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Lamotrigine Induced Pancytopenia

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Abstract: **Lamotrigine is an anticonvulsant that the Food and Drug Administration (FDA) has approved for the epilepsy and depression of bipolar disorder. A few cases of lamotrigineinduced pancytopenia have been previously reported on, but the pathophysiology and clinical manifestations are not yet known. The present report describes the clinical history, radiography, hematology, microbiology, bone marrow sample, and histology of a case of Lamotrigine -induced pancytopenia.**

Keywords: **Lamotrigine, anticonvulsant ¸ pancytopenia.**

I. INTRODUCTION

Pancytopenia is a medical condition occurs due to damage to stem cells or to the bone marrow microenvironment leading to bone marrow failure. Bone marrow damage may be caused by infections, drugs, toxins, neoplasia, myelodysplasia, bone marrow necrosis, osteosclerosis, myelo-fibrosis or immune-mediated mechanisms, or it may be idiopathic. Bone marrow aspiration reveals a mix of necrotic lysing cells, macrophages and stromal cells. Depending on the cause, the bone marrow may recover and be repopulated, usually within 3 weeks after the original marrow injury, or the disease may progress to the chronic form[2] .

Lamotrigine is an anticonvulsant that the Food and Drug Administration (FDA) has approved for the treatment of epilepsy and depression in bipolar disorder. Though skin rashes, dizziness, and headache are the most well known side effects of lamotrigine, blood crisis such as eosinophilia, neutropenia, and thrombocytopenia have also been reported. Furthermore, a few cases of lamotrigine-induced pancytopenia have been reported, but its exact pathophysiology is as yet unknown. Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), may be fatal or life threatening. Early signs may include rash, fever, and lymphadenopathy. These reactions may be associated with other organ involvement, such as hepatitis, hepatic failure, or acute multi organ failure[1] .

Therefore, it is necessary to be aware of the possibility of pancytopenia during the treatment of epilepsy or bipolar disorder with lamotrigine. We report here on a case of pancytopenia with patient who was treated with lamotrigine.

II. CASE REPORT

A 47 years old male patient who is known to have Old CVA, Epilepsy on Lamotrigine, presented with history of fatigability, dizziness, fever, and generalized body rash for 30 days. Clinical examination revealed that patient is febrile (38.8oC) and tachycardia (110 bpm). Lamotrigine was discontinued on admission, The initial results of laboratory tests showed white blood cells (4.9 x 10^3/µL), Hemoglobin (5.5), platelets (82 x 10^3/µL) (table 1). Iron was 88 ugm/dl, TIBC 169ugm/dl, Ferritin 1362 ng/ml, INR 1.8. Liver enzymes showed AST 54 IU/L , ALT 22 IU/L, LDH 3413 IU/L. Urea 74 mg/dl, Creatinine 1.4 mg/dl.

Further workup was done to investigate the cause of pancytopenia, peripheral bloods smear showed normocytic normochromic anemia with marked anisopoikilocytosis. And leucocytes series show normal count, absolute neutropenia and absolute eosinophilia, and thrombocytopenia .Hepatitis serology, HIV came negative, direct and Indirect Coomb's test came negative. Vitamin B12 was within normal ranges. Anti-Cardiolipin IgM , IgG and ANA are negative. Blood cultures, Urine cultures, Sputum cultures, are negative. Pan C.T was done to rule out malignancies and the results were unremarkable.

Bone marrow aspirate and biopsy was normal and reveal Left shifted Myelogenesis and Erythrogenesis with marked increase in eosinophilic precursors, increase in megaloblast and increase in megakaryocytes with dysplastic changes. Patient was discharged on Day 12 after management of fever and rash. Follow up 1 week later on when patient visited OPD, much improvement was seen as clinically and in laboratory as in [table A] (Day 19).

In this case, the patients' hematologic abnormalities were normalized within 3 weeks after lamotrigine discontinuation, which corresponds with the previous case reports. Since all other causes of pancytopenia were excluded, and the presence of rash and eosinophilia which improved after lamotrigine discontinuation, and because fast recovery is unusual for the cases of pancytopenia which is caused by other diseases, we believe that lamotrigine was the cause of pancytopenia in this patient.

TABLE I: Results of blood analysis in patient treated by Lamotrigine

Hematology	Day 1	Day2	Day 3	Day 5	Day 6	Day 7	Day 8	Day 9	Day10	Day11	Day12	Day19
Erythrocytes	1.7	1.9	2.2	1.9	2.2	2.3	2.2	2.4	2.7	2.7	2.8	3.25
Leucocytes	4.9	4.8	7	4.1	4.5	4.1	3.1	3.3	4.1	4.6	5.1	4.2
%neutrophils		48.1	32.6		15	10.5	13.9					
%Lymphocytes		32.4	38.4		35	35.9	38.1					
%Monocytes		2	2.4		3	5.9	5.3					
%Eosinophils		17.1	26.3		47	47.2	39.9					
%Basophils		0.4	0.28		0	0.5	2.8					
Hemoglobin	5.5	6.1	7.2	6.5	7.1	7.2	6.8	7.8	8.5	8.2	9.2	10
Hematocrit	16.2	18.3	20.3	19.1	20.7	20.8	19.9	22.7	24.2	23.4	26.7	30.3
MCV	92.6	94	88.6	97	91.2	90	90	92.7	89	88.6	95	93.2
MCH	31.4	31.5	31.4	33	31.3	31.2	30.8	32.2	31.3	31.1	32.7	30.8
MCHC	34	33.5	35	34	34.3	34.6	34.2	34.8	35	35	34.5	33
Platelets	82	62	56	46	36	37	68	62	62	69	95	351
%Reticulocytes					2.6	1.98				0.86		
LDH	3413		3045	2454		2750	2999	2406	2254	1888	1566	

III. CONCLUSION

To conclude, it is beneficial for the clinicians to aware the possibility of an occurrence of pancytopenia in patients treated by lamotrigine, although it is rare and this condition was reversible in our case.

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