

## Lamotrigine-Induced Neutropenia in a Woman With Seizure Disorder

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**Abstract-**Lamotrigine is an anticonvulsant medication belonging to the phenyltriazine class that modulates calcium and potassium channels and inhibits voltage-sensitive sodium channels. Additionally, lamotrigine inhibits dihydrofolate reductase. The U.S. Food and Drug Administration has approved the medication for the maintenance treatment of bipolar type I disease and seizure disorder. Various case reports has reported hematologic adverse effects with lamotrigine therapy.<sup>1-8</sup> Here we have described a 24-year-old seizure disorder patient who developed neutropenia while on lamotrigine.

### Case Report

Mrs A, a 24-year-old Indian woman presented to Medicine Department at SMS Medical Coolege Jaipur with fever for last 5 days. Fever was high grade ( 102-103°F) , associated with chills , continuous , decreased on taking Tab PCM , with no diurnal variations associated with generalized weakness and bodyache . Fever was not associated with cough, cold, sore throat, pain abdomen , diarrhea , vomiting, yellowish discoloration of eyes, burning micturition , decreased urine output, neck pain , altered behavior , focal neurological deficit , headache , blurring of vision / double vision / deviation of angle of mouth. There was no history of chest pain , shortness of breath/ palpitations, recurrent oral ulcers , photosensitivity , swollen joints, significant weight loss, and unusual vaginal discharge , local itching or irritation.

The past history revealed that the patient has adult onset seizure disorder and is taking Lamotriginand Clobazam from last 15 days. Systemic examination and clinical examination was normal except that fever was noted in examination.

The blood test results showed revealed anaemia and progressive leucopenia and neutropenia (white blood cell count was 3000/mm<sup>3</sup> on first day, 2200/mm<sup>3</sup> on second day and , 1000/mm<sup>3</sup> on third day . The ANC was 1342/mm<sup>3</sup> on first day, 1170/mm<sup>3</sup> on second day and, 300/mm<sup>3</sup> on third day). The haemoglobin was 8.2 gm/dl. The fever profile was negative for dengue, Widal and Chikungunya . USG whole abdomen revealed no abnormality except mild splenomegaly. Blood culture was sterile. CECT chest, abdomen and head revealed no abnormality. Autoimmune and Thyroid profile was negative. Bone marrow aspirate revealed small islands of haematopoiesis showing normoblastic erythroid hyperplasia and presence of abundant megakaryocytes however, myeloid series is markedly suppressed S/o Agranulocytosis. Bone marrow aspirate CS revealed Acinetobacter species sensitive to imipenem, and colistin. Urine CS revealed Enterococcus species 100000 CFU/ml which was sensitive to ampicillin, tetracycline, vancomycin, linezolid. In view of continuous fever and neutropenia all viral panel was sent which also came negative.

In view of continuous fever and neutropenia inj Filgrastin was added (for 7 days) and considering diagnosis of drug induced febrile neutropenia Lamotrigine was stopped and Levetiracetam was started in replacement. Patient was taken on Artesunate, Meropenem, Linezolid and Caspofungin.

After 2 days clinical and lab parameter started improving and fever subsided. After completing these treatments, his general appearance remained satisfactory and neutrophil counts remained within normal limits. He was discharged on the 7th day.

**Discussion-** Published reports of lamotrigine-induced neutropenia<sup>1-4</sup> and agranulocytosis<sup>5-8</sup> have demonstrated normalization of blood counts with drug discontinuation alone. In our case, there was a definite association between lamotrigine therapy and neutropenia. The brief normalization of blood counts following stopping lamotrigine was noted.

Although the mechanism of action of lamotrigine-induced hematologic abnormalities is unknown, a combination of immunoallergic, direct medullary toxicity, and granulopoiesis-inhibiting effects has been suggested.<sup>1</sup> There are also reports on lamotrigine-associated macrocytic anemia,<sup>9</sup> leukopenia,<sup>10-12</sup> and thrombocytopenia,<sup>12</sup> which suggest a common possible mechanism involving enzymatic inhibition of dihydrofolate reductase by lamotrigine. It is plausible that one or more of the above pathophysiologic mechanisms were

involved in our patient. With the normalization of blood counts with discontinuation alone, we did not attempt a bone marrow aspiration.

**Conclusion-** Based on the clinical course, we concluded that the leukopenia and neutropenia are associated with lamotrigine. Monitoring of WBC should be kept in mind when administering lamotrigine.

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