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CASE REPORT

Sulfasalazine-Induced DRESS Syndrome: A Case Report

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Abstract

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a rare but potentially fatal drug hypersensitivity reaction. We report a 13-year-old male with enthesitis-related arthritis who developed DRESS three weeks after initiating sulfasalazine therapy. He presented with diffuse erythematous rash, facial edema, oral ulcerations, and marked eosinophilia. The diagnosis was established using RegiSCAR criteria after excluding alternative causes. Prompt discontinuation of sulfasalazine and initiation of corticosteroids led to rapid clinical improvement. This case highlights the importance of early recognition and management of sulfasalazine-induced DRESS in pediatric patients.

Key Words

Juvenile Idiopathic Arthritis, Drug Hypersensitivity Syndrome, HLA Antigens, Disease Modifying Antirheumatic drug

Introduction

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a rare but potentially life-threatening drug-induced hypersensitivity reaction characterized by delayed onset of symptoms, including fever, rash, lymphadenopathy, hematologic abnormalities (such as eosinophilia), and internal organs involvement, particularly of the liver and kidneys. The estimated incidence ranges from 1 in 1,000 to 1 in 10,000 drug exposures, with a mortality rate of approximately 10%.[1]

Sulfasalazine, a sulfonamide-based disease-modifying antirheumatic drug (DMARD), is widely used to treat chronic inflammatory disorders such as rheumatoid arthritis and juvenile idiopathic arthritis [JIA]. However, its use is occasionally complicated by severe hypersensitivity reactions, including DRESS syndrome.[2] To the best of our knowledge, there are no large-scale epidemiological studies on sulfasalazine-induced DRESS in the Indian population, highlighting the value of this case as a contribution to Indian pharmacovigilance literature.

JIA is a group of chronic arthritis affecting children under 16 years of age. Enthesitis-related arthritis (ERA) is a subtype characterized by inflammation of entheses (sites where tendons or ligaments insert into the bone) and is often associated with HLA-B27 positivity.[3] First-line treatments for ERA include nonsteroidal anti-inflammatory drugs (NSAIDs) and DMARDs like sulfasalazine.[4]

Pediatric DRESS is less common and may mimic systemic JIA flare or macrophage activation syndrome, leading to diagnostic delay.[5] In children, the incidence of DRESS syndrome is lower than in adults.[6] Here, we present a case of a 13-year-old male with ERA who developed DRESS syndrome three weeks after initiating sulfasalazine therapy, emphasizing diagnostic vigilance and early management.

Case Report

A 13-year-old male presented with a one-year history of inflammatory bilateral knee pain&plantar pain with difficulty in walking. There was no significant past or family history of autoimmune disease. In MSK (Musculoskeletal) examinationrevealed that there was restricted motion of affected joints,plantar tenderness and pedaledema. The USG of the heel revealed plantar fasciitis. Laboratory tests revealed an elevated

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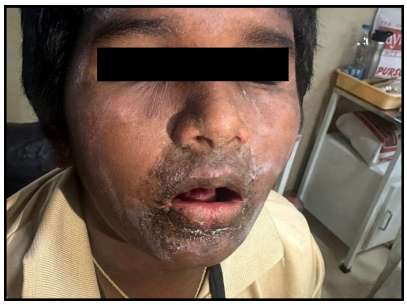
erythrocyte sedimentation rate and C-reactive protein levels, with negative HLA-B27 supported the diagnosis of ERA and the patient was started on sulfasalazine 500 mg, folic acid 5 mg a day, with nonsteroidal anti-inflammatory drugs for pain relief.

After three weeks, he developed a diffuse erythematousexfoliative rash that began on the face,as shown in **Figure 1,** and spread to the trunk and limbs, accompanied by facial edema, oral ulcerations, and fever (38.5 °C). He was referred to dermatology for evaluation. Investigations revealed leukocytosis (57,230/mm³) with eosinophilia and mildly elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST), as presented in **Figure 2**. Renal function was normal. Viral studies (HHV-6/EBV/CMV) were not performed. Differentials diagnosis included viral exanthems, systemic JIA flare, and SJS/TEN, which were ruled out based on eosinophilia, absence of mucosal necrosis, and delayed onset following sulfasalazine exposure.

Figure 1. Clinical presentation of sulfasalazine-induced DRESS syndrome showing diffuse erythematous exfoliative rash and facial edema at initial evaluation.



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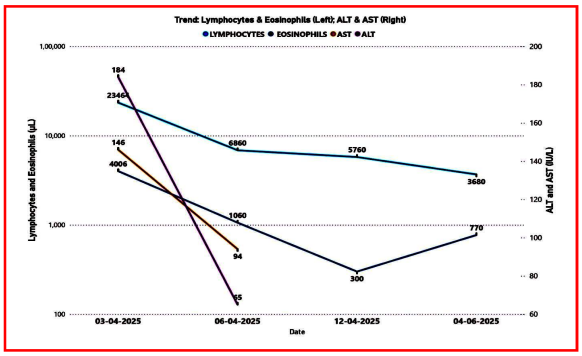

Figure 2 : Trend of lymphocyte count, eosinophil count, and liver enzymes (ALT and AST) over time following withdrawal of sulfasalazine and initiation of corticosteroid therapy.

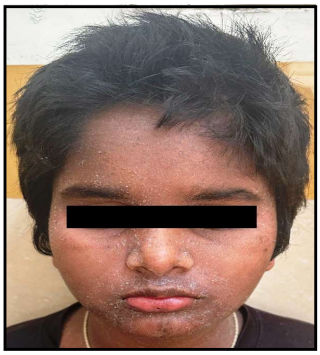

Figure 3 : Significant resolution of cutaneous lesions and reduction in facial edema after withdrawal of sulfasalazine and initiation of systemic corticosteroid therapy.

A diagnosis of DRESS syndrome secondary to sulfasalazine was made based on Regi SCAR score of 7 (Definite: 6 and above), confirming a definite case of DRESS syndrome.[7] The detailed scoring is mentioned in **Table 1.** Causality assessments supported the association: the **Naranjo algorithm (score = 5)** and the **WHO–UMC scale** classified it as *probable*,[8] The **Modified Schumock and Thornton scale** indicated that the event was *not preventable*.[9]

The drug was immediately discontinued, and intravenous corticosteroids and antihistamines were initiated alongside supportive fluid and nutritional therapy. Oral lesions healed, facial edema decreased, and the rash with pruritus resolved within three days. Liver enzymes normalized, and the patient was discharged on a tapering course of oral corticosteroids. He was instructed to attend regular follow-up appointments for continued management of ERA. There was no re-challenge with sulfasalazine, and the patient has remained clinically stable without recurrencepost treatment, as illustrated in **Figure 3**.

Discussion

DRESS syndrome is a severe idiosyncratic drug reaction with variable onset and presentation, typically occurring within 2 to 8 weeks after drug exposure.Its delayed onset often makes diagnosis challenging.[1]

Although the pathophysiology of DRESS is complicated and not fully understood, involves a strong T-cell activation caused by a drug-specific immunological response that is frequently associated with specific human leukocyte antigen (HLA) alleles.[10] This cascade culminates in a cytokine storm, with elevated IL-5 levels contributing to the hallmark eosinophilia.

Exposure to high-risk medications like anticonvulsants, antibiotics, allopurinol, and sulfonamides like sulfasalazine significantly increases the risk of DRESS syndrome.

Table 1. Application of the Regi SCAR DRESS Validation Scoring System to this Patient.

Criteria	Case findings	Score
Fever =38.5 °C	Present (38.5 °C recorded)	+1
Enlarged lymph nodes	Not observed	0
Eosinophilia	4,500 /mm³ (˜ 4.5 × 10? /L) ? >1.5 × 10?/L	+2
Atypical lymphocytes	Not reported	0
Skin rash extent =50 % BSA	Diffuse rash involving face, trunk, and limbs	+1
Rash suggestive of DRESS (exfoliative, facial edema)	Exfoliative rash with facial edema	+1
Skin biopsy suggestive of DRESS	Not performed	0
Internal organ involvement	Mild hepatic (elevated ALT/AST)	+1
Resolution =15 days	Resolved within 3 Months	+1
Exclusion of other potential causes (e.g., infection)	Unknown	0

Genetic predisposition, including specific HLA alleles and variations in drug-metabolizing enzymes, further increases susceptibility. In juvenile patients, underlying immune dysregulation also plays a significant role.[11]

Our case is consistent with earlier juvenile findings, such as those of Kuchinskaya *et al*. (2023), where a 12-year-old patient with JIA developed DRESS syndrome three weeks after starting sulfasalazine, with hepatic involvement and a good response to steroid treatment.[12] The clinical presentation in this case aligns with findings from Blackley *et al*. (2024), who reported that pediatric DRESS most often presents with fever, facial edema, rash, eosinophilia, and hepatic involvement, features also evident in our patient.[13] These similarities reinforce sulfasalazine as a well-established precipitant of DRESS across age groups, whereas differences highlight possible immunogenetic factors specific to ERA.Prompt withdrawal of the offending drug and initiation of systemic corticosteroids led to rapid clinical improvement in our patient, consistent with pediatric DRESS literature. Early steroid therapy is essential for controlling inflammation, preventing progression of organ involvement, and reducing the risk of relapse, benefits that were clearly observed in this case.[11]This case highlights the need for clinician awareness of sulfasalazine-induced DRESS in children, emphasizing early recognition, prompt drug withdrawal, and corticosteroid therapy to prevent severe organ involvement.

Conclusion

In children with juvenile idiopathic arthritis, sulfasalazine can rarely cause DRESS syndrome. Recovery depends on early detection, timely discontinuation of medication, and corticosteroid therapy. This case highlights the importance of close monitoring during the initial weeks of treatment to prevent serious hypersensitivity reactions.

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