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Case Report: Steven Johnson Syndrome (SIS) Induced By Antibiotics: A Detailed Analysis

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Abstract

Background: *Stevens-Johnson Syndrome SJS is a rare but very serious mucocutaneous disease primarily caused by medications that includes antibiotics. This case report is about a 35-year-old male who suffered from SJS due to treatment for urinary tract infection using co-trimoxazole.*

Case Presentation: *The patient began with symptoms of flu, later on followed by rapid progression of erythematous rash and painful mucosal involvement. On clinical examination, there were blisters, skin detachment involving 10% of the body surface area, and oral and ocular mucosal lesions. This reaction developed in a temporal association with co-trimoxazole therapy, making the drug a likely cause. She was systemically treated with corticosteroids and supportive care and showed marked recovery in two weeks from hospitalization.*

Conclusion: *This case underlines the importance of early suspicion of SJS in patients receiving antibiotic treatment. Removal of the offending drug and timely initiation of multi-disciplinary management will only improve the outcome in such patients.*

Keywords: *Stevens-Johnson Syndrome, co-trimoxazole, drug hypersensitivity, antibiotic-induced reactions.*

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I. Introduction

Stevens-Johnson Syndrome or SJS, is a severe and potentially life-threatening cutaneous-mucosal reaction. It is usually caused by medications and among these, antibiotic agents have been implicated including co-trimoxazole, sulfonamides, beta-lactams, and fluoroquinolones. SJS is characterized by less than 10 percent BSA, differing from its more dangerous counterpart TEN which exceeds 30 percent BSA. Both are included in SCARs.[1,2,3]

Isolated instances of SJS caused by drugs, including the use of antibiotics, have received more attention in clinical practice as such use of antibiotics is widespread and there appears to be a rising incidence of such cases. However, it must be kept in mind that certain patients, for example HIV infection, malignancy, and genetic predispositions - including HLA-B*1502 allele, among others are at higher risk, but SJS can just as easily present in other patients without those risk factors. Early identification of SJS and withdrawal of the offending drug help improve the outcomes. We describe herein one case of SJS caused by co-trimoxazole, and discuss the pathophysiology of the condition. It is against this background that we draw attention to some of the issues associated with the clinical management of the syndrome.[4,5,6]

II. Case Study

Patient Information

The patient is a 35-year-old South Asian male, living in an urban environment and employed as an office worker. He has no known allergies to drugs and does not suffer from any chronic medical conditions. His use of medication is limited to the occasional intake of over-the counter pain relievers like ibuprofen, typically for minor discomfort. His family medical history does not indicate any known dermatological issues or drug hypersensitivity reactions. Overall, his health history is stable, with no significant ongoing medical concerns or conditions requiring regular management.

Presenting Complaint

The patient presented to the emergency department (ED) with fever, malaise, and a widespread painful rash involving the skin and mucous membranes. He reported that these symptoms began 10 days after the initiation of co-trimoxazole, which was prescribed for an uncomplicated urinary tract infection (UTI).

History of Present Illness

The patient was prescribed co-trimoxazole (800 mg sulfamethoxazole + 160 mg trimethoprim) for UTI. Approximately eight days into therapy, the patient developed mild flu-like symptoms, including fatigue and fever. These symptoms were followed by the appearance of a rash, initially localized to the trunk but rapidly progressing to involve the face, neck, and extremities. The rash was associated with burning and discomfort, with subsequent blistering and skin detachment in some areas. The patient also reported significant pain and ulceration in the mouth, difficulty swallowing, and conjunctivitis.

The patient promptly discontinued the antibiotic therapy upon noticing the rash and sought medical attention two days later as the condition worsened. By the time of admission, approximately 10% of the patient's BSA was affected, with mucosal involvement including the oral cavity, eyes, and genital region.

Clinical Examination

- **Vitals on Admission:**
  - Blood Pressure: 110/70 mmHg
  - Pulse: 95 bpm
  - Temperature: 38.5°C
  - Respiratory Rate: 18 breaths/min
- **General Appearance:** The patient appeared in moderate distress due to painful skin lesions.
- **Dermatological Examination:**
  - Erythematous macules with central blistering and detachment of the epidermis were present, primarily on the trunk, upper extremities, and face.
  - Positive Nikolsky's sign (gentle lateral pressure on the skin led to sloughing).
  - Blisters and peeling skin covered approximately 10% of the patient's BSA.
- **Mucosal Involvement:**
  - **Oral mucosa:** Diffuse erosions and ulcers on the lips, buccal mucosa, and tongue, with crusting and bleeding.
  - **Ocular involvement:** Bilateral conjunctivitis with redness and tearing but no corneal ulceration.
  - **Genital involvement:** Mild erythema and ulceration on the penile mucosa.

Investigations

- **Complete Blood Count:**
  - Hemoglobin: 12.6 g/dL
  - White Blood Cell Count: 14,200/mm³ (Neutrophils 80%)
  - Platelets: 215,000/mm³
- **Renal Function:**
  - Serum creatinine: 1.2 mg/dL
  - Blood urea nitrogen (BUN): 18 mg/dL
- **Liver Function:**
  - AST: 45 U/L
  - ALT: 38 U/L
- **C-Reactive Protein (CRP):** 17 mg/L (elevated)
- **Serum Electrolytes:** Mildly elevated potassium levels (5.2 mmol/L)
- **Blood Cultures:** Negative for bacterial growth
- **Skin Biopsy:** Histopathological examination revealed full-thickness epidermal necrosis, subepidermal blister formation, and lymphocytic infiltration at the dermoepidermal junction, consistent with a diagnosis of SJS.

Diagnosis

From history, physical examination, and skin biopsy, Stevens-Johnson Syndrome was made as the clinical diagnosis. The temporal association between giving co-trimoxazole and onset of symptoms in this case strongly supported the drug as the causative agent.

Management

Immediate Measures:

- **Discontinuation of Antibiotic:** Co-trimoxazole was stopped immediately on admission and permanently discontinued.
- **Hospital Admission:** The patient was admitted to the ICU to be monitored closely because of the prospect of the disease condition rapidly worsening.
- **Supportive Care:**
  - Intravenous fluids were given to help maintain hydration and electrolytes imbalance.

- Wound care involved sterile dressings and application of emollients to avoid secondary infections.
- Oral care was administered through chlorhexidine mouth wash along with topical anesthetics for oral ulcers.
- In view of the management and assessment of ocular involvement, an ophthalmology consultation was sought.

Pharmacological Management

- **Systemic Corticosteroids:** Methylprednisolone 1 mg/kg/day intravenous was started to decrease the inflammation and immunological response. This was due to the early stage of the disease and the level of mucocutaneous involvement where the administration of corticosteroids was indicated.
- **Antihistamines:** Diphenhydramine dose 25 mg was repeated every 8 hours for symptomatic treatment of pruritus and inflammation.
- **Pain Management:** The patient was also on paracetamol 1 g every 6 hours for pain and fever management.
- **Antibiotic Prophylaxis:** Although controversial, prophylactic antibiotics were withheld, with close monitoring for signs of secondary infection (fever, leukocytosis, or worsening skin lesions).
- **Eye Care:** Lubricating eye drops and topical corticosteroids were given to avoid corneal involvement and to reduce the inflammation of the conjunctiva.

By day three, the patient's fever had resolved, the inflammation, as well as the erythema of the skin, was reduced, and Nikolsky sign remained positive, but no new lesions appeared. Steroid therapy was tapered during five days while the state of the patient stabilized.Re-epithelialization of the wound started by the first week of treatment with considerable healing of the skin and mucosal lesions by day 10. He was discharged after 12 days of hospitalization and was advised to follow up as an outpatient with dermatology and ophthalmology. Followed up at one month, he has complete recovery with regression of skin and mucosal lesions and without any ocular sequelae.

III. Discussion

Overview of Stevens-Johnson Syndrome

Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN) are severe forms of drug-induced mucocutaneous reactions. Although rare, with an annual incidence of 1–6 cases per million, the case fatality rate of SJS can be up to 10%, further rising with TEN, which is associated with greater areas of skin peeling. SJS characteristically presents within 1-3 weeks after a drug has been started, and common culprits include antibiotics, antiepileptics, and NSAIDs.[7,8]

Antibiotic-Induced Stevens-Johnson Syndrome

Most drugs involved in SJS are antibiotics, which include sulfonamides- co-trimoxazole, beta-lactams, and fluoroquinolones. The use of co-trimoxazole, a sulfonamide antibiotic, was significantly associated with the development of SJS in this patient. Besides the history and clinical findings that pointed to the incriminating role of co-trimoxazole, other possible causes such as infections were excluded.

Pathophysiology

SJS is simply an immune-mediated hypersensitivity reaction mediated through apoptosis of keratinocytes. The exact mechanism is not known, but most implicate drug-specific cytotoxic T lymphocytes and natural killer cells. These immune cells cause widespread keratinocyte apoptosis and subsequent shedding of the epidermis by inducing cytokines (e.g., TNF-α, IFN-γ) and granzyme B. Specific alleles of HLA, in particular HLA-B*1502, have been associated with at least increasing the risk of developing SJS in particular populations.[9,10,11]

Diagnosis and Differential Diagnosis

Diagnosis of SJS is clinical, especially with acute onset of painful erythematous skin rash and mucocutaneous involvement along with a positive Nikolsky sign. Differential diagnoses include erythema multiforme, DRESS with eosinophilia and systemic symptoms, staphylococcal scalded skin syndrome, and autoimmune blistering disorders such as pemphigus vulgaris. Skin biopsy still has a role in establishing the diagnosis which would include necrotic keratinocytes and subepidermal blistering.

Management Challenges

Multidisciplinary management is very crucial in the care of SJS, and it is usually supportive care along with wound management and discontinuation of offending drug. Use of systemic corticosteroids is still not definite, although mixed evidence has been reported on their usefulness. Their onset early in the disease might possibly reduce mortality and disease progression according to some studies, yet others advise against their use due to danger of complications like secondary infections.[12,13]

Prognosis

Therefore, early diagnosis and treatment are crucial in the improvement of prognosis in SJS. In this case study, the patient had a favorable outcome with the patient achieving a complete recovery after appropriate medical management and discontinuation of co-trimoxazole. Those that worsen prognosis are age, comorbidities, and extent of the surface involvement; they can worsen from complications including ocular damage and scarring in high grade disease.[14,15]

IV. Conclusion

This case report underlines the very critical need for early identification and treatment of Stevens-Johnson Syndrome, more so in cases caused by antibiotics, such as co-trimoxazole. Antibiotics are used by patients extensively in the modern world, and thus, such use should be a high suspicion for severe cutaneous adverse reactions in patients presenting with mucocutaneous symptoms following drug exposure. Improvement in patient outcomes is centered around discontinuation of the offending agent, intensive supportive care, and multidisciplinary management. The timely intervention to prevent fatal outcomes and reduce morbidity by effectively improving the patient's condition in this report underscores the relevant factors in such cases. As SJS can be life-threatening, awareness of the condition with ensured vigilance by the healthcare providers plays an important role in reducing its impact. Further research is needed to clarify the mechanisms involved in drug hypersensitivity and to lay the foundations for optimal strategies for its prevention, early detection, and treatment.

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