STEVENS-JOHNSON SYNDROME DUE TO SULFASALAZINE- A CASE REPORT

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Summary

Sulfasalazine is a sulfur containing drug used mainly in rheumatoid arthritis and ulcerative colitis. There are rare reports of Stevens Johnson Syndrome (SJS) due to sulfasalazine. In this article, the authors report a case of SJS due to sulfasalazine and establish the causality, severity and preventability of the reaction. The reaction developed four weeks after initiating the treatment. The drug was stopped and the patient was managed symptomatically with systemic and topical steroids. Though dermatological reactions such as SJS due to sulfasalazine are rare, one should keep in mind the possibility of SJS and advice the patient accordingly while prescribing this drug.

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Introduction

Sulfasalazine is a sulfur containing drug approved by the United States Food and Drug Administration (US FDA) in the management of rheumatoid arthritis, and in ulcerative colitis (both in active as well as maintenance).[1] Adverse Drug Reactions (ADRs) due to sulfasalazine occur in 10-45% of the patients with ulcerative colitis and are primarily related to the presence of sulfa moiety.[2] The most commonly reported ADRs include nausea and vomiting, abdominal discomfort, head ache, fever and skin rash.[3] It is known to cause both dose dependent and dose independent (hypersensitivity type) ADRs. The hypersensitivity type of ADRs include skin rash, aplastic anemia, hepatic and pulmonary dysfunction and autoimmune hemolysis.[3] Dermatological reactions due to sulfasalazine include drug eruptions, rashes, skin discoloration and rarely Toxic Epidermal necrolysis (TEN) and Stevens- Jonson Syndrome (SJS).[1] We here by report a case of SJS due to sulfasalazine in a 48 year old woman four weeks after initiation of therapy. We also established the causality, severity and preventability assessments of the psychotic reaction as per the Naranjo scale,[4] Hartwig scales[5] and the Modified Schummock and Thornton scales[6] respectively.

Case report

A 48 year old female patient was diagnosed as Rheumatoid arthritis (RA factor positive) in a private hospital and the patient was prescribed Tab. Sulfasalazine 500 mg twice daily for 28 days, Tab. Ranitidine 150 mg twice daily for 15 daya and Tab. Nimesulide 100 mg once daily for 15 days. Patient took Ranitidine and Nimesulide for 15 days and continued to take Sulfasalazine.

On 28th day of therapy with sulfasalazine, patient noticed rash all over the body, over the lip and genitila and also joint swelling (both wrists). She went to the private hospital again where she was prescribed with Tab. Ibuprofen+Paracetamol, Tab. Ciprofloxacin and Fluticasone ointment. Four days after the developmet of rash, she presented to the emergency department of our hospital. On examination, there were erythromatous, crusted plaques on lips, genitila and conjunctiva with mild fever.

There were few erosions over inner side of vulva and oral mucous membrane and tongue. Itchy, erythematous papules and macules over the body were present. A diagnosis of SJS secondary to sulfasalazine and the patient was managed accordingly. Sulfasalazine was also stopped. The patient was given Inj. Dexamethasone, followed byTab. Prednisolone was given and tapered gradually and stopped, and Betadine gargle. The eye complication was managed as per the Ophthalmologist advice. The lesion subsided gradually following the treatment and the patient was discharged after 11 days of treatment in the hospital.

Upon reporting the ADR to the Pharmacovigilance cell, the Pharmacists carried out the Causality assessment, severity assessment and preventability assessment of the ADR as per the Naranjo scale, Hartwig scale and the Modified Schummock and Thornton scales respectively. The causality assessment revealed the ADR to be ‘Probably’ associated with the drug. Similarly the severity assessment revealed the ADR to be ‘Moderate Level 4 (b)’ suggesting that the ADR is the reason for hospital admission. It was found that the ADR was ‘not preventable’.

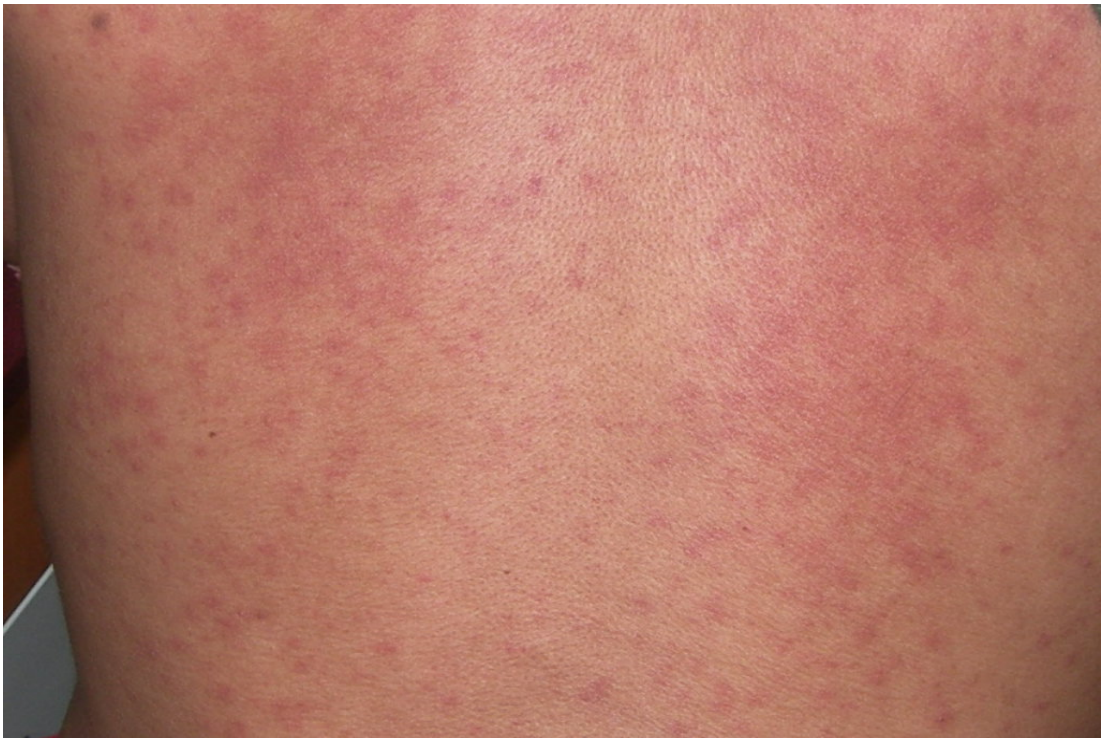

Figure 1. Erythematous macules and papules in the back

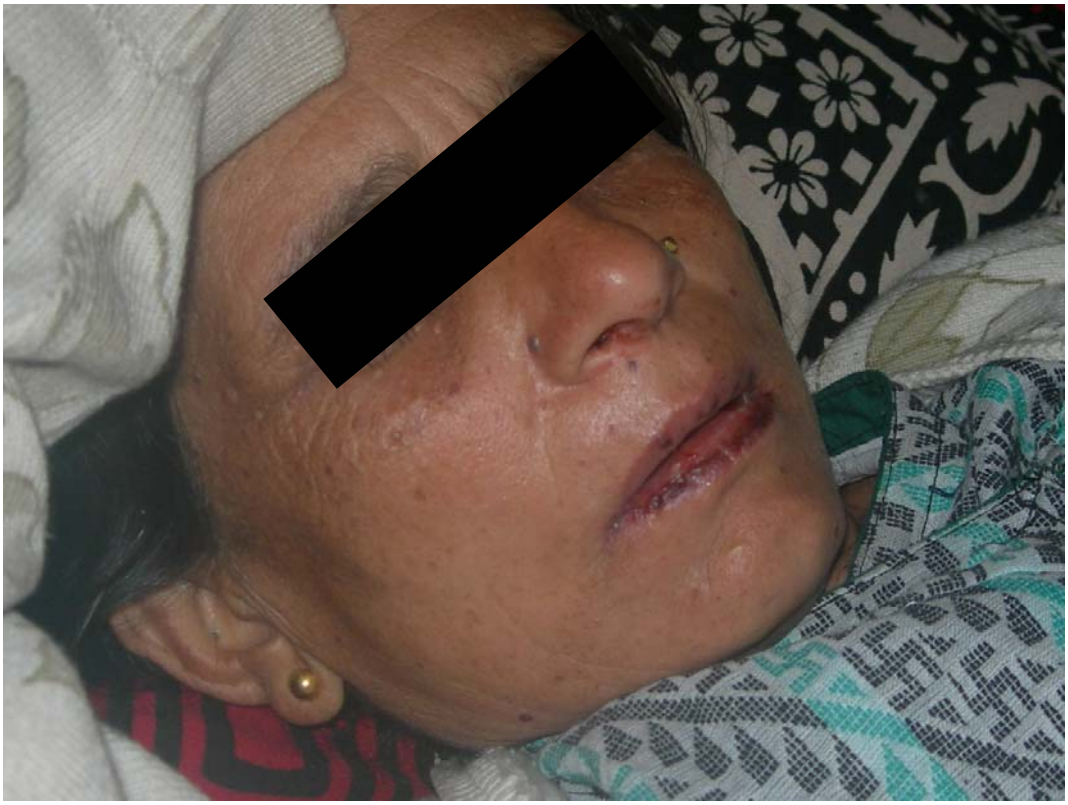

Figure 2. Erythematous crusted plaque on lip. Few scaling on eye lid is also seen

Discussion

SJS is a blistering disorder that is usually more severe than erythema multiforme.[7] The incidence of SJS ranges from 1.2 to 6 per million per year and carries around 5% mortality. 8 Sulfonamides, anticonvulsants, allopurinol, pyrazolone derivatives, oxicams, and chlormezanone are the drugs most frequently associated with Stevens-Johnson syndrome.[9] Drugs are the most common cause for SJS.[10] The initial presentations of SJS are often a sore throat, malaise, and fever. 7 In our patient, there were no such classical symptoms. The reaction developed spontaneously. SJS due to sulfasalazine is rare. Borras-Blasco et al reported a case of Photo-induced SJS associated with sulfasalazine therapy in a 34-year-old malewith no predisposing factors. The patient presented to the emergency department because of severe erythema confined to sun-exposed areas which was later confirmed by skin biopsy. The patient improved following the cessation of therapy and was discharged.[11] Sulfasalazine induced systemic lupus bullous skin eruptions typical of Steven's-Johnson and erythema multiforme syndrome have been described in two patients.[12]

SJS within a few days, in addition to erosion of multiple mucous membranes, small blisters developing on dusky or purpuric macules or atypical target lesion. [7] In our case, the patient had erythromatous, crusted plaques on lips, genitila and conjucntiva and also few erosions over inner side of vulva and oral mucous membrane and tongue along with itchy, erythematous papules and macules over the body. A systemic steroid is the mainstay in the management of SJS. In our case, the patient was managed with systemic and topical corticosteroids initially and later with oral steroids. The patient responded to the treatment well and got discharged after 11 days of treatment. Rechallenging the patient with the suspected drug is never justifiable [10] as it can be even fatal. In our case also the patient was not rechallenged.

Carrying out the causality assessment using standard methods is one of the best ways to establish the causal relationship between drug and effect. The Naranjo algorithm [3] is used widely in carrying out the causality assessment of ADRs. It is based on the score calculated on the basis of points given for each of ten questions that comprises the table. In our case, the causality assessment revealed that the ADR to be 'probably' attributed to sulfasalazine.

In order to take appropriate initiatives towards management of the ADR, it is necessary to study the severity of the ADRs. Hartwig scale [5] is widely used for the purpose. This scale categorizes the reported adverse drug reactions into different levels as mild, moderate or severe based on the treatment and whether or not hospitalization was required for the management of the ADRs. In our patient, the ADR was found to be of 'Moderate Level 4 (b)' suggesting that the ADR is the reason for hospital admission.'

The preventability assessment provides an idea to find whether a particular ADR could be preventable. A commonly used scale for this purpose is the Modified Schumock and Thornton scale. [6] In our case this ADR was found to be 'not-preventable.'

Conclusion

SJS is a life threatening cutaneous ADR and sometimes it is fatal in severe SJS. Though reports of SJS due to sulfasalazine are rare, one should be careful while prescribing this drug to a patient. Patients should be counseled thoroughly regarding the possibility of dermatological manifestations due to this drug and should be educated regarding the detecting of the ADR when the initial symptoms appear. Upon occurrence of the ADR, the drug should be stopped immediately and the patient should be managed as a medical emergency. Since it is a life threatening ADR, the patient should never be rechallenged.

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