wjpmr, 2023,9(7), 125-128

SJIF Impact Factor: 5.922

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Review Article

ISSN 2455-3301

WJPMR

DRUG-INDUCED REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (DRESS) SYNDROME: A REVIEW

V. Nandini[1]*, P. Supriya[1], Dr. K. Tirumala Naik[2], M. Navya Sai[3] and M. Prathyusha Bai[4]

[1]Pharm. D Intern, Krishna Teja Pharmacy College, Tirupati, Andhra Pradesh, India.
[2]Clinical Preceptor & Associate professor, Krishna Teja Pharmacy College, Tirupati.
[3,4]Pharm. D Interns, Krishna Teja Pharmacy College, Tirupati, Andhra Pradesh, India.

***Corresponding Author: V. Nandini**

Pharm. D Intern, Krishna Teja Pharmacy College, Tirupati, Andhra Pradesh, India.

Article Received on 12/05/2023 **Article Revised on 02/06/2023** **Article Accepted on 22/06/2023**

ABSTRACT

Drug-induced hypersensitivity syndrome (DIHS), commonly referred to as DRESS syndrome (Drug-Induced Reaction with Eosinophilia and Systemic Symptoms), is a severe and potentially fatal adverse drug reaction. It is characterized by a delayed onset, occurring 2 to 8 weeks after initiating medication. The syndrome involves a complex interplay of factors, including medication exposure, genetic predisposition, and viral reactivation. The pathophysiology of DRESS syndrome is not fully understood, but it is believed to be an immune-mediated reaction involving T-cell activation. The clinical presentation of DRESS syndrome is diverse, with symptoms including rash, fever, eosinophilia, and organ involvement. Prompt diagnosis and withdrawal of the offending medication are essential for successful treatment. Systemic corticosteroids are commonly used, and the prognosis varies depending on the severity of the syndrome. This review provides an overview of the epidemiology, pathophysiology, clinical presentation, evaluation, treatment, and prevention strategies for DRESS syndrome.

KEYWORDS: Drug induced hypersensitivity syndrome, adverse drug reaction, genetic predisposition, fulminant hepatitis, drug reaction with eosinophilia and Systemic symptoms syndrome, hepatic necrosis, immune mediated reaction.

INTRODUCTION

Definition: DRESS syndrome, also called as drug-induced hypersensitivity syndrome (DIHS), it is a distinct, severe, idiosyncratic reaction to certain drugs characterized by a prolonged latency period. It is a potentially life-threatening ADR.[1,2,3] It can cause injury or even death and affects both adults and children. It often happens 2 to 8 weeks after starting a medicine.[4]

Epidemiology

The Drug reaction with eosinophilia and systemic symptoms syndrome affects both children and adults. [5] The prevalence of DRESS syndrome is generally low, with estimates of risk after exposure to triggering medicines ranging from 1 in 1,000 to 1 in 10,000 individuals.[1] A 10% mortality rate is associated with this disease, primarily due to fulminant hepatitis with hepatic necrosis.[3] For new users of phenytoin and carbamazepine, the probability of developing hypersensitivity within 60 days of the first or second prescription was calculated to be 2.3-4.5/10,000 and 1-4.1/10,000, respectively.[6]

Pathophysiology

Recent years have seen significant improvements in our understanding of DRESS pathogenesis. A delayed type IVb, and occasionally an IVc, hypersensitivity reaction, DRESS is a severe, idiosyncratic, T cell driven drug reaction. The complicated combination of medication (or vaccine or biologic) exposure, genetic predisposition, and viral reactivation is thought to be the cause of DRESS. The "Swiss cheese" model of aligned hazards is supposed to explain why some people experience this illness while others do not, while having the same exposure.

This model needs to consider the fact that there are probably still unidentified risk factors and situations that predispose people to this disease.[7]

Although the specific pathophysiology of DRESS syndrome is yet unknown, cases using anticonvulsants consider the intricate interplay of three factors:

1. A lack or anomaly of the epoxide hydroxylase enzyme, which detoxifies the byproducts of aromatic amine anticonvulsants;
2. A herpes virus family associated with sequential reactivation; and

3. An ethnic predisposition with certain human leukocyte antigen (HLA) alleles.

Reactive metabolites and the theory of inadequate drug metabolism:

DRESS syndrome risk is increased by certain mutations in genes encoding drug detoxifying enzymes. It's possible that certain genetic predispositions are passed down through autosomal dominant inheritance.

Racial and family predispositions that have been seen in patients of African descent may be explained by this. The etiology of DRESS syndrome brought on by anticonvulsants has been linked to excessive reactive metabolite production.

Epoxide hydroxylase is often responsible for detoxifying these harmful compounds. Epoxide hydroxylase-related genetic abnormalities lead to the buildup of hazardous metabolites, which can trigger immune reactions.

Immunologic mechanism: It is generally known that DRESS syndrome is an immune-mediated reaction because it affects a small percentage of patients, is associated by eosinophilia, and modifies the lymphocytic response. A delayed cell-mediated immune response is very plausible because it has to be sensitized and can be replicated through skin tests. Tumor necrosis factor and interleukin-6 are two of the proinflammatory cytokines that are Increased in the DRESS syndrome.

Genetic predisposition: The development of DRESS syndrome is more likely in people with particular HLA haplotypes. A higher probability of white patients acquiring the abacavir-induced DRESS syndrome has been linked to the HLA-B*5701 allele. Japanese individuals are more likely to develop the DRESS syndrome in response to carbamazepine, according to research by Kashiwagi et al. In the Chinese population, HLA-B*5801 was found to have a substantial association with the DRESS syndrome caused by allopurinol, according to Hung et al.

Reactivation of herpes viruses: Human herpes virus (HHV) reactivation and host immune response to the virus are linked to systemic signs of DRESS. Since HHV-6 can be found in the blood of roughly 60–80% of DRESS patients, HHV-6 reactivation has been incorporated into the diagnostic standards for DIHS created by Japanese specialists. Epstein-Barr virus (EBV), cytomegalovirus (CMV), and HHV-7 reactivation are three other herpes viruses that may be linked to systemic symptoms and flare-ups of DRESS. In order to explain viral participation, two theories have been proposed: (i) Immunological reaction against the medication with secondary viral reactivation connected to a cytokine storm; and (ii) Early viral reactivation in charge of the majority of DRESS syndrome characteristics.

There is proof that specific medications that activate DRESS can directly cause viral multiplication in T cells in a culture dish. But the majority of experts support the idea that virus reactivation is just a bystander effect. The importance of virus activation in the pathophysiology of DRESS is still unknown, even though the identification of HHV reactivation may be helpful in the diagnosis of DRESS.[8]

Uncertainty surrounds the precise pathogenic function.

In a refractory DRESS disease patient, the JAK-STAT (Janus kinases-signal transducer and activator of transcription proteins) signaling pathway was recently revealed to be activated. Additionally, IL-5 might be crucial to the pathogenesis of DRESS. In 88% of cases, the causing substance can be identified.[9]

Clinical presentation

A complex syndrome with a wide range of clinical symptoms is called DRESS syndrome. The clinical manifestations often take 2 to 8 weeks to show after the triggering medication is introduced. [2] There are several possible offending medicines. DRESS syndrome is commonly accompanied by the use of the following drugs: antibiotics, antiviral drugs, anticonvulsants, mexiletine, allopurinol, antidepressants and biologic agents. [1] Rash, fever, eosinophilia (absolute eosinophil count [AEC] 500/L), and organ injury (usually liver and/or kidney, but other organs such as the lung, heart, gastrointestinal system, or others can be affected) are among the clinical symptoms of DRESS syndrome.[10]

Systemic involvement may include hepatitis, pneumonitis, myocarditis, pericarditis, nephritis, colitis.[11]

Etiology

a) Common causes: There is a greater number of drugs which can cause DRESS syndrome.[6]

- ✓ Antibiotics: linezolid, ampicillin, cefotaxime, dapsone, ethambutol, and ampicillin.
- ✓ Antiviral drugs: Abacavir, Zalcitabine, and nevirapine
- ✓ Anticonvulsants: Phenytoin, phenobarbital, valproic acid, carbamazepine, zonisamide and lamotrigine.
- ✓ Antidepressants: Bupropion and Fluoxetine.[1]
- ✓ Antiretroviral drugs.[12]

b) Risk factors: Pharmacogenetic susceptibility and Immunosuppression.[13]

Evaluation

The patient should have a thorough evaluation to determine the diagnosis, determine the severity, and for monitoring purposes.[6]

Any patient who has taken a new medicine during the last two to eight weeks and exhibits both a skin eruption and a fever should be evaluated for DRESS syndrome. It is strongly advised to carry out a series of thorough

laboratory investigations and monitor often in suspicious instances.[9]

- CBC with diff
- BMP
- LFTs
- Coags
- ESR
- CRP
- Viral hepatitis panel
- Biopsy.[11]

Blood is taken for testing, and a skin biopsy may be done. High levels of eosinophils, a type of white blood cell, are frequently detected in blood test. [4]

Prognosis

The majority of DRESS syndrome patients fully recover with early diagnosis, medication withdrawal, and adequate treatment. One spectrum of the disease resolves quickly, but a more severe spectrum may have substantial, lifelong systemic effects. The clinical result varies significantly. [3] The signs and symptoms of DRESS might linger for weeks after stopping the offending substance, with a typical recovery time of 6 to 9 weeks. [7]

Management

The cornerstone of treating DRESS syndrome is the prompt discontinuation of the culprit medication and the administration of systemic corticosteroids.[14] If it is unclear which substance is to blame, it may be necessary to stop using several medications.[4]

The usage of seven distinct drug groups is most frequently associated with the DRESS syndrome, a reaction to some incriminated medicines.

- Anticonvulsants like phenytoin, carbamazepine, phenobarbital, valproic acid and mexiletine.
- Antidepressants like amitriptyline and desipramine.
- Sulfonamides and sulfones like dapsone, sulfasalazine, sulfamethoxazole and trimethoprim.
- Anti-inflammatory drugs like diclofenac, piroxicam, sundilac and ibuprofen.
- Anti-infectives such as doxycycline, terbinafine, Abacavir, minocycline and linezolid.
- Angiotensin converting enzyme inhibitors like enalapril and captopril.
- Beta blockers such as celiprolol and atenolol.[15]

Steroid creams are used for rash in mild occurrences. It may be necessary to take oral or intravenous immune-suppressing drugs (such as corticosteroids, cyclosporine) for a more severe rash or when organs are affected. Treatment is gradually reduced over several weeks to months in order to stop DRESS syndrome from returning.[4]

Prevention

The main prevention of DRESS syndrome is not yet well-established. The following primary preventative strategies are possible:

- Agents known to be linked to the DRESS syndrome should be gradually increased in dosage.
- DRESS syndrome patients' family may benefit from genetic counseling. [16]

CONCLUSION

DRESS syndrome is a severe and potentially life-threatening adverse drug reaction characterized by a delayed onset and immune-mediated reaction. It involves a complex interplay of medication exposure, genetic predisposition, and viral reactivation. Prompt diagnosis and withdrawal of the offending medication are crucial for successful treatment. Systemic corticosteroids are commonly used, and the prognosis varies depending on the severity of the syndrome. Further research is needed to better understand the pathophysiology and develop effective preventive strategies for DRESS syndrome. Healthcare professionals should be aware of this syndrome and consider it in patients presenting with a skin eruption, fever, and organ involvement after starting a new medication.

ACKNOWLEDGEMENT

We are very thankful to Dr. K. Tirumala Naik, Pharm. D, Clinical preceptor and Associate professor, Department of pharmacy practice, Krishna Teja Pharmacy College, Tirupati. We sincerely thank him for his immense support and valuable suggestions to complete our article. We are very glad to pursue our article under his guidance.

REFERENCES

1. Olopaade J, Tee- melegrito RA. What to know about DRESS Syndrome (Internet). Medicalnewstoday. com (cited Nov 3). Available from https://www.medicalnewstoday.com/articles/dress-syndrome-symptoms-causes-and-treatments#treatment, 2021.
2. Choudhary S, McLeod M, Torchia D, Romanelli P. Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome. The Journal of clinical and aesthetic dermatology, 2013 Jun; 6(6): 31.
3. 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 Jan; 63(1): 30.
4. Krantz MS, Phillips EJ. Drug Reaction with Eosinophilia and Systemic Symptoms. JAMA dermatology, 2023 Jan 11.
5. Corneli HM. DRESS syndrome: drug reaction with eosinophilia and systemic symptoms. Pediatric Emergency Care, 2017 Jul 1; 33(7): 499-502.
6. 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 Jan; 63(1): 30.
7. Stirton H, Shear NH, Dodiuk-Gad RP. Drug reaction with eosinophilia and systemic symptoms (DReSS)/Drug-Induced hypersensitivity syndrome (DiHS)—readdressing the DReSS. Biomedicines, 2022 Apr 26; 10(5): 999.
8. 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 Jan; 63(1): 30.
9. Alotaibi M, Alotaibi MA. Drug-Induced Reaction with Eosinophilia and Systemic Symptoms: A Review. Cureus, 2023 Mar 2; 15(3).
10. Wolfson AR, Zhou L, Li Y, Phadke NA, Chow OA, Blumenthal KG. Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome identified in the electronic health record allergy module. The Journal of Allergy and Clinical Immunology: In Practice, 2019 Feb 1; 7(2): 633-40.
11. Drug rash with eosinophilia and systemic symptoms syndrome [Internet]. Wikem.org (cited 2021 Feb 22). Available from: https://wikem.org/wiki /Drug_rash_with_eosinophilia_and_systemic_sympt oms_syndrome.
12. Kerure A. DRESS Syndrome - Causes, Signs and Symptoms, Treatment [Internet]. Lybrate.com (cited 2023 Jan 10). Available from: https://www.lybrate. com/topic/dress-syndrome-know-the-signs-of- it/3d712a195d730596dfb 1aeb89844c420.
13. Drug reaction with eosinophilia and systemic symptoms [Internet]. Amboss.com (cited 2022 Oct 21). Available from: https://www.amboss.com /us/knowledge/Drug_reaction_with_eosinophilia_an d_systemicsymptoms.
14. Husain Z, Reddy BY, Schwartz RA. DRESS syndrome: Part II. Management and therapeutics. Journal of the American Academy of Dermatology, 2013 May 1; 68(5): 709-e1.
15. Almasry IM, Al Sabah H, Lazarevic V, Albathali AA, Alnaki A, AlSumait A. Successful Management of Some Challenging Cases of DRESS Syndrome with Intravenous Immunoglobulins, Case-Based Review Article. J Clin Exp Dermatol Res., 2020; 11: 541.
16. Gibson CM, Daaboul Y, Korjian S. DRESS syndrome primary prevention [Internet]. wikidoc.org (cited 2016 July 20). Available from: https://www.wikidoc.org/index.php/DRESS_syndro me_primary_ prevention#:~:text=Primary %20prevention%20measures%20may%20include% 20the%20following%3A,of%20patients%20with%2 0DRESS%20syndrome.