mutter, A. Shelley, B. Worley, T. Ramsay, A. Saavedra, R. Parker, F. Stewart, Systemic interventions for treatment of Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and SJS/ TEN overlap syndrome, Cochrane Database Syst. Rev. (3) (2022).
- [13] S. Singh, S. Jakati, S.S. Shanbhag, A.M. Elhusseiny, A.R. Djalilian, S. Basu, Lid margin keratinization in Stevens-Johnson syndrome: review of pathophysiology and histopathology, Ocul. Surf. 21 (2021) 299–305. Jul 1.
- [14] L. Seminario-Vidal, D. Kroshinsky, S.J. Malachowski, J. Sun, A. Markova, T. M. Beachkofsky, B.H. Kaffenberger, E.N. Ergen, M. Mauskar, A. Bridges, C. Calhoun, Society of Dermatology Hospitalists supportive care guidelines for the management of Stevens-Johnson syndrome/toxic epidermal necrolysis in adults, J. Am. Acad. Dermatol. 82 (6) (2020) 1553–1567. Jun 1.
- [15] I. Torres-Navarro, Á. Briz-Redón, R. Botella-Estrada, Systemic therapies for Stevens–Johnson Syndrome and Toxic Epidermal Necrolysis: a SCORTEN-based systematic review and meta-analysis, J. Eur. Acad. Dermatol. Venereol. 35 (1) (2021) 159–171 (Jan).
- [16] K. Kridin, M.C. Brüggen, S.L. Chua, A. Bygum, S. Walsh, M.C. Nägeli, V. Kucinskiene, L. French, F. Tétart, B. Didona, B. Milpied, Assessment of treatment approaches and outcomes in Stevens-Johnson syndrome and toxic epidermal necrolysis: insights from a pan-European multicenter study, JAMA Dermatol. 157 (10) (2021) 1182–1190. Oct 1.
- [17] N. Parizad, R. Goli, N. Faraji, M. Mam-Qaderi, R. Mirzaee, N. Gharebaghi, R. Baghaie, H. Feizipour, M.M. Haghighi, Effect of guided imagery on anxiety, muscle pain, and vital signs in patients with COVID-19: a randomized controlled trial, Complement. Ther. Clin. Pract. 43 (2021) 101335. May 1.
- [18] N. Talebiazar, B. Choobianzali, A. Hassanpour, R. Goli, S. Shakorzadeh, M. Ghalandari, The effect of hypnotherapy on the hospital anxiety in three children with cancer: a case report, Int. J. Surg. Case Rep. 93 (2022) 106961. Apr 1.
- [19] M. Jasemi, R. Goli, R.E. Zabihi, H. Khalkhali, Educating ethics codes by lecture or role-play; which one improves nursing students' ethical sensitivity and ethical performance more? A quasi-experimental study, J. Prof. Nurs. 40 (2022) 122–129. May 1.
- [20] N. Aghakhani, N. Faraji, V. Alinejad, R. Goli, J. Kazemzadeh, The effect of guided imagery on the quality and severity of pain and pain-related anxiety associated with dressing changes in burn patients: a randomized controlled trial, Burns 48 (6) (2022) 1331–1339. Sep 1.
- [21] R. Goli, M. Arad, M. Mam-Qaderi, N. Parizad, Comparing the effects of geranium aromatherapy and music therapy on the anxiety level of patients undergoing inguinal hernia surgery: a clinical trial, Explore 18 (1) (2022) 57–63. Jan 1.
- [22] N. Parizad, R. Goli, R. Mirzaee, R. Baghaie, H. Habibzadeh, Satisfaction with nursing care and its related factors in patients with COVID-19: a descriptive correlational study, J. Educ. Health Promot. (2021) 10.
- [23] B. Choobianzali, S. Shakorzadeh, R. Goli, Oral hydration therapy is an alternative approach to prevent nausea and vomiting in patients with COVID-19: a letter to the editor, Int. J. Surg. Case Rep. 91 (2022) (Feb).
- [24] N.A. Talebi-Azar, B.C. Anzali, R.A. Goli, COVID-19 and its mental health effects on nurses and health workers–a narrative review, Pak. J. Med. Health Sci. 14 (2020) 1453–1456.
- [25] H. Feizipour, R. Goli, N. Gharebaghi, A. Kiani, Comparing mental health status between health staffs with and without direct contact with the covid-19 virus in hospital wards: a descriptive-analytical study, Nurs. Midwifery J. 20 (10) (2023) 830–841.
- [26] M. Arad, L. Alilu, H. Habibzadeh, H. Khalkhali, R. Goli, Effect of spiritual intelligence training on nurses' skills for communicating with patients-an experimental study, J. Educ. Health Promot. 11 (2022).
- [27] P. Ghodsi Astan, R. Goli, M. Hemmati Maslakpak, J. Rasouli, L. Alilu, The effect of evidence-based nursing education on nurses' clinical decision making: a randomized controlled trial, Health Sci. Rep. 5 (5) (2022) e837 (Sep).
- [28] M.A. Jasemi, R.E. Rasoulgoli, H. Khalkhali, Effects of teaching nursing codes of ethics through lecture on moral sensitivity and moral performance of nursing students-a single blind, Quasi Exp. Study Pak. J. Med. Health Sci. 14 (2) (2020) 1276–1280.
- [29] R. Goli, N. Faraji, H. Maroofi, A. Hassanpour, Effect of spiritual care on the quality of life in patients who underwent intracranial hemorrhage surgery: a randomized controlled trial, Int. J. Surg. 110 (1) (2024) 167–175. Jan 1.
- [30] Molaee H., Goli R., Faraji N., Dizaji N.N., Bagheri M., Shakorzadeh S., Hassanpour A., Imanzadeh F., Lameei R. The effect of acupressure on sleep quality in patients with leukemia: a single-center, randomized controlled trial. Annals of Medicine and Surgery.:10-97.
- [31] M. Arad, R. Goli, N. Parizad, D. Vahabzadeh, R. Baghaei, Do the patient education program and nurse-led telephone follow-up improve treatment adherence in hemodialysis patients? A randomized controlled trial, BMC Nephrol. 22 (2021) 1–3 (Dec).
- [32] S. Heidari, N. Parizad, R. Goli, M. Mam-Qaderi, A. Hassanpour, Job satisfaction and its relationship with burnout among nurses working in COVID-19 wards: a descriptive correlational study, Ann. Med. Surg. 82 (2022) 104591. Oct 1.