

Pyridoxine Dependent and Pyridoxine Responsive Seizures

Pyridoxine dependent seizures (PDS) are a recognized, though rare, cause of intractable seizures in infancy(1). Life-long pyridoxine supplementation in pharmacological doses (15 mg/kg/day) is required. However, early onset seizures responsive to pyridoxine (Pyridoxine responsive seizures, PRS) also exist, which can successfully be treated by immediate pyridoxine repletion without the need for subsequent daily pyridoxine supplementation(2). The purpose of this communication is to highlight the need to differentiate between these two entities, so as to avoid misdiagnosis and prevent inappropriate life-long treatment.

A 71-day male infant with a normal birth and family history was admitted with recurrent seizures since three day of age. The seizures were generalized tonic and multifocal clonic, lasting a few minutes and occurring once every 3-4 days. Despite three admissions at different hospitals and use of various anticonvulsants, seizure control was not achieved. Previous investigations including transfontanelle USG, EEG, CT Scan head, hematological and biochemical workup and, serum antiepileptic drug levels were unremarkable. On admission, the seizures subsided with intravenous diazepam and therapy with phenobarbitone was started. His physical examination, hematological and biochemical workup, CSF examination, and ocular examination did not reveal any abnormality. After two days, the child had more episodes of seizures, despite a serum

phenobarbitone level in the therapeutic range.

In view of resistant seizures and a normal workup, 100 mg Pyridoxine (Inj. Vitneurin®) was given intravenously followed by 15mg/kg/day pyridoxine orally. No alteration in vital signs was noted during or after the infusion. There were no further seizures over the next three days, and all other medications except pyridoxine were stopped by the fourth day. Brain MRI and EEG done over the next seven days were normal and there was no recurrence of seizures. He was discharged on oral pyridoxine. To confirm the diagnosis of PDS, the child was readmitted after one month for 'Pyridoxine Withdrawal'(1). Oral pyridoxine was stopped but there was no recurrence of seizures over the next seven days. In view of the failure of recurrence of seizures on pyridoxine withdrawal, a diagnosis of pyridoxine responsive seizures (PRS) was made and the baby sent home without any medications. He is now 27-month- old, developing normally and has had no further seizures.

Recent recognition of varied and late presentations of PDS has led to the recommendation for pyridoxine-trial for all children with early onset (<3 year age) intractable seizures or status(3,4). This has been found to be helpful in diagnosing previously unsuspected cases of PDS. However, response of seizures to the use of intravenous (or oral) pyridoxine and continued seizure control by pyridoxine monotherapy is not sufficient in itself to make a diagnosis of PDS. A definitive diagnosis of PDS can only be made by documenting recurrence of seizures on pyridoxine with-

drawal, that again respond to pyridoxine(1-3). Patients in whom there is initial response to pyridoxine but seizures do not recur on pyridoxine withdrawal are labeled as 'Pyridoxine responsive seizures'(2-4). Out of 15 patients with initial response to pyridoxine, Baxter reported six (40%) that did not have seizure recurrence after pyridoxine withdrawal(4). Therefore, a formal trial of pyridoxine is recommended as the only way to establish a diagnosis of PDS.

PRS may be due to either a transient pyridoxine deficiency, or a benign seizure disorder coincidentally ceasing with pyridoxine. Benign familial neonatal convulsions, benign idiopathic neonatal convulsions, and benign neonatal sleep myoclonus were ruled out in this child due to an incompatible clinical picture. Although maternal or the infant's pyridoxine/pyridoxal phosphate levels could not be done, pyridoxine deficiency seems to be the most likely reason for seizures in this child. Low intakes of pyridoxine have been reported in pregnant and lactating women and may lead to a transient deficiency in their breastfed infants(5). Children with PRS have been reported not to have any distinguishing features from those with PDS except for the absence of a family history and a good developmental outcome (2), both of which were seen in this child.

This case amply demonstrates the infrequent use of pyridoxine in our country among neonates with early onset resistant seizures. Despite three admissions at different hospitals and intractable seizures of neonatal onset, this patient had not received a trial of pyridoxine. We also wish to reiterate that not giving a 'pyridoxine trial' can leave a treatable

cause of intractable epilepsy undiagnosed. However, and more importantly, not carrying out a trial of 'pyridoxine withdrawal' can give a wrong label to the child and expose him to life-long pyridoxine therapy with its attendant recognized and unrecognized risks(6).

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