Available online on 15.04.2022 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Full Text Article

Case report

Phenytoin Induced Drug Rash with Eosinophilia and Systemic Symptoms: A rare paediatric case report

Aishwarya S Pattanshetti, Agadi Hiremath Viswanatha Swamy, Prasad N. Bali, Sanatkumar B Nyamagoud*

Department of Pharmacy Practice, KLE College of Pharmacy, Vidyanagar, Hubballi. A Constitute Unit of K.L.E Academy of Higher Education and Research, Belagavi, Karnataka, INDIA

Article Info:

Article History:

Received 19 February 2022
Reviewed 14 March 2022
Accepted 20 March 2022
Published 15 April 2022

Cite this article as:

Pattanshetti A, Bali PN, Phenytoin Induced Drug Rash with Eosinophilia and Systemic Symptoms: A rare paediatric case report, Journal of Drug Delivery and Therapeutics. 2022; 12(2-s):1-4

DOI: http://dx.doi.org/10.22270/jddt.v12i2-s.5416

*Address for Correspondence:

Dr. Sanatkumar B Nyamagoud, Assistant Professor, Department of Pharmacy Practice, KLE College of Pharmacy, Vidyanagar, Hubballi. KLE Academy of Higher Education and Research, Belagavi-590010, Karnataka, INDIA.

Abstract

Purpose**:** Dress Syndrome (Drug rash with eosinophilia and systemic symptoms) is a severe adverse drug reaction characterised by rash, fever, lymphadenopathy, and organ involvement. It is a severe, one-of-a-kind adverse medication reaction. DRESS is the most rarely seen severe adverse drug reaction, and it affects approximately 1 in a thousand to 1 in a ten thousand patients who take the drug. It is found that the mortality rate is nearly 10 %. The main objectives include - learn the importance of DRESS syndrome, recognize the signs and symptoms of DRESS, to know what diagnostic studies are indicated and to provide accurate treatment.

Methods: The case of 11-year-old girl who came with history of head injury and was given phenytoin to treat it. Later she came with a complaint of numerous urticated papules and plaques on her trunk, neck, both upper and lower limbs, and febrile since 4days. And we used the Regi SCAR scoring system that grades DRESS cases as 'no', 'possible', 'probable' or 'definite' groups for diagnostic criteria of DRESS. And we also applied Naranjo's causality assessment scale in the following case study.

Results and conclusion: In the initial recognition of DRESS syndrome and the immediate withdrawal of offending drugs and continuing with a supportive therapy and corticosteroids as needed. Systemic corticosteroids can reduce symptoms of hypersensitivity reactions.

Keywords: Drug Reaction with Eosinophilia and Systemic Symptoms, Phenytoin, Exfoliation of Skin, Corticosteroids.

INTRODUCTION

Drug rash with eosinophilia and systemic symptoms (DRESS) is a severe form of drug reaction characterized by fever, skin rash, lymphadenopathy, hematological abnormalities and internal organ involvement 2 to 8 weeks after a drug is first used. [1]

It is recently coined the term "drug rash with eosinophilia and systemic symptoms" (DRESS) to better understand drug hypersensitivity reactions and distinguish them from drug-induced pseudo lymphoma [2].

DRESS is the most rarely seen severe adverse drug reaction, and it affects approximately 1 in a thousand to 1 in a ten thousand patients who take the drug. It is found that the mortality rate is nearly 10 %. The true incidence of DRESS is difficult to predict because epidemiological data on illness incidence and underlying factors are limited [5].

The syndrome usually develops within two months after drug introduction. Fever, often high (38-40°C), which is the most common symptom and rash are the first signs, especially when related to antiepileptic drugs. The face, upper trunk and upper extremities are initially affected, with subsequent progression to the areas of necrosis, edema and mitotic figures but no Reed-Sternberg cells or capsular invasion. This Histopathological pattern can simulate a malignant lymphoma. [3]

It is difficult to diagnose, as many of its clinical features mimic those found with other serious systemic disorders. However, early recognition of the syndrome with the cessation of the causative drug is essential in improving patient outcome. [4]

CASE REPORT

A 11-years-old female with a history of head injury one and half month back, for which she was being treated with tab. Phenytoin, following which child developed maculopapular rash all over the body since 3days initially started over neck then spread to involve face, trunk, upper limb, lower limb, over a period of 8 to 12hours, redness in the oral cavity since 2 days also complained with lymphadenopathy, now she was brought complaints of fever since 15 days and rash over body since 10 days. She had a history of hospital admission a month back in KIMS Hubli in a view of fall, admitted for 15days. CT and EDH were normal. And discharged with tab phenytoin.

She was conscious, oriented to time, place and person. Head to toe test was performed where only face involves maculopapular lesions all over the body along with palms and soles. The anthropometry parameters which includes childs weight was 35kg, height was 137cm, BMI was 18.6kg. on

systemic examination per abdomen, respiratory system, cardiovascular system was normal, central nervous system includes cranial nerves, motor reflexes were nothing abnormalities detected, hence there is no involvement of organ damage. This based on subjective data a provisional diagnosis of drug induced acute urticaria, adverse drug reaction secondary to phenytoin, rickettsia fever was made and following specific laboratory tests was performed to establish diagnosis.

On day of admission she had intermittent fever (100.9°F), blood pressure (92/60mmHg), pulse rate (121bpm), respiratory rate (22cpm), oxygen saturation (98%), pulse volume was good. She has lymphadenopathy. The peripheral smear test was usually normal with impression of normocytic normochromic, with eosinophilia and elevated absolute eosinophilic count of 500cells/cmm. Her liver function test was elevated such as aspartate aminotransferase was 593µL, alanine transaminase 519µL, alkaline phosphatase 316IU/L. The troponin I was decreased (<0.012ng/ml). The urine routine was analysed with presence of urine protine, 2 to 3 pus cells in urine and ketone bodies were also present in urine. On fifth day of admission she was sent for dermatologist opinion, on current examination she was seen with multiple urticated papules coalesce to form plaque avascular necrosis and exfoliation of skin distributed over trunk, neck, upper limbs, lower limbs. Palms and soles were spared; in oral cavity mucositis was present. Dermatologist gave an impression based on clinical presentation drug reaction eosinophilia and systemic symptoms was made. Thus advised to avoid offending drug, application of calamine lotion and liquid paraffin all over body three times a day, inj. Dexona 1.5cc BD IV for 3 days, Inj Chlorphenamine twice daily. Based on subjective and objective data the patient was diagnosed with phenytoin induced drug reaction eosinophilia and systemic symptoms.

They advised discontinue the offending drug. The patient was treated with Intravenous fluid, Inj Chlorpheniramine 0.8mg/kg (2cc) stat as antiallergic, Tab Paracetamol 500mg if necessary for onset of fever, Inj Ranitidine 1cc twice a day, Inj Lorazepam iv 0.5mg/kg/day if necessary for epileptic episodes, Tab Azithromycin once a day 10mg/kg/day and Inj Piperacillin-tazobactam IV thrice daily 100mg/kg/day as prophylaxis. Over 7 days of admission her condition significantly improved then she was sent home. The patient was seen one month after her discharge, at the time fever and rashes were resolved and her liver enzymes were normalized.

DISCUSSION

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a serious and potentially fatal adverse reaction to therapeutic medications. [6] When DRESS syndrome is in the differential diagnosis, one should also consider other dangerous causes of severe cutaneous drug reaction such as Stevens-Johnson syndrome and toxic epidermal necrolysis. These typically occur sooner after drug exposure than does DRESS syndrome, within 1–3 weeks. [7]

The incidence of DRESS due to antiepileptics is in the range of 1:1000 to 1:10.000 in general population and of 0.4:1000 in hospital settings. In younger children the incidence of DRESS seems to be lower than in adults, although the real incidence is not known. The overall mortality rate is of 10% with a lower percentage in children than in adults.[6]

Jeremic I et al., explains about diagnostic criteria for dress, as includes if a macro popular rashes developed more than 3 weeks, clinical symptoms present after 2 weeks of discontinuing and fever is more than 38˚C, Liver abnormalities like ALT is more than 100IU/L with other organ involvement, haematological abnormalities and Leucocytes are in abnormal range, Atypical Lymphocytes is found to be more than 5%, abnormal Eosinophilia with Lymphadenopathy and HHV-6 reactivation symptoms. [8] In our study patient was having maculopapular rash all over the body for 2weeks initially started over neck then spread to involve face, trunk, upper limb, lower limb, over a period of 8 to 12hours, redness in the oral cavity for a week, liver abnormalities like ALT, AST, ALP were elevated, absolute eosinophilic count was increased with lymphadenopathy.

Most used diagnostic criteria Register for Severe Cutaneous Adverse to Drugs criteria (RegiSCAR) (Tables 1) Mortality is estimated to be 10%-20%. Therefore, it is very important to recognize DRESS syndrome as early as possible, stop treatment with causative drug and to start appropriate therapy with systemic steroids. [8]

Assessment using Regi-SCAR-group diagnostic criteria for DRESS revealed that overall >5 score indicating definite cause for DRESS syndrome. (Table 1) [8] Causality assessment was performed using Naranjo's causality assessment scale. It was encountered that phenytoin was the definitive cause of DRESS with an overall score of >9. (See Table 2) [9]

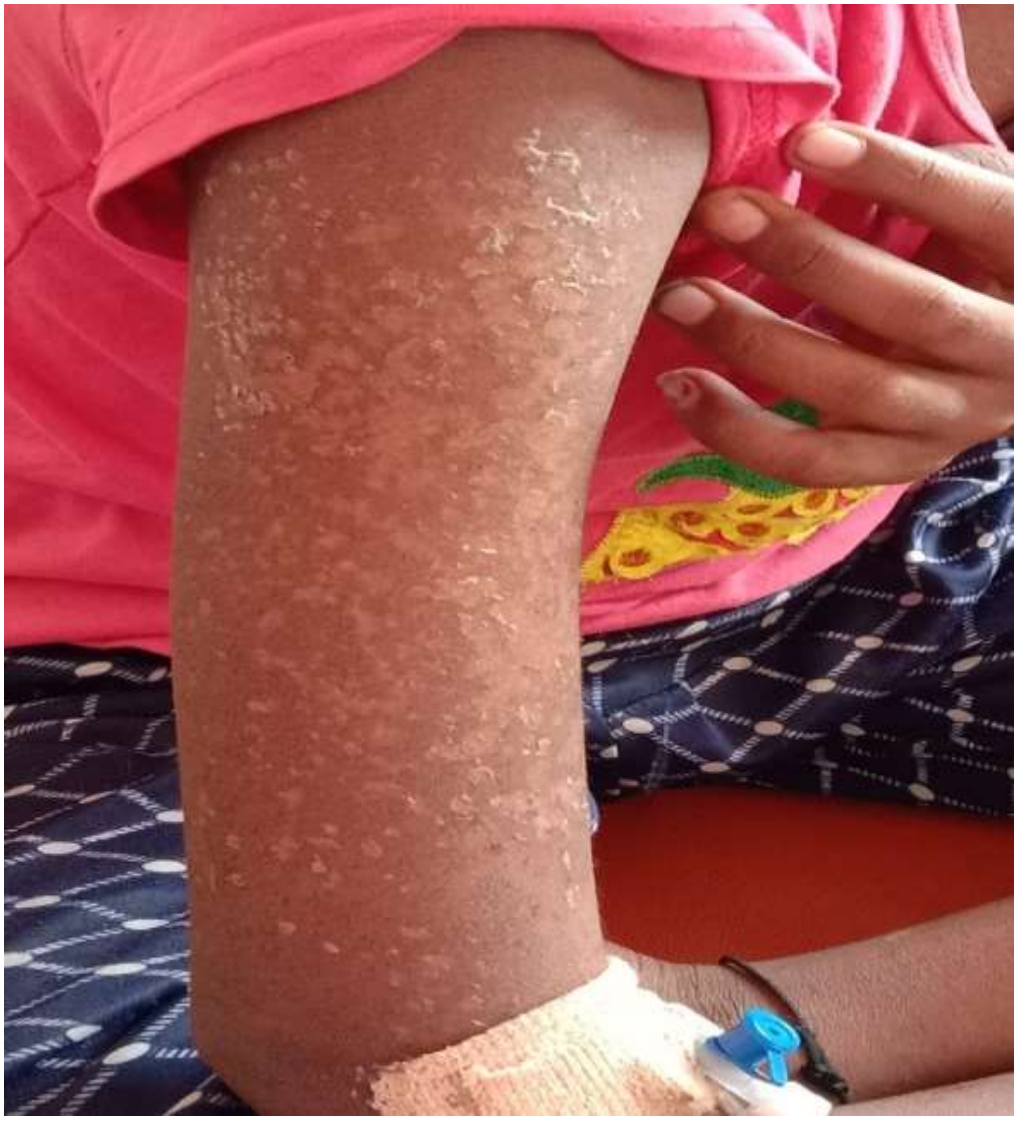
Abhishek De et al., DRESS syndrome usually begins within 2 months of ingestion of the offending drug, most often 2–6 weeks after its first use. However, symptoms may occur more rapidly and be more severe upon re-exposure. For phenytoin, the mean interval to onset is 17–21 days. Our study describes the similar clinical features such as patient developed a DRESS syndrome for more than 15 days of phenytoin ingestion, and symptoms occurred rapidly and be more severe upon re-exposure. [10]

Table 1: Regi-SCAR-group diagnostic criteria for DRESS. [8]

Diagnostic criteria's	No	Yes	Unknown
Fever >38°C	-1	1	-1
Enlarged lymph nodes	0	1	0
Eosinophilia	0	1	0
700-1499 or 10% - 19.9%. >1500 or >20%	0	2	0
Atypical lymphocytes	1	0	0
Skin rash >50% extent Atleast 2 of edema, infiltration, purpura or scaling. Biopsy suggesting DRESS.	0 0 - 1	1 1 1 0	0 0 0 0
Internal organ involvement One Two or more Resolution in more than 15days	0 0 2 0	 1 0 1	 0 - -1
Atleast 3 biological investigations done and negative to exclude alternative diagnosis.	0	1	0
Final score: <2 no DRESS., 2-3 possible DRESS., 4-5 probable DRESS., >5 definite DRESS.			

Table 2: Naranjo's causality assessment scale: [9]

QUESTIONS	YES	NO	DO NOT KNOW	SCORES
Are there previous conclusive reports on this reaction?	+1	0	0	1
Did the adverse event appear after the suspected drug was administered?	+2	-1	0	2
Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	1
Did the adverse reaction reappear when the drug was readministered?	+2	-1	0	2
Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	+2	0	2
Did the reaction reappear when a placebo was given?	-1	+1	0	1
Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?	+1	0	0	1
Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	1
Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	0
Was the adverse event confirmed by any objective evidence?	+1	0	0	1



Figures 1: Erythematous maculopapular rash on upper limbs.

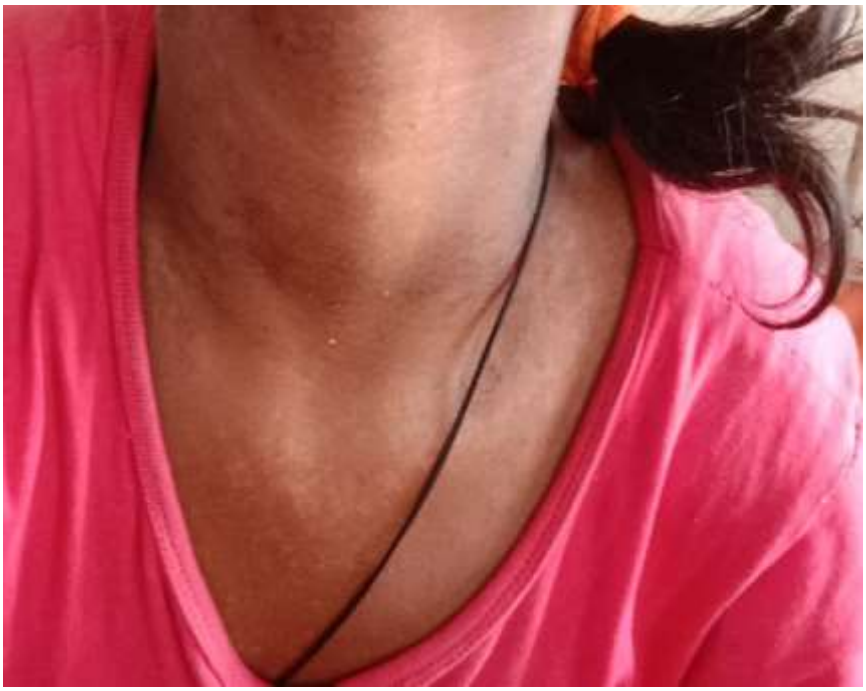


Figure 2: Erythematous maculopapular rash over the neck

Immediate withdrawal of causative drug, institutional treatment, and supportive measures, standard wound care, multidisciplinary approach, and prompt initiation of systemic steroid helped in resolution of the symptoms, as indicated can reduce the morbidity and mortality to minimum**.** early recognition of DRESS syndrome and withholding and/or changing the medication is necessary to prevent potentially fatal outcomes in special population like pediatrics.

Acknowledgement: The author thanks KLE College of Pharmacy, Hubballi and Karnataka Institute of Medical Sciences KIMS, Hubballi for all the support.

Conflict of interest: The authors declare no potential conflicts of interest with respect to research, authorship, and /or publication of this article.

Funding: No Funds, Grants or Other Support Was Received.

Contribution: AP: Preparation of Manuscript; AP, PB: Decision Making; AP: DATA Collection; All the Authors were Involved in Patient Care. AP, PB is the guarantor for this paper.

REFERENCES

1. Deka, N.M., Dass, R., Das, B.K. et al. Phenytoin Induced DRESS Syndrome. Indian J Pediatr 2013; 80:266. https://doi.org/10.1007/s12098-012-0751-7

2. Kim C, Choi G, Yun C, Kim D. Drug Hypersensitivity to Previously Tolerated Phenytoin by Carbamazepine-induced DRESS Syndrome. Journal of Korean Medical Science. 2006; 21(4):768. https://doi.org/10.3346/jkms.2006.21.4.768

3. Criado P, Criado R, Avancini J, Santi C. Drug reaction with Eosinophilia and Systemic Symptoms (DRESS) / Drug-induced Hypersensitivity Syndrome (DIHS): a review of current concepts. Anais Brasileiros de Dermatologia. 2012; 87(3):435-449. https://doi.org/10.1590/S0365-05962012000300013

4. Oliveira A, Carvalho R, Martins A, Reis J. Acute Hepatitis in the DRESS Syndrome. GE Portuguese Journal of Gastroenterology. 2016; 23(6):304-308. https://doi.org/10.1016/j.jpge.2016.06.001

5. Cacoub P, Musette P, Descamps V, Meyer O, Speirs C, Finzi L et al. The DRESS Syndrome: A Literature Review. The American Journal of Medicine. 2011; 124(7):588-597. https://doi.org/10.1016/j.amjmed.2011.01.017

6. Mori F, Caffarelli C, Caimmi S, et al. Drug reaction with eosinophilia and systemic symptoms (DRESS) in children. Acta Biomed. 2019; 90(3-S):66-79. Published 2019 Jan 29. https://doi.org/10.23750/abm.v90i3-S.8167

7. Oelze L, Pillow M. Phenytoin-induced Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) Syndrome: A Case Report from the Emergency Department. The Journal of Emergency Medicine. 2013; 44(1):75-78. https://doi.org/10.1016/j.jemermed.2011.05.052

8. I J, P O. Possible DRESS Syndrome in a Patient with Systemic Sclerosis and Rheumatoid Arthritis during Treatment with Lamotrigine. Archives of Medicine. 2018; 10(6). https://doi.org/10.21767/1989-5216.1000288

9. Jihana S, Parathoduvil AA, Purushothaman S. "An analysis of seriousness, predictability and preventability of adverse drug reactions reported at a tertiary care teaching hospital in Kerala, India: a retrospective observational record based study." International Journal of Basic & Clinical Pharmacology [Online], 2018; 7(12):2433-2438.

10. De A, Rajagopalan M, Sarda A, Das S, Biswas P. Drug reaction with eosinophilia and systemic symptoms: An update and review of recent literature. Indian Journal of Dermatology. 2018; 63(1):30. https://doi.org/10.4103/ijd.IJD_582_17