An Unusual Side Effect Of A Commonly Used Antiepileptic Drug

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Sir,

Levetiracetam is a commonly used anticonvulsant drug. Though it is considered as a benign drug; asthenia, headache, somnolence and nervousness are documented common side effect. Agranulocytosis is reported as a rare side effect with an incidence of 1.2%, but almost always it is of moderate severity.¹ Here we present a case of severe degree of agranulocytosis due to Levetiracetam.

A 22 year male student had a history of single episode of generalized tonic-clonic seizure 15 days back for which he was started on Tab. levetiracetam. Patient developed generalized bodyace and high fever without chills and rigors after about 10 days of therapy. There was no history of sore throat, jaundice, abdominal pain, oliguria, dysuria, bleeding tendency. On examination, there was no pallor, icterus, petechiae or lymphadenopathy. Systemic examination was normal. Investigations (according to days of admission) are given in Table 1.

X-ray chest, ECG, urine routine microscopy, USG abdomen and pelvis were normal. CT scan and MRI of brain and EEG studies were normal. As there was neither any focus of infection nor patient was on any other drugs which could cause severe agranulocytosis, the Levetiracetam was suspected as a cause for the same. According to WHO-UMC scale the association between the drug and agranulocytosis was of category probable/likely and therefore was stopped. Patient was started on Inj. G-CSF (filgrastim- 300 microgm). Inj. Cefazidime (1 gm TDS) and Vancomycin (1 gm BD) on day 2 of admission in view of high grade fever. Severity assessment using Hartwig and Seigel scale was 5/7. Bone marrow biopsy was planned but was not done as patient started showing improvement after 4 days of therapy. For seizures patient was started on Tab. Clobazam 10 mg on day 2 of admission. Patient remained seizure-free in the ward and was afebrile after 7 days of treatment. Absolute neutrophil count (ANC) improved and patient was discharged. Patient remained symptom-free on follow-up.

Levetiracetam is a pyrrolidine derivate commonly used as anticonvulsant drug which is approved as adjunctive therapy for new onset generalized tonic-clonic convulsions as well as for partial tonic-clonic seizure with or without secondary generalization. Amongst side effects nasopharyngitis, somnolence, headache, asthenia, nervousness are very common, but agranulocytosis or even pancytopenia, vision abnormality, abnormal liver function, allergic reaction including drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome and behavioural problems have been reported as a rare side effects.² The agranulocytosis is defined as absolute neutrophil count (ANC) <1500/cu mm with mild between 1000 to 1500/cu mm; moderate between 500 to 1000/cu mm; severe is <500/cu mm; very severe is <200/cumm. Agranulocytosis in adult is mostly due to acquired causes like infections especially viral infections, autoimmune conditions, inflammatory disorders and drugs.³

Among the various drugs causing agranulocytosis chemotherapeutic drugs are most common. Apart from these drugs some antibiotics like sulphonamide, chloramphenicol: some anticonvulsant like carbamazepine; other drugs like prophylthioracil, insecticides etc can also cause agranulocytosis.

Though the association between Levetiracetam and agranulocytosis is there and incidence is 1.2% and almost all cases detected are of young age with moderate severity and most common time duration is within one month of starting of therapy. The mechanism for development of this side effect is not exactly known but most likely it involves an idiosyncratic reaction. So, we had a young patient who developed agranulocytosis due to Levetiracetam within one month of initiation but of very severe degree.

Therefore it is advisable to do complete blood count as a part of initial evaluation and it could be done periodically after starting the drug especially for initial six months.

References

1. Agranulocytosis due to Levetiracetam: a study of 5,132 patients on Levetiracetam; eHealthMe; Feb 11, 2014.