Introduction

Since its introduction, clozapine has been associated with haematological abnormalities, with most common abnormality being leucopenia, and other less commonly reported haematological abnormalities include agranulocytosis, neutropenia, thrombocytopenia, leukocytosis, and thrombocythoaemia.\[1\] However, there are few reports of eosinophilia associated with the use of clozapine.\[2‑6\]

In this report, we present two cases of eosinophilia associated with clozapine and discuss the clinical implications of detection of eosinophilia in patients receiving clozapine.

Case 1

Miss X, a 32-year female, diagnosed with schizoaffective disorder, hypothyroidism, drug induced polycystic ovary disease, and migraine presented with a relapse while on Quetiapine 800 mg/day, Lithium Carbonate 900 mg/day, Thyroxine 150 mcg/day, Amitriptyline 75 mg/day, and Metformin 1 g/day. Her treatment history revealed that she had not responded to three antipsychotic trials in the past and resultanty was considered for clozapine. Preclozapine investigations in the form of heamogram, liver function test, renal function test, fasting blood glucose level, electroencephalogram and electrocardiogram did not reveal any abnormality. However, lipid profile was deranged for which she was advised dietary modifications, regular physical activities; metformin was continued in consultation with the endocrinologist. Clozapine was started at the dose of 25 mg/day and her heamogram was monitored. After about 2 weeks (13th day of clozapine), while she was on clozapine 150 mg/day, her haemogram showed an eosinophil count of 9% with an absolute eosinophil count of 936/cmm. At this time her physical examination did not reveal any rash or any other abnormality to suggest any infection or allergic reaction. In view of the increased eosinophil count, she was investigated further in form of complete blood count, urine microscopic examination and culture, peripheral blood smear for malarial parasite and a chest roentgenogram, all of which were found to be within the normal range except for persistence of increased eosinophil count. Her investigations for impending myocarditis in form of Troponin-T and Creatine Kinase (CK- MB) also did not reveal any abnormality. In view of the response to clozapine and no symptoms suggestive of any infective or allergic pathology, clozapine was continued and the dose was gradually increased to 200 mg/day along with an empirical trial of mebendazole. However, on 26th day of clozapine her eosinophil count increased to 42% with absolute eosinophil count of 6090/cmm along with leucocytosis (total leucocyte count of 14500/cmm). All other

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Quick Response Code:
Website: www.jfmpc.com
DOI: 10.4103/2249-4863.152269

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Eosinophilia whenever develops is usually seen during the initial phase of treatment with clozapine, usually within first 4 weeks of therapy. As with other blood dyscrasia with clozapine, various mechanisms have been proposed to be responsible for clozapine associated eosinophilia. Commonly proposed mechanisms include type-I hypersensitivity reaction, which is supported by evaluated IgE levels in few reports and stimulation of T-lymphocytes.

Clozapine-associated eosinophilia is understood as two different forms: First transient benign eosinophilia and second eosinophilia with end organ damage. The eosinophilia has been shown to be associated with myocarditis, pancreatitis, colitis, toxic hepatitis, and pleural effusions. Other reports have also linked eosinophilia to predict neutropenia.

With regard to the management of clozapine-associated eosinophilia, literature suggests that decision of continuation of clozapine is determined by the presence or the absence of other organ damage. The literature emerging from the case reports suggests that invariably clinicians have opted to stop clozapine in the presence of end organ damage. However, in the absence of end organ damage the eosinophilia is usually benign and transient. Accordingly, whenever eosinophilia is noticed it is important to evaluate the patient for the presence of any specific organ damage and decision making should take the same into account. In occasional cases, authors have also rechallenged patients with clozapine even after an episode of clozapine and have used it successfully with only few cases of recurrence of eosinophilia along with other organ damage.

There are no clear cut monitoring guidelines for eosinophilia while using clozapine. However, clinicians should give due importance to the eosinophil count while reviewing the hemogram.

Both our patients developed eosinophilia during the initial phase of the treatment and further evaluation did not reveal any other organ damage and, hence, clozapine was continued in the second case and in the first case rechallenged with clozapine did not lead to the recurrence of eosinophilia. Our cases add to the existing literature that in the absence of other organ damage clozapine can be continued safely. However, close monitoring should be done.

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How to cite this article: Aneja J, Sharma N, Mahajan S, Chakrabarti S, Grover S. Eosinophilia induced by clozapine: A report of two cases and review of the literature. J Fam Med Primary Care 2015;4:127-9.

Source of Support: Nil. Conflict of Interest: None declared.