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Case Study

CARBAMAZEPINE INDUCED SLE-A RARE AND SERIOUS ADR

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ABSTRACT

Carbamazepine is a commonly used antiseizure medication. Carbamazepine-induced SLE (Systemic Lupus Erythematosus) is a very rare phenomenon. Drug-induced SLE is an autoimmune disease caused by long-term use of certain drugs. Carbamazepine is a drug with low risk for causing lupus symptoms. The process that leads to drug-induced SLE are not entirely understood. A very few cases are reported with carbamazepine association with SLE. Herein we report a case of 4 y old girl with SLE induced by carbamazepine showing a causality score of 8 by Naranjo ADR probability scale.

Keywords: Carbamazepine, Systemic Lupus Erythematosus, Drug induced

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INTRODUCTION

Carbamazepine (CBZ), is sold commonly under the brand name Tegretol. It is mainly used in the treatment of epilepsy and neuropathic pain. It is not effective for absence seizures or myoclonic seizures. It can be used as a second line agent in Bipolar Affective Disorder. The mechanism of action is (1) Drug stabilises inactivated state of Na^+ channels, thereby making neurones less excitable. (2) May reduce the action of nucleus ventralis of the thalamus or decreases synaptic transmission or summation of temporal stimulation leading to neuronal discharge [1].

Common side effects are nausea and drowsiness. The other serious side effects includes skin rashes and decreased Bone marrow function. Lupus-like symptoms such as muscle pain, joint pain, fever, rashes and occasionally pleuritis and pericarditis develops as a long term side effects mainly due to induction of autoantibodies [2].

A predisposing factor for developing drug-induced SLE is N-acetylation speed or the rate at which body can metabolize the drug. This is greatly decreased in patients with genetic deficiency of N-acetyl transferase enzyme. This is because such patients will have more metabolites in their urine than fast acetylators.

Systemic Lupus Erythematosus is a chronic inflammatory disease that has a protean manifestation. More than 90% of cases is seen in women. SLE, an autoimmune disorder characterised by multisystem inflammation with the generation of autoantibodies. Serum nuclear antibodies (ANA) are found in nearly all individuals with active SLE. In childhood onset SLE there are several clinical symptoms more commonly found than in adults, including rash, mucocutaneous involvement, renal involvement, proteinuria, urinary cellular casts, seizures, thrombocytopenia, fever and lymphadenopathy [3].

Some drugs are responsible for causing SLE, with the highest risk drugs including procainamide and hydralazine. Carbamazepine is a drug with low risk for causing lupus symptoms. Management depends on the individual patient's condition, the severity of disease and its manifestations. It is important to recognise early the drugs causing SLE symptoms [4]. Symptoms of SLE will disappear within weeks after medication use is discontinued. This case report highlights carbamazepine-induced SLE in a 4 y old girl with seizures, after 10 mo of carbamazepine therapy

CASE REPORT

A 4 y old girl child with normal birth and development, had a history of seizures from 3 y of age with complex partial seizure semiology and was on medication Tegretal (Carbamazepine) and Frisium (Clobazam)) which was started 10 mo back. She was admitted in the hospital with fever, tiredness, early morning stiffness, joint pain and rash. On examination her vitals where stable. Clinical examination revealed cervical and axillary nodes++, Synovitis of right knee and ankle, pallor+Hepatosplenomegaly present; blood showed active inflammation.

Lab values: CRP: 48.9, ESR: 77 mm/hr, ANA 3+, AntiSDNA+. Nucleosomes+Rib P proteins+.

USG abdomen was done which showed (1) Mild hepatomegaly with relative hypoechogenicity, (2) Mild increase in renal cortical Echogenicity, (4) Particles in urinary bladder possibility of cystitis, (5) mild free fluid in abdomen

EEG showed R parietal spikes; MRI showed R parietal lobe CSF signal intensity with mild volume loss. Due to high CRP and mild pleural effusion she was started on injection IV Ceftriaxone 1g BD.

Pediatric Rheumatology assessment agreed with the possibility of Drug-Induced SLE (Carbamazepine) and hence carbamazepine was stopped and a dose of Frisium was hiked. No other anticonvulsants could be added due to the possibility of HLA activation similar to CBZ.

Patient condition improved after 4 d of withdrawal of the drug. During discharge, no significant involvement in the form of renal or liver was noted. She was commenced on Tab Hydroxy-chloroquine 100 mg OD, Tab. Naproxen 250 mg ½ TID and discharged with a plan to add leviteracetam if a seizure occurs.

DISCUSSION

Carbamazepine-induced SLE is not very frequent. According to *Degiovgio et al.*, the minimum prevalence of CBZ induced SLE IS 2-3/100,000 [5]. The characteristic features of CBZ induced SLE are:

For dominant in young females symptoms mainly of fever, rash, arthalgia and leukopenia without the involvement of kidney or central nervous system, prompt improvement after cessation of CBZ with or without prednisolone administration only a few cases of CBZ induced SLE are reported.

Currently, theories propose that SLE develops when genetically predisposed individuals are exposed to some environment or chemical agents such as drugs or metabolites of the drugs. These agents inhibits T-cell DNA methylation, increased lymphocyte function-associated antigen and adoptive transfer of T cell that makes autoreactive and causes lupus-like symptoms. The mechanism by which these cells causes autoimmunity is unknown [6].

In this case, we used Naranjo ADR probability scale for the causality assessment and showed a score of 8 (Probable). A Rechallenge could

not be performed due to the severity of the reaction and inherent risk. Carbamazepine was withdrawn and patient condition improved after 4 d. As a part of management hydroxychloroquine and naproxen was given.

CONCLUSION

Carbamazepine has a low risk for causing SLE. But the prompt knowledge about this reaction is important in clinical practice. The main problem in the treatment is that other anticonvulsant drug which causes HLA activation could not be prescribed if the patient is allergic to CBZ. So adequate knowledge of clinical pharmacist/ clinicians is important in handling such situations for the rational choice of drugs and disease management.

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CONFLICT OF INTERESTS

Declared none

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