**Contemporaneous Sulfasalazine-Induced Stevens-Johnson Syndrome and Cholestatic Liver Injury: A Sporadic Case Report**

**Abstract**

**Background:**
Stevens-Johnson syndrome (SJS) and drug-induced liver injury (DILI) are rare but potentially life-threatening adverse drug reactions. Sulfasalazine is known to cause either condition individually, but their simultaneous occurrence is exceedingly rare.

**Case Presentation:**

We report the case of a 56-year-old female with psoriatic arthritis who developed a severe hypersensitivity reaction shortly after initiating sulfasalazine. Clinical features included facial erythema, mucosal ulceration, conjunctivitis, and hepatocellular liver injury. Skin biopsy confirmed Stevens-Johnson Syndrome. Laboratory investigations excluded infectious, autoimmune, and metabolic liver causes. Sulfasalazine was withdrawn, and treatment with intravenous corticosteroids and immunoglobulin led to clinical improvement.

**Management and Outcome:**

The patient received dexamethasone, IVIG, and supportive care with a multidisciplinary team. Liver enzymes normalized, mucocutaneous lesions resolved, and the patient was discharged in stable condition.

**Conclusion:**
Stevens-Johnson syndrome and idiosyncratic liver injury are rare but established adverse effects of sulfasalazine. Our case highlights the importance of early identification of the offending agent in Stevens-Johnson syndrome and drug-induced liver injury, and the prompt management of the patient’s condition using steroids and other supportive measures such as fluid management. Early recognition, drug discontinuation, and multidisciplinary care are critical to ensuring a favorable outcome.

**Keywords**

Stevens-Johnson syndrome, Drug-Induced Liver Injury, Sulfasalazine, Psoriatic Arthritis, Hypersensitivity Reaction.

**Introduction**

Sulfasalazine is combination of salicylic acid and sulphapyridine, used in the treatment of rheumatoid arthritis, psoriatic arthritis and ulcerative colitis. Despite its efficacy in treating these various disease conditions, sulfasalazine is often associated with a range of adverse effects. Stevens-Johnson syndrome/ toxic epidermal necrolysis (TENS) and sulfasalazine induced liver injury are some of the more severe and rare adverse effects of this drug. Stevens-Johnson syndrome and TENS are adverse effects of sulfasalazine with incidence of 0.4 to 1.2 in a general population. In both clinical conditions, it involves the loss of sheet-like skin and mucosal membranes along with other systemic symptoms. These cutaneous reactions are classified based on the percentage body surface area affected. Stevens-Johnson syndrome is referred to as a minor form of TENS with < 10% of BSA being affected. A proposed mechanism of action for this reaction is the possible interaction of drug-associated antigen/active metabolite with the major histocompatibility complex (MHC) type 1. The reaction is a T-cell mediated immune reaction with keratinocyte apoptosis induced by CD8+ cells.1

Sulfasalazine induced liver injury have features similar to that of drug-allergy, typically manifested as sudden onset of rashes along with elevated liver enzymes. Mechanism involved behind this idiosyncratic liver injury is a hypersensitive reaction toward the metabolites of sulfasalazine.2 The co-occurrence of both these adverse reactions is extremely rare and early cessation of drug is crucial in minimizing morbidity and mortality. Here, we present a clinically significant case of a patient who developed both SJS/TEN and sulfasalazine-induced liver injury concurrently. The case highlights on the importance of early recognition and immediate withdrawal of the offending drug to minimize further complications and ensure patient safety.3

**CASE PRESENTATION**

A 56-year-old female patient, known history of hypertension, type 2 diabetes mellitus and psoriatic arthritis was admitted in the department of general medicine with complaints of swelling and redness of face since 3 days and redness over the neck and chest since 2 days. A detailed medical history was taken and it was recorded about 3 years back, patient experienced high blood pressure and started on ayurvedic drug with last dose taken till March 2025. She was diagnosed with psoriasis 2 years back and was started on coal tar and halobestasol proprionate cream weekly and treatment continued till first week of March 2025. In February 3rd week, patient noted swelling over her right hand and after medical consultation was diagnosed with psoriatic arthritis. She was informed to stop coal tar and halobestasol proprionate cream and started on Tab.Apremilast 10mg which was increased to 30 mg on 1st March and Tab. sulfasalazine 500mg was added. About 2 months back, she was diagnosed with type 2 diabetes mellitus and prescribed Tab.vildagliptin+metformin. On march 18th, patient experienced fever onsets and bitter taste and took Tab.Rabeprazole and Tablet containing pancreatic enzymes. The next day, she noticed rashes and redness on her face and was taken over to her nearby hospital. There she was treated with steroids along with antihistamines. Even after initial treatment, rashes progressed with ongoing fever, erythema on chest and mucosal involvement of both eyes and oral cavities. Due to severity of her condition and lack of symptom relief, she was referred to our hospital.

**CLINICALFINDINGS**

Initial laboratory investigations along with skin biopsy (as shown in table 1) was conducted which was suggestive of Stevens-Johnson Syndrome/toxic epidermal necrolysis? erythema multiform. Her inflammatory markers were also found to be elevated. Urine routine analysis showed numerous pus cells and bacteria present. Urine culture was sent and showed growth of Candida with doubtful significance. In view of increased inflammatory markers and risk of infection, blood culture was also sent which showed no growth. Cardiac panel and lipid profile was found to be within normal range. Liver function test was found to elevated (table 1). R factor was calculated and at presentation was approximately 9.6, indicating a hepatocellular pattern of drug-induced liver injury (DILI). Ultrasound abdomen was done and showed grade 1 fatty liver .Gastroenterology consultation sought suggested viral panel testing and liver biopsy in view of significantly elevating liver enzymes. Rheumatology consultation was also sought to rule out any autoimmune causes for elevated liver enzymes. Blood samples were also sent for autoimmune profiling and autoimmune hepatitis antibodies test which was later found to be negative. Ophthalmology consultation was sought for complaints of eye discharge (yellow and purulent) and conjunctival congestion.

Table 1: Summarizes the laboratory findings recorded at the time of hospital presentation

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Parameter** | **Normal Range** | **DAY1****21/3/25** | **DAY6****26/3/25** | **DAY10****30/3/25** | **DAY14****3/4/25** | **DAY19****8/4/25** |
| **Hematological Parameters** |  |
| Hemoglobin | 12–16 g/dL (F) | 12.8 g/dL |  12.0g/dL  | 11.0g/dL | 9.9g/dL | 10.2g/dL |
| White Blood Cell Count (WBC) | 4,000–10,000 /µL |  5490/µL |  5660/µL | 7480/µL | 8860/µL | 9460/µL |
| Platelet Count | 150,000–450,000 /µL | 1.92/µL | 3.27/µL | 4.15/µL | 2.71/µL | 2.75/µL |
| **Inflammatory Markers** |  |
| C-Reactive Protein (CRP) | <8 mg/L | 64.5mg/L | 12.5mg/L | 7.16mg/L | 97.3mg/L | 17.1mg/L |
| Erythrocyte Sedimentation Rate | <20 mm/hr (F) | 59mm/hr |  42mm/hr | 35mm/hr | 73mm/hr | 76mm/hr |
| **Glycemic Control Parameters** |  |
| HbA1c | <5.7% (non-diabetic) | 6.5 |
| **Liver Function Tests** |  |
| Total Bilirubin | 0.1–1.2 mg/dL |  0.7 mg/dL | 5.8mg/dL | 7.1mg/dL | 7.1mg/dL | 2.6mg/dL |
| Direct Bilirubin | 0-0.2 mg/dL | 0.4 mg/dL | 4.6mg/dL  | 5.4mg/dL | 3.4mg/dL | 2.1mg/dL |
| Total protein | 6-8g/dL | 6.8g/dL | 5.3g/dL | 5.8g/dL | 5.2g/dL | 5.7g/dL |
| S Albumin | 3.5-5g/dL | 3.6g/dL | 2.9g/dL | 2.5g/dL | 2.7g/dL | 2.9g/dL |
| S Globulin  | 2.5-3.5g/dL | 3.2g/dL | 2.4g/dL | 3.3g/dL | 2.5g/dL | 2.8g/dL |
| Alanine transaminase (ALT) | 0–33 U/L | 325 U/L | 326U/L | 271 U/L | 235U/L | 135U/L |
| Aspartate transaminase (AST) | 5–40 U/L | 493 U/L | 236 U/L | 167 U/L | 141U/L | 83U/L |
| Alkaline phosphatase (ALP) | 35–140 U/L | 144U/L | 240U/L | 319U/L | 254U/L | 220U/L |
| Gamma-glutamyl transferase (GGT) | 0–42 U/L | 368U/L | 392 U/L | 596 U/L | 719 U/L | 439 U/L |
| Prothrombin Time (PT) | 12-16 Seconds | 15.3 s | 14.5 s | 14.4 s | 13.8 s | 13.8 s |
| INR | 1 | 1.12 | 1.05 | 1.04 | 1 | 1 |
| **Other Relevant Tests** |  |
| ANA, SMA, LKM Antibodies | Negative | Negative  |
| RA Factor | <20 IU/ml | 28.7 |
| Hepatitis A/B/C /E Panel | Negative | Negative |
| Skin Biopsy | — | **A skin punch biopsy from the left side of the face performed, showed full-thickness epidermal necrosis with dyskeratotic cells and marked dermal edema. Features favour Stevens Johnson Syndrome/toxic epidermal necrolysis.** |
| Liver Biopsy | — | Drug-induced liver injury: **cholestasis, steatosis, ballooning, feathery degeneration, canalicular and hepatocellular cholestasis with no fibrosis.** |
| **ANA –** Antinuclear Antibody**; SMA** **– Smooth Muscle Antibody; LKM** **– Liver Kidney Microsomal Antibody, RA FACTOR-Rheumatoid factor** |

**MANAGEMENT**

Patient was initially managed with injection dexamethasone 4mg twice daily and injection pheniramine 25 mg twice daily for rashes and swelling along with other supportive fluids. Inj.Meropenem 1g thrice daily was added as secondary prophylaxis for infections. In view of elevated liver enzymes, tab. Ursodeoxycholic acid 300mg twice daily and capsule Vitamin E 400mg once daily was started. Patient started experiencing frequent episodes of loose stools and was given tab. Rifaximin 400 mg twice daily and probiotic-prebiotic capsules once daily. Multivitamin and nutritional supplements along with other supportive measure were also given. Tab.fluconazole 50mg once daily was added against fungal infection (Candida). As patient had history of type 2 diabetes mellitus and her elevated HbA1c, she was started on Inj.glargine 6 units given at night.

From ophthalmology side, in view of conjunctival congestion, she was treated using the following: homatropine hydrobromide eye drops twice daily, moxifloxacin eye drops and ointment hourly till 10pm and soft paraffin cream hourly till 10pm. Eyelids were cleaned using sterile water.

Skin erythematous erosion was treated by applying mupirocin cream for facial erosions. Clotrimazole mouth paint for white precipitates on tongue. Triamcinolone acetonide cream thrice daily was used for red buccal erosions. For rashes on face desonide cream twice daily and for those on body, lotion containing betamethasone dipropionate and zinc sulphate, along with another lotion containing clobetasone, miconazole, and fusidic acid, was used.

In view of stevens-Johnson syndrome, patient was administered IVIG infusion (20g/200ml) on day 4 of hospital stay. IVIG infusion was given for three days and patient showed improvement in her condition and her skin lesions also started to improve.

Her conjunctival congestion started showing improvement by day 2 with left eye showing few epithelial erosions and no evidence of uveitis in both eyes. Frequency of drug administration was reduced to every 2 hours in view of this improvement. Within the next four days, her vision started improving along with both corneas becoming clear. Skin erosions also started showing reduction as supportive care continued. No further red rashes and new lesions were seen. Steroid was tapered in view of improving condition and later converted to oral tablets for ease of administration.

Patient became symptomatically stable, her blood inflammatory markers reduced, skin lesions improved and liver function tests showed an improving trend and was discharged with antibiotics, insulin and liver protectants along with skin and eye ointments. Steroid tablets (tab. Prednisolone 8mg in tapering doses) were also given. On follow up after discharge, her lesions resolved and liver functions also improved. The patient was asked to continue with the discharge medications along steroid (tab. Prednisolone 4mg in tapering doses).

**DISCUSSION**

Stevens-Johnson syndrome and idiosyncratic liver injury are both complications of sulfasalazine often occurring at early onset of drug or in in our case as a delayed reaction. While both complications are individually recognized adverse reactions to sulfasalazine, their simultaneous manifestation, as observed in our patient, is uncommon and poses a complex therapeutic challenge. Our patient developed mucocutaneous erosions, conjunctival congestion, and elevated liver enzymes approximately two months after initiating sulfasalazine, suggesting a delayed hypersensitivity reaction. This delayed onset and pattern of involvement differ from the case reported by Nada Zizi et al., where a 33-year-old female developed epidermal detachment and mucocutaneous lesions within two weeks of sulfasalazine initiation; however, liver dysfunction was not reported in their case, distinguishing our case due to its added hepatic component.4 Similarly, Binayak Chandra et al. documented a 48-year-old female with sulfasalazine-induced SJS who presented with skin and mucosal involvement but without hepatic injury.5 Both the cases utilized systemic corticosteroids for treatment, with tapering schedules and ophthalmologic interventions for conjunctival involvement, reflecting consistent management strategies. In contrast to our case on hepatoxicity, Rodolfo et al. reported sulfasalazine-induced hepatotoxicity in a 19-year-old female who presented with elevated liver enzymes and biopsy-confirmed hepatic necrosis but without dermatological manifestations, indicating that while sulfasalazine can cause either condition independently, concurrent presentation as seen in our case remains atypical.6 Furthermore, our patient demonstrated favourable outcomes with a combination of high-dose intravenous corticosteroids and IVIG, a treatment approach supported by Michaels et al. This dual therapy likely contributed to rapid clinical stabilization and resolution of symptoms.7 Unlike cases that relied solely on corticosteroids, our inclusion of IVIG may have accelerated recovery, especially give the severity and overlap of systemic involvement. The hepatotoxicity observed in our patient aligns with the observations of Jobanputra et al. and Masood et al., who emphasized sulfasalazine’s potential to induce liver injury and the importance of timely drug withdrawal and supportive therapy.8-9 Taken together, while aspects of our case mirrors with those described in the other literature, the delayed onset of both SJS and hepatic injury, along with their simultaneous presentation and multi-organ involvement, makes it distinct. This case highlights the importance of recognition even beyond the typical early treatment window, immediate cessation of the offending drug, and a multidisciplinary treatment strategy including corticosteroids, IVIG, liver support and ophthalmologic care to achieve favourable outcomes.

**CONCLUSION**

Although Stevens-Johnson syndrome and hepatoxicity are the established adverse effects of sulfasalazine, their simultaneous occurrence is rare and often under reported. Our case highlights the importance of early identification of offending agent in Stevens-Johnson syndrome and drug induced liver injury and the prompt management of patient condition using steroids and other supportive measures like fluid management. Although the role of steroids and IVIG in these adverse reactions is controversial, our patient showed rapid improvement with administration of systemic cortical steroid which only further accelerated using IVIG. This case also emphasizes on the need for individualized assessment and vigilance when initiating sulfasalazine therapy especially in individuals with history of polypharmacy.

**CONSENT**

The author has obtained consent to conduct the study.

**DISCLAIMER (ARTIFICIAL INTELLIGENCE):**

Author(s) hereby declares that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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