Case Report

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Internal Medicine Section

Carbamazepine Induced Thrombocytopenia

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ABSTRACT

Antiepileptic Drugs (AEDs) are commonly associated with haematological disorders, including anaemia, thrombocytopenia, neutropenia and even bone marrow failure. Fatal disorders like aplastic anaemia are uncommon. On exploring through the literature, older AEDs are more associated with haematological alterations than newer AEDs, and careful monitoring is warranted especially with phenytoin, carbamazepine and valproate. The exact cause of these alterations is not established, though immune mechanisms and pharmacology of individual drugs are the proposed mechanisms, a further research along this path is underway. Of worth mentioning here, this predilection of older AEDs towards haematological disorders is pronounced in children compared to adults. We present here a case of congenital heart disease with history of brain abscess and seizures, on carbamazepine who presented to our hospital with toothache. Routine screening prior to tooth extraction revealed thrombocytopenia. Further evaluation revealed the association of carbamazepine and thrombocytopenia, which mandated discontinuation of drug and switching patient to alternative AED.

Keywords: Antiepileptic drugs, Cyanotic congenital heart disease, Haematological alterations

CASE REPORT

A 40-year-old male presented to the Out Patient Department of Oral Medicine with one week history of toothache. He was diagnosed with a tooth ailment for which he was advised tooth extraction. He was referred to the Department of Medicine in view of polycythemia and thrombocytopenia. The patient is a known case of cyanotic congenital heart disease. He also gave history of brain abscess 16 years ago which was surgically drained. During that admission, patient was started on AEDs. He was lost to follow up for the last 16 years but has continued to take the AEDs regularly. The last known attack of seizures were six years prior to present admission, which the patient attributed to missed doses of medication.

He was on phenobarbitone and carbamazepine at the time of current admission. On examination, the patient had features of chronic hypoxia like grade 3 clubbing and central cyanosis. The lab parameters showed polycythaemia, which was expected, but the patient also had thrombocytopenia that could not be explained by his clinical condition. His 2D echocardiogram was suggestive of congenitally corrected transposition of great arteries with a severe pulmonary stenosis and a large ventricular septal defect mimicking the fallot physiology along with AV/VA discordance. The patient was evaluated for the cause of thrombocytopenia and carbamazepine, which is known to cause haematological alterations, was considered as a possibility. The Naranjo algorithm was applied and a score of 7 was suggestive of a probable association ofcarbamazepine to the thrombocytopenia. The drug was discontinued on day 3 of hospital stay. On admission his platelets were 45,000/cu.mm along with presence of giant forms. After cessation of drug, one week later, the platelet count showed a significant improvement to 82,000 platelets/cu.mm.

The patient was taken up for tooth extraction and was given a course of amoxicillin and clavulunate. Patient's AEDs were optimised; levetericetam and phenobarbitone were prescribed at weight adjusted dosages. Patient also underwent multiple phlebotomy procedures for polycythaemia. At the time of discharge, the platelet count returned to normal levels, 1.21 lacs platelets/cu.mm. The patient was followed up two weeks later and his platelet count was found to be 99,000/cu.mm along with giant forms [Table/Fig-1].

Lab Parameters	Day 1	Day 3	Day 5	Day 8	Day 11	On Discharge (Day 14)	Follow up (Day 28)
Haemoglobin (g/dl)	23.5	23.0	20.6	22.1	21.0	21.3	21.0
Platelets (per cu.mm)	45,000 Giant forms+	49,000 Giant forms+	53,000	60,000	82,000 Giant forms+	1,21,000	99,000 Giant forms+

[Table/Fig-1]: Lab parameters.

DISCUSSION

Carbamazepine has been used since the 1960s to treat trigeminal neuralgia. In 1974 it was approved as an anti-epileptic. Chemically, it is an iminostilbene derivative. The carbamyl group at the first position is responsible for its potent anti-seizure activity [1]. In India, it is used as a first line drug for the management of partial as well as generalized tonic clonic seizures [2]. It's rare but severe haematological side effects include agranulocytosis, thrombocytopenia and aplastic anaemia [3].

Sudden withdrawal of anti-seizure medication is a precipitating factor for seizures. However in this case, the patient was on multiple drug therapy and the dose of phenobarbitone was increased when carbamazepine was stopped. Later, the anti-seizure medication was optimized. Other precipitating factors were eliminated. An autoimmune mechanism has been postulated as the cause of low platelet counts aspatients on carbamazepine are noted to develop drug dependent reactive platelet antibodies [4]. These results are to be verified by two or more independent laboratories and for a definitive carbamazepine induced immune thrombocytopenia [5]. Hence, careful monitoring of the platelets becomes a necessity for patients on treatment with this drug [6]. If the thrombocytopenia persists after the cessation of drug, differential diagnoses are to be considered. A diagnosis of Immune Thrombocytopenic Purpura (ITP) can be made by exclusion if no improvement is noted.

Carbamazepine and phenobarbitone are enzyme inducers and alter the metabolism of the other drug by decreasing it levels. However, it is classified as a minor interaction according to which the chances of interaction are not clinically significant. The half-life of carbamazepine is dependent on the usage of the drug. Patients on long term treatment metabolize it faster and half-life is 8-12 hours. The therapeutic level when measured just before the morning dose i.e. trough level is 4-8 mcg/ml [7]. Although a carbamazepine level was not done, within 5 half-lives the drug reaches negligible therapeutic concentration [8], which inthis case is within three days. This is substantiated by the increasing trend in platelets of our case observed from day 5. The half-life of platelets is 7-10 days. Hence, it is required to wait at least seven days to note a significant improvement and a return to normal levels, although, an upward improving trend can be noted as early as four days [9].

CONCLUSION

In India, carbamazepine is used frequently at its anti-epileptic dose. Carbamazepine induce disolated thrombocytopenia is preventable by careful monitoring of haematological parameters uring follow up. At review, platelet counts should be repeated and anti-seizure medication can be optimized accordingly.

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