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Case Report

Ethosuximide associated drug reaction with eosinophilia and systemic symptoms syndrome masqueraded as adenovirus infection

Emi R. Abraham[1]*, Serena M. Varghese[2], Gopika M. Chandran[2], Dinu Varghese[1]

[1]Department of Clinical Pharmacology, Rajagiri Hospital, Aluva, Kerala, India
[2]Department of Pediatrics, Rajagiri Hospital, Aluva, Kerala, India

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***Correspondence:**
Dr. Emi R. Abraham,
Email: emiabraham7@gmail.com

ABSTRACT

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome is a serious adverse reaction due to drugs. Due to the rarity of this condition particularly in children, DRESS can be often misdiagnosed. An 8-year-old boy was referred to our paediatrics department with the complaints of persisting fever and rashes. He was tested positive for Adenovirus infection and was provisionally diagnosed with urticaria due to viral infection, for which he was started with antiviral and antipyretics. The child was also recently diagnosed with Myoclonic Absence Epilepsy and was started on syrup Ethosuximide. Despite being treated with antiviral and antipyretics his fever spikes were consistent with itchy rashes. Multidisciplinary medical consultations were done to finally rule out DRESS associated with Ethosuximde and the drug was stopped. The child showed significant improvement from the next day with no further episodes of fever spike. Hence, we present this case to provide an alert for the need of early differential diagnosis of DRESS syndrome in case of concomitant viral infection.

Keywords: DRESS syndrome, Ethosuximide, Adenovirus

INTRODUCTION

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a serious adverse reaction due to drugs, usually presented after 1 to 12 weeks after the administration of the causative drug. The clinical presentation usually begins with fever (between 38°C to 40°C), rashes followed by systemic involvement and end organ damage. Initially the rashes are morbilliform macular type that appears in the face, abdomen and upper limbs, they later become purpuric.[1,2] Due to the rarity of this condition particularly in children, DRESS can be often misdiagnosed. We report the first case of DRESS syndrome associated with Ethosuximide and concomitant Adenovirus infection.

CASE REORT

An eight-year-old boy presenting with the complaints of fever, rashes and sore throat was referred to our paediatrics department from a local hospital due to the falling trends of platelet and white blood cells, despite being treated with Inj Dexamethasone, antihistamines and Inj Ceftriaxone. On clinical examination he had generalized erythematous urticarial rashes (Figure 1) over his body. His peripheral smear showed normocytic normochromic blood picture with lymphocytopenia. The child was diagnosed with myoclonic absence epilepsy 13 days back and was started on syrup ethosuximide 150 mg twice daily.

His initial blood test showed Transaminitis (SGOT/SGPT-116 U/l/100U/l). Influenza and respiratory syncytial virus (RSV) results were negative, whereas the Adenovirus test was positive. Hence, he was provisionally diagnosed with urticaria due to viral infection. The child was started on intravenous fluids, oral azithromycin, oseltamivir, and other supportive therapies. Considering the severity of the itchy rashes, a dermatology consultation was placed, following by which topical steroids and oral antihistamines were added to relieve itching. A skin biopsy

was also suggested if the symptom persists. Despite these measures the child's fever spikes (39.5°C on the 3rd day of hospital admission) remained consistent. Therefore, sample was sent to rule out dengue, typhoid fever, leptospirosis, and epstein barr virus infection, however, they were all negative. An abdominal ultrasound revealed cholelithiasis and hepatomegaly, without cholecystitis. Considering the possibility of hemophagocytic lymphohistiocytosis (HLH), paediatric hemato-oncology consultation was sought. Wherein, a bone marrow biopsy was suggested.

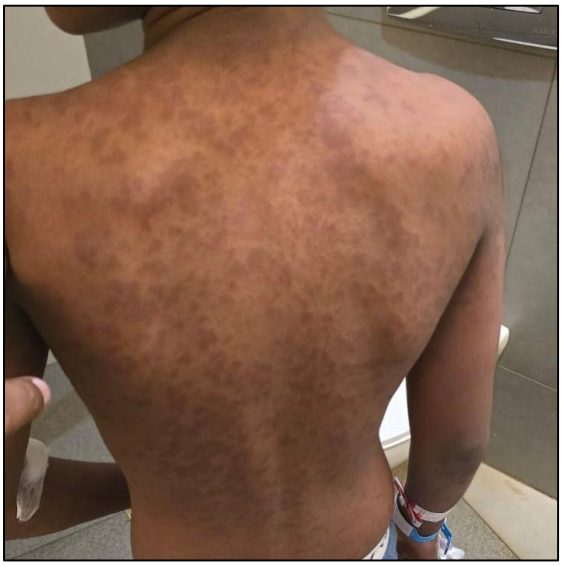

Figure: 1 Urticarial rash at the time of admission.

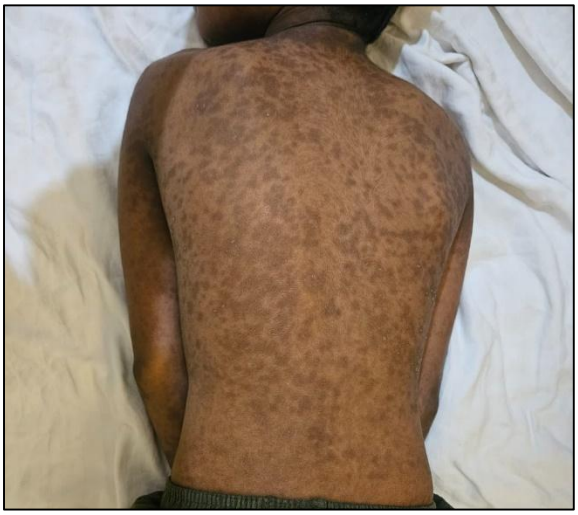

Figure: 2 Resolving hyper pigmented lesions at the time of discharge.

Repeated liver function test showed a decreasing trend in lactate dehydrogenase (604 U/l to 443 U/l) and a mild increase in absolute eosinophil counts (0.5% to 0.8%). As the inflammatory markers remained negative along with the improved platelet counts, bone marrow examination was deferred. Considering only a mild elevation of ferritin (330 ng/ml) and normal triglycerides/fibrinogen levels, HLH was also dismissed (Table 1). An Echo-cardiogram was done to rule out coronary involvement suspecting atypical Kawasaki disease, but no significant findings were observed.

Despite being administered with antipyretics and topical steroids his fever spikes and urticarial rashes persisted. Clinical pharmacology consultation was also sought considering the possibility of an allergic reaction to ethosuximide. Eventually the possibility of DRESS syndrome was suggested taking into account of eosinophilia and transaminitis. Finally, it was opined to de-challenge Ethosuximde on day 5. The child became afebrile on the following day. His rashes and itching subsided within 2 days of abstinence from ethosuximide, leaving behind the hyper pigmented lesions over his body (Figure 2). Moreover, the child improved symptomatically and no new episodes of fever spikes were reported.

Table: 1 Shows the blood parameters of the patient throughout the hospital stay.

Parameters	Normal range	D1	D2	D4
Alkaline Phosphatase	153-367 U/l	125	118	-
SGOT	0-34 U/l	116	137	-
SGPT	10-49 U/l	100	173	-
Ferritin	20-250 ng/ml	363.6	-	-
LDH	125-220 U/l	604	-	443
Eosinophils	0-5%	-	-	16.9

Table: 2 RegiSCAR scoring.

Clinical and laboratory criteria	RegiSCAR scoring
Fever >38.5°C	0 (yes)
Enlarged lymph nodes	1
Eosinophilia	1
Atypical lymphocytes	0 (no/unknown)
Skin rash >50% of BSA	1
Skin rash suggesting DRESS	1
Biopsy suggesting DRESS	0 (unknown)
Organ involvement	1 (liver)
Resolution >15 days	0 (yes)
ANA, blood culture, serology for HAV/HBV/HCV, chlamydia, mycoplasma	0 (no)
Total	5
RegiSCAR	Probable

DISCUSSION

The incidence of DRESS syndrome varies from one per 1000 to one per 10,000 cases of medication exposures. Although the accurate rate is obscure, it is likely lower in children when compared to adults.[3] Owing to the unpredictability of its clinical presentations, a European standard known as the registry of severe cutaneous adverse

reactions (RegiSCAR), was developed to clinically diagnose DRESS syndrome. The RegiSCAR score calculated for this patient is 5 (Table 2), which implies a probable case of DRESS syndrome. The estimated Naranjo Adverse Drug Reaction Probability Scale score is 7, concluding that the drug would be the probable cause for the reactions. Although aromatic anticonvulsants are more frequently linked with DRESS syndrome, here a succinimide anticonvulsant-ethosuximide has caused the reaction. Additionally in a literature review, 6 children out of 154 (3.9%) who received Ethosuximide experienced moderate to severe rash.[4] However, only one case of a 7-year-old boy with Ethosuximide-related DRESS syndrome has been documented until now.[5]

A number of factors including drug, virus, and genetics appear to drive this unique syndrome. Although the role of viruses in the pathogenesis of DRESS syndrome is not unravelled, according to a literature review around half of the cases with DRESS syndrome also had a reactivation of viral infection.[6,7] In this case the Adenovirus might be the probable instigating factor for triggering DRESS syndrome. So far only two case reports of DRESS syndrome with concomitant influenza and chikungunya virus infection have been reported.[8,9]

CONCLUSION

DRESS syndrome is mostly seen in adult population, whereas it can also affect children. Due to the delayed presentation of clinical symptoms and their similarities with other common infectious diseases, the early diagnosis of DRESS syndrome is always challenging. Hence, this case report contributes as a source of information on the concomitant adenovirus infection and DRESS syndrome. We anticipate the case may provide an alert for the early differential diagnosis of this unusual syndrome.

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REFERENCES

1. Calle AM, Aguirre N, Ardila JC, Villae RC. DRESS syndrome: A literature review and treatment algorithm. World Allergy Organ J. 2023;16:100673.
2. Cardoso CS, Vieira AM, Oliveira AP. DRESS syndrome: a case report and literature review. Case Rep. 2011;2:3898.
3. Manieri E, Dondi A, Neri I, Lanarie M. Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome in childhood: a narrative review. Front Med. 2023;10:1108345.
4. Hiransuthikul A, Rattananupong T, Klaewsongkram J, Rerknimitr P, Pongprutthipan P, Ruxrungtham K. Drug-induced hypersensitivity syndrome/drug reaction with eosinophilia and systemic symptoms (DIHS/DRESS): 11 years retrospective study in Thailand. Allergol Int. 2016;65:432–8.
5. Werbel T, Castrovinci P, Contestable J. Ethosuximide-induced drug reaction with eosinophilia and systemic symptoms with mediastinal lymphadenopathy. Pediatr Dermatol. 2019;36:99-101.
6. Mori F, Caffarelli C, Caimmi S. Drug reaction with eosinophilia and systemic symptoms (DRESS) in children. Acta Bio Medica Atenei Parm. 2019;90:66–79.
7. Sharifzadeh S, Mohammadpour AH, Tavanaee A, Elyasi S. Antibacterial antibiotic-induced drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome: a literature review. Eur J Clin Pharmacol. 2021;77:275–89.
8. Girijala RL, Ramamurthi A, Wright D, Kwak Y, Goldberg LH. DRESS syndrome associated with influenza virus. Bayl Univ Med Cent Proc. 2019;32:277-8.
9. Sil A, Bhattacharjee MS, Chandra A, Pramanik JD. Sulfasalazine-induced drug reaction with eosinophilia and systemic symptoms (DRESS) with concomitant acute chikungunya virus infection: possible role of new viral trigger. BMJ Case Rep. 2021;14:244063.

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