Pancytopenia secondary to levetiracetam administration is infrequent but possible. Here, we report a case of pancytopenia associated with levetiracetam in a 4-month-old infant. However, increased incidence of upper respiratory tract infections (URTIs) has been reported frequently. It appears that URTI is a heralding side effect of pancytopenia and tip of the iceberg.

**KEYWORDS:** Adverse drug reaction, infection, levetiracetam, neutropenia, pancytopenia

**BACKGROUND**

Levetiracetam is an anticonvulsant medication used to treat epilepsy. It inhibits partial and secondarily generalized tonic–clonic seizures. Double-blind, placebo-controlled trials with either refractory partial-onset seizures or uncontrolled generalized tonic–clonic seizures associated with idiopathic generalized epilepsy revealed that addition of levetiracetam to other anti-seizure medications was superior to placebo. Levetiracetam also has efficacy as an adjunctive therapy for refractory generalized myoclonic seizures. Insufficient evidence is available about its use as monotherapy for partial-onset or generalized epilepsy. However, there is a growing trend toward using levetiracetam as monotherapy in children with first convulsion or epilepsy.[1,2] This warrants further analysis in a well-controlled, prospective study.

It is thought to stimulate synaptic vesicle protein 2A, inhibiting neurotransmitter release by agonists of ryanodine receptor and inositol triphosphate receptor. Common side effects include aggression, agitation, coma, drowsiness, reduced consciousness, slow breathing, and upper respiratory tract infections (URTIs; pharyngitis, rhinitis, increased cough, influenza, and sinusitis).[3,4]

Although the efficacy, safety, and tolerability profile of levetiracetam is well known in the treatment of adult patients with epilepsy, data in children are somewhat limited.

Here, we report a case of pancytopenia, with major decrease noted in neutrophil series, followed by platelet and erythrocyte series, related to levetiracetam.

**HISTORY**

A 4-month-old male infant developed four episodes of convulsions for which he was admitted in a peripheral center and was prescribed levetiracetam as first-line monotherapy in dose of 20 mg/kg/day. Convulsions were controlled after starting levetiracetam. His blood reports were: hemoglobin (Hb), 12.5 g/dL; total leukocyte count (TLC), 9600/µL; differential leukocyte count (DLC)- polymorph (P) 55, lymphocyte (L) 37, monocyte (M) 5, eosinophil (E) 3; absolute neutrophil count (ANC), 5280/µL; and platelet count (PC), 1.6 lacs/µL.

However, after 5 days of therapy, he developed swelling of lower limbs, followed by abdominal distension after 1 week of starting therapy. Eight days after starting therapy, he was referred to our setup and presented with shock, hyponatremia, and acute prerenal failure with edema.

**EXAMINATION**

On admission, the child was lethargic. His pulse was 190/min, respiratory rate was 60/min, and blood pressure was 62/38 mm Hg. His capillary refill time was

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**How to cite this article:** Gohil JR, Agarwal TS. Levetiracetam adverse drug reaction: Pancytopenia. J Pediatr Neurosci 2018;13:116-7.
prolonged at 4s. Respiratory system revealed grunting, subcostal indrawing, and bilateral crepitations. His abdomen was distended and he had umbilical hernia; liver span was 10 cm in midclavicular line. He had swelling of lower limbs.

**INVESTIGATIONS**

His Hb was, 9.5 g/dL; TLC, 1,070/µL; DLC- P 25, L 70, M 2, E 3; ANC, 265/µL; PC, 68,000/µL; Na+, 127 mmol/L; K+, 4.8 mmol/L; Ca2+, 6.56 mg/dL; complement reactive protein (CRP), 989 mg/dL; D-dimer >20 ng/mL; urea, 86 mg/dL; and creatinine was, 1.9 mg/dL. He had pancytopenia, with ANC decreasing from 5280 to 265/µL, platelets decreasing from 1.6 lacs/µL to 68,000/µL, and Hb decreasing from 12.5 to 9.5 g/dL, with hyponatremia, acute prerenal failure, and septic shock.

**COURSE**

He was diagnosed as a case of right-middle-lobe pneumonia with septic shock, pancytopenia, and multiorgan dysfunction. He succumbed after 10 h of admission, despite receiving intravenous fluids, vasopressor, ventilator support, and broad-spectrum antibiotics. Blood culture was negative.

**DISCUSSION**

Antiepileptic drugs such as phenytoin have been known to cause blood dyscrasia, including pancytopenia. Pancytopenia secondary to levetiracetam administration is infrequent but possible. The present case demonstrates development of pancytopenia associated with levetiracetam in an infant. On literature review, four other cases of pancytopenia with the use of levetiracetam have been reported. However, all these cases were in elderly age group.[5]

Levetiracetam has often been associated with increased incidence of URTI.[3,4] Fulminant infection secondary to levetiracetam associated pancytopenia may only be the tip of the iceberg; with milder cases frequently presenting as URTI. It appears that URTI may be a heralding side effect of pancytopenia.

The decision to start levetiracetam must weigh the risk of seizure recurrence against the possible side effect—pancytopenia—of the drug.

**CONCLUSION**

We, thus, recommend using safer antiepileptic drugs as first-line treatment for the control of convulsions in the pediatric and neonatal age group as per their approved indication. Levetiracetam should not be used as first-line monotherapy for partial and secondarily generalized tonic–clonic seizures in children.

**Financial support and sponsorship**

Nil.

**Conflict of interest**

There are no conflicts of interest.

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