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Case Study

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A CASE REPORT ON NAVIGATING THE COMPLEXITIES OF PHENYTOIN-INDUCED DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (DRESS) SYNDROME

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ABSTRACT

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a severe hypersensitivity reaction associated with various medications, including anticonvulsants like phenytoin. We report a case of a 64year old male patient who developed DRESS syndrome following phenytoin therapy for seizure. The patient presented with complains of fever with rashes and itching. He also had an episode of vomiting and gradually progressed to involve multiple organ systems. Laboratory investigations revealed that eosinophils counts were 9% and elevated ESR level. His RFT was deranged with mildly elevated creatinine, which is consistent with a diagnosis of DRESS syndrome. Phenytoin was promptly discontinued and the symptoms were subsided. Our case underscores the importance of recognizing DRESS syndrome as a potential adverse reaction to phenytoin and highlights the challenges associated with its diagnosis and management.

KEYWORDS: DRESS syndrome, drug-induced hypersensitivity syndrome, phenytoin, adverse drug reaction.

INTRODUCTION

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a rare but potentially life-threatening adverse drug reaction characterized by fever, skin rash, lymphadenopathy, and multiorgan involvement. Also known as phenytoin hypersensitivity syndrome, was most commonly associated with phenytoin use. Although it is classically caused by anticonvulsants and sulfonamides, many other drugs have been implicated. Its pathophysiology is not completely understood at this time.[1]

Its etiology has been linked with lymphocyte activation, drug metabolic enzyme defects, eosinophilia, and human herpesvirus-6 reactivation. DRESS has a later onset and longer duration than other drug reactions, with a latent period of 2 to 6 weeks. It may have significant multisystem involvement, including hematologic, hepatic, renal, pulmonary, cardiac, neurologic, gastrointestinal, and endocrine abnormalities. This syndrome has a 10% mortality rate, most commonly from fulminant hepatitis with hepatic necrosis.[2]

Phenytoin, a commonly used medication for the management of seizures, has been implicated as a causative agent in DRESS syndrome due to its metabolic and immunologic effects. Preventive measures, including genetic screening and provider education, can help mitigate the impact of this severe adverse drug reaction. As research continues to elucidate the underlying mechanisms, our ability to prevent and treat DRESS syndrome will undoubtedly improve, enhancing patient safety and care.[3]

CASE

A 64year old male who is a known case of CAD, Hypertension, DLP and Seizure, he was presented with complains of fever with rashes and itching also he had 1 episode of vomiting and laboratory investigations revealed that eosinophils counts were 9% and elevated ESR (54) level. RFT was deranged with mildly elevated creatinine. He was taking T. Phenytoin 100mg once daily for seizure disorder and he developed above mentioned complains. Dermatology consultation was sought and they gave impression as DRESS syndrome to phenytoin and suggested to stop phenytoin and prescribed with steroids. After the medication discontinued, within a period of time his complains were subsided and laboratory values were within normal limits. During the course of hospital stay, he was treated iv fluids, antibiotic (T. Doxycycline), steroids (T. Prednisolone), epileptics, OADs, antihypertensive and other supportive measures. Regular monitoring of vitals and blood sugars were done. Patient was stable and discharged.

DISCUSSION

Phenytoin-induced DRESS syndrome is a multifactorial hypersensitivity reaction involving genetic susceptibility,

metabolic activation of phenytoin, immune system dysregulation, and potential viral reactivation. Genetic factors such as HLA-B*1502 and CYP2C9 polymorphisms contribute to the risk, while the accumulation of toxic metabolites triggers an immune response that leads to systemic inflammation and organ damage. Our case report was similar to a study conducted by **M. Yazicioglu *et.al*** there the patient presented with erythematous pruritic maculopapular confluent eruption, fever and Laboratory results revealed WBC count 9400/mm3, eosinophils7%; lymphocytes 68%, LFT was abnormal.[4] Another study conducted by **MNM Rodriguesorcid *et.al*** in which the patient had fever and maculopapular cutaneous lesions. He presented lymphocytosis with eosinophilia and severe acute hepatitis 24 hours after admission day. Hepatic transaminases returned to reference levels after phenytoin withdrawal[5] which were similar to our case in which the patient had complains of fever with rashes and itching. Laboratory investigations revealed that eosinophils counts were 9% and elevated ESR (54) level. RFT was deranged with mildly elevated creatinine.

Phenytoin-induced DRESS syndrome is believed to stem from a hypersensitivity reaction triggered by the drug. When phenytoin is metabolized in the liver, it generates metabolites that can bind to proteins, forming drug-protein complexes. These complexes are recognized as foreign by the immune system, sparking an immune response characterized by the activation of T lymphocytes and the release of cytokines and inflammatory mediators. Consequently, In our study, our patient experienced rashes and itching all over the body which was similar to the observations seen in the study done by **Yung-Tsu Cho *et al*** which showed widespread inflammation and tissue damage occur in various organs, leading to the characteristic manifestations of DRESS syndrome, including rash, fever, hepatitis, nephritis, and lymphadenopathy.[6] Genetic predisposition may also influence an individual's susceptibility to developing this syndrome. Management involves prompt withdrawal of phenytoin, supportive care, and monitoring for potential complications, highlighting the importance of early recognition and intervention in this potentially serious adverse drug reaction.

CONCLUSION

In conclusion, Phenytoin-induced Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome is a critical and potentially fatal hypersensitivity reaction that necessitates prompt diagnosis and intervention. The syndrome's hallmark features include a widespread rash, hematologic abnormalities such as eosinophilia, and multi-organ involvement, which can lead to severe complications if not addressed quickly. Immediate discontinuation of phenytoin and supportive care, often including corticosteroids, are essential steps in management. The primary management strategy involves the immediate discontinuation of phenytoin, coupled with supportive care and, in many cases, the administration of systemic corticosteroids. Early recognition and appropriate treatment are paramount to improving patient outcomes and preventing long-term sequelae associated with this serious drug reaction.

ABBREVIATIONS

1. **DRESS:** Drug reaction with eosinophilia and systemic symptoms
2. **ESR:** Erythrocyte Sedimentation Rate
3. **CAD:** Coronary Artery Disease
4. **RFT:** Renal Function Test.

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CONFLICTS OF INTEREST

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