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LETTER TO EDITOR (VIEWERS CHOICE)

ATYPICAL PYRIDOXINE DEPENDENT EPILEPSY IN A NEWBORN

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Pyridoxine dependent epilepsy is one kind of refractory seizures which presents as encephalopathy from in utero to late infancy and sometimes into adulthood.[1] Pyridoxine dependent epilepsy is an autosomal recessive disorder caused due to abnormality of enzyme glutamic acid decarboxylase which results in reduced synthesis of inhibitory neurotransmitter gamma-aminobutyric acid (GABA).[2] Due to its rarity and the absence of appropriate biochemical tests, the diagnosis of pyridoxine dependent epilepsy is not always easy.[3] Though catastrophic, pyridoxine dependent seizures readily respond to administration of pyridoxine with the cessation of seizures usually within minutes after administration of pyridoxine. If not identified early, this leads to fatality in most cases and survivors will be left with severe intellectual disability. We present a neonate with a birth weight of 4.3 kg delivered via cesarean section who presented to us with uncontrollable seizures on day 7 of life with encephalopathy without any significant antenatal and postnatal history. The baby was normal for 2 days after birth and on day 3 of life, the mother noticed that the baby had a staring look, refusal of feeds with involuntary movement of limbs. The baby was then taken to a pediatrician who identified them as seizures and started the child on intravenous (IV) phenobarbitone and IV antibiotics consisting of cefotaxime and amikacin. The child was referred to us on day 7 of life in view of uncontrollable resistant seizures. On presentation to us, the child had tonic posturing without up rolling of eyeballs. The systemic examination was normal. On investigations, hemoglobin was 15.5 gm/dl, white cell count 9200 cells/cumm (neutrophils 45%, lymphocytes 55%, basophils 5%) and platelet count was 500,000 cells/cumm. Cerebrospinal fluid (CSF) showed protein 85 mg/dl (normal up to 120 mg/dl), 5-6 mononuclear cells/HPF (normal up to 14 cells/HPF) and glucose 56 mg/dl (corresponding blood sugar was 78 mg/dl). CRP was 8.4 mg/L (normal up to 15.8 mg/L). Serum calcium was 8.8 mg/dl (normal 7 to 12 mg/dl), magnesium 2.2 meq/L (normal 0.65 to 1.05 meq/L), lactate 4.2 mmol/l (normal 1.1 to 2.3 mmol/l) and pyruvate 0.27 mg/dl. Blood culture and urine culture did not grow any organism. EEG and MRI brain were normal. The child continued to have uncontrolled seizures for which the child was started on IV phenobarbitone followed by IV phenytoin, IV levetiracetam (increased to a maximum of 60 mg/kg/day). But the child deteriorated further requiring mechanical ventilation and injection midazolam infusion but the seizures were not controlled. Antibiotics were upgraded to IV Meropenem and IV Vancomycin on day 2 of admission. A trial of IV pyridoxine was given at 30 mg/kg/day on day 3 of hospitalization along with multivitamin infusion and was continued.[2] The baby continued to have seizures and finally, the multivitamin infusion was stopped after 7 days due to non-response. On day 9 of pyridoxine administration, the seizures stopped for the very first time. Unsure of the cause of response, anti-epileptics were weaned in the order of Inj levetiracetam followed by Inj phenytoin and finally Inj phenobarbitone. The seizures did not recur even after weaning of all anti-epileptics. We continued pyridoxine suspecting it to be a case of pyridoxine dependent epilepsy. Subsequently, pyridoxine was shifted from injectable therapy to oral therapy. During the observation period, mother forgot to administer pyridoxine once and the baby again had a seizure for which oral pyridoxine was given and this time the seizures stopped within an hour suggestive of classical pyridoxine dependent seizures.[4] Laboratory tests in form pipecolic acid and alpha-amino adipic semi aldehyde could not be done due to non-availability.

Infants with classical neonatal pyridoxine dependent seizures have fits soon after birth but other atypical presentations are also reported. Other manifestations include hepatomegaly, visual agnosia, squint, articular apraxia.[3] Pyridoxine dependent seizures should be suspected in an infant less than 3 years with seizures with no abnormal antenatal or natal history and a possible elder sibling death due to uncontrollable seizures.[5] Baxter proposed new criteria to diagnose pyridoxine dependent epilepsy which includes (i) seizures cease within 7 days of administration of pyridoxine (ii) recur when pyridoxine supplementation is withdrawn (iii) ceases again when pyridoxine is given again.[6] Similarly, our patient had a response to pyridoxine after 9 days, had a recurrence of seizure on missing a dose and again seizures stopped on giving pyridoxine.

Due to its rarity and in the absence of appropriate biochemical tests the diagnosis of pyridoxine dependent epilepsy is not always easy.[3] Early testing of biomarkers including pipecolic acid and alpha-amino adipic semi aldehyde may prevent delay in diagnosis of pyridoxine dependent epilepsy.[8] We could not do the

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biomarkers in our patient due to non-availability. Once the diagnosis is confirmed, therapy should be continued indefinitely. The dose of pyridoxine recommended varies from 5 to 300 mg/kg/ day.[7] We thus report, that one may need to continue pyridoxine supplementation in pyridoxine dependent seizures for a long time as a response can take a longer time.

Compliance with Ethical Standards

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