

PHENYTOIN INDUCED EXANTHEMATOUS RASH WITH SEVERE LEUKOPENIA AND ANEMIA-A CASE REPORT.

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Key words: - Adverse drug Reaction (ADR), Phenytoin, Rash, Anemia, leukopenia, Common Terminology Criteria for Adverse Events (CTCAE).

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Introduction: -

Phenytoin is the most common and widely used antiepileptic drug. It is used for the prevention and treatment of generalized seizures, partial seizures and status epilepticus. Cutaneous reactions are a common adverse effect associated with antiepileptic drugs (AEDs) and a cause of treatment discontinuation. Such reactions range from mild rashes to more serious conditions such as Stevens-Johnson syndrome and toxic epidermal necrolysis^[1]. With phenytoin, for instance, skin rashes occur in up to 16% of patients at the beginning of therapy^[2].

Hematological problems have been rarely reported with phenytoin and includes granulocytopenia, agranulocytosis, pancytopenia, thrombocytopenia, leukopenia [3].

Phenytoin interferes with the absorption or proper distribution of folic acid, therefore it results in Anemia^[4]. Here we are presenting a case on phenytoin induced Rash with leukopenia and Anemia.

Case Description: - A 34-years-old female patient came with complaints of low-grade fever since 15 days and rash over body of 4 days duration. Fever was low-grade, continuous, not associated with chills, and decreased on medication. Rash was itchy and was associated with swelling and painful ulceration of the lips. The patient had history of seizures 1 month back, 3 episodes per day lasted for 10 minutes with post ictal confusion and frothy discharge from mouth. As she was developing seizures continuously then she consulted a physician and got prescribed with Phenytoin -100mg-TID. On using phenytoin for 1 week, she developed ulcers on the lips and Rash all over the body. Her hematological states WBC 1,800 cells/cumm & haemoglobin 8.3g/dl.

Discussion: -

Phenytoin is an anti-epileptic drug. Most of the patients are hypersensitive to this drug. Initially it begins with Exanthematous Rash, untreated condition may lead to SJS (Stevens Johnson syndrome) further leads to TEN (Toxic epidermal necrolysis). In SJS the skin detachment is of 10% while in TEN the skin detachment occurs more than 30%^[5]. Phenytoin is metabolized by CYP450. The presence of Allele HAL B*51:01 has increased the risk of 5 to 26% of Exanthematous Rash^[6]. Therefore it is recommended to screen the patients initially for the above mentioned allele and then prescribe the drug under

discharge medication. Common Terminology Criteria for Adverse Events (CTCAE) v5.0 was used to classify the Rash and was to be grade-3. Fever and Rash are the most common manifestations of 90-100% of phenytoin exposures^[7]. Phenytoin metabolism interrupts the vitamin-B12 synthesis, which plays a key role in production of normocytic & normochromic Erythrocytes^[4]. Some similar studies shows that incidence of DRESS with Anti-convulsant drugs 47.4%, Antibiotics-18.4%, NSAID's -13.2%, allopurinol-5.2%, others-15.8%^[8]. Pathophysiology of SJS and TEN is still yet unclear, the Arene oxides are the metabolites of the aromatic anti convulsants. When these arene oxides are not rapidly detoxified with the epoxide hydrolases. These metabolites acts as the haptens and render the keratinocytes antigenic by binding to them^[9]. In this patient there was an elevated leucocytic count which is an evidence of inflammation and decreased hemoglobin levels.



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Conclusion: - Each drug have its own adverse effect. Phenytoin is a frequently used anticonvulsant. Rarely it may cause ADRs such as Rash. Therefore it is important to educate the patient regarding the offending drug and to avoid further exposure. Clinical pharmacists and physicians must be aware of such reaction, so that we can prevent the Adverse reaction before it occurs.

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