

Pyridoxine Dependent Early Epileptic Encephalopathy in a Newborn: Case Report

Yenidoğan Bir Bebekte Piridoksin Bağımlı Erken Epileptik Ensefalopati

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ABSTRACT Pyridoxine-dependent seizures, characterized by various intractable seizure types, usually occur during the first hours of life. Typically, pyridoxine-dependent seizures are unresponsive to anticonvulsant drugs and they respond only to immediate administration of pyridoxine hydrochloride. We have reported a 5-day-old boy who was presented with flexor type tonic spasms with clustering beginning in the first hours of his life. The spasms were refractory to several anticonvulsant drugs but they responded well to pyridoxine treatment. This report emphasizes the importance of considering pyridoxine-dependent epileptic encephalopathy in newborn babies who are unresponsive to anticonvulsant drugs.

Key Words: Vitamin B6 deficiency; infant, newborn; epilepsy

ÖZET Piridoksin bağımlı konvülsiyonlar farklı ve dirençli tiplerde nöbetlerle karakterizedirler. Genellikle doğumdan sonraki ilk dönemlerde ortaya çıkar. Piridoksin bağımlı nöbetler tipik olarak antikonvülzanlara yanıt vermezler ve sadece piridoksin uygulaması sonrası düzelirler. Doğumdan sonraki ilk saatlerde başlayan ve uygulanan tedavilere cevap vermeyen fleksör tip tonik kasılmalarla karakterize 5 günlük erkek olgu sunuldu. Tonik kasılmalar uygulanan birçok antikonvülzan ilaca dirençli olmasına rağmen piridoksin uygulaması sonrası tamamen düzeldi. Bu olgu sunumunda birçok antikonvülzan ilaca dirençli yenidoğan bebeklerde piridoksin bağımlılığı ve uygulamasının öneminin vurgulanması amaçlandı.

Anahtar Kelimeler: B6 vitamini eksikliği; bebek, yenidoğan; epilepsi

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Vitamin B6 or pyridoxine is necessary in the metabolism of proteins, red blood cells and central nervous system. The deficiency can result in anemia and convulsions in infants.¹ Pyridoxine dependent seizures (PDS), known as an autosomal recessively inherited disorder, are rarely seen. They are not controlled by anticonvulsant drugs in infancy and early childhood.² The prevalence is estimated at 1 in 100 000 to 700 000.³ Since the first description of PDS in 1954, most of the reports worldwide were either single cases or a series of a few cases.⁴

In this study, we have reported a newborn baby who presented with generalized tonic spasms with clustering during the first hours of life. Initially unresponsive to several anticonvulsant therapies, the spasms remitted with pyridoxine within a few minutes.

CASE REPORT

A 5-day-old boy was presented with generalized flexor type tonic spasms with clustering beginning in the first hours of his life as well as respiratory distress, vomiting and irritability. The spasms were refractory to phenytoin sodium, phenobarbital, and clonazepam and midazolam infusion.

The history of this case has revealed that the second child of healthy consanguineous parents (the parents were first-degree cousins) was born via vaginal delivery at 38 weeks' gestation. The pregnancy was uneventful and the mother did not use any prescribed or over-the-counter medication, or vitamin supplementation. Antenatal baby's movements were normal according to the mother. His birth weight was 2820 grams (10-25 p) and his head circumference was 35 cm (50 p).

After 5 days of uncontrolled seizures, the patient was transferred to our hospital. His EEG showed suppression-burst patterns, characterized by high-voltage bursts alternating with almost flat suppression phases. Laboratory studies (complete blood count, serum biochemistry, and urinalysis) and cranial ultrasonography of the brain were normal. Urine and blood samples were collected for metabolic analysis within normal results.

At this stage, he was given a trial of intramuscular 100 mg pyridoxine and the seizures have stopped within 5-6 minutes. The child had no hypotension, bradycardia, or apnea and did not need resuscitation. There was no seizure recurrence in follow-up. He was discharged three days later and treated with oral pyridoxine (15 mg/kg/day). The patient was seizure free 4 months after being released from hospital and his neuromotor development was delayed by two months according to his age group. He failed to exhibit exact head control at prone position and mild hypotonic. The control EEG showed no abnormality and the baby's mental development was normal. No further seizures occurred.

DISCUSSION

PDS is a disorder of GABA metabolism, probably due to a defective binding of pyridoxal phosphate

coenzyme with glutamate decarboxylase, the rate-limiting enzyme in GABA synthesis.^{5,6} The typical natural history of PDS begins within hours of birth with fits which are difficult to control with anti-convulsant drugs. However, 'turn off' occurs within minutes of the administration of parenteral pyridoxine, after which the baby is often floppy and unresponsive for a period.⁷

PDS is an autosomal recessive disorder for which the clinical features are classified into the early-onset, with the typical group presenting within the first few days of life. However, the onset can also occur after the neonatal period.⁸ Vomiting, breathing difficulties, hyper alertness, and irritability may be observed. Mills et al. reported 13 patients from eight unrelated families with pyridoxine-dependent epilepsy and the parents in six of the families were consanguineous.⁹ The patient in our case study is the second child of consanguineous parents (the parents were first-degree cousins). The baby was admitted to hospital due to respiratory distress, vomiting, convulsion and irritability.

The disease may appear with neonatal epileptic encephalopathy with severe seizures that do not respond to anticonvulsant drugs, as in the case of our patient. The most common seizure type is generalized tonic clonic seizures that progress to the status of epilepticus. Other types of seizures reported in the literature include brief partial seizures, atonic and myoclonic seizures, and infantile spasms.¹⁰ Our patient presented with generalized seizures, tonic spasms that are flexor type with clustering.

The most noteworthy interictal pattern consists of bursts or runs of high-voltage relatively bilaterally synchronous 1-4 Hz activity with intermixed spikes or sharp waves. The other pre-pyridoxine paroxysmal EEG abnormalities include focal spikes or sharp waves, multi-focal spikes and single sharp waves recorded over a whole quadrant or over a whole hemisphere.^{10,11}

Our patient's EEG showed suppression-burst patterns with abnormal background activity, spike and polyspike.

Diagnosis of suspected PDS can be confirmed by administering from one to five times of 100 mg

parenteral pyridoxine (ideally under electroencephalography and vital sign monitoring) during a clinical seizure. Diagnosis can also be confirmed by demonstrating prompt resolution of the clinical and electrographic features of the event or giving 10-15 mg/kg per day of oral pyridoxine to a patient who experiences frequent seizures and noting complete control of the events within a week.⁶ Hypoplasia of the posterior part of the corpus callosum and cerebellar hypoplasia are the most typical structural abnormalities, identified by CT and/or MRI scans.¹² In our patient, cranial CT and/or MRI could not be obtained, but cranial ultrasonography of the brain were normal.

Generalized seizures of our patient were not controlled despite the use of anticonvulsant drugs. The diagnosis was made by administering

one 100 mg dose of pyridoxine intramuscularly, which stopped the seizures within a few minutes.

The recommended maintenance daily treatment dose of pyridoxine ranges from 2 to 200 mg/day.² Our patient was discharged with maintenance dosage of pyridoxine, 75 mg a day orally, and other anticonvulsants were stopped.

In conclusion, PDS should be considered in any newborn or infant with unresponsive to conventional anticonvulsant treatment and in this patients pyridoxine should be given immediately. Pyridoxine treatment should certainly be maintained so as not to impair mental development. Early diagnosis and treatment of PDS is very important for the neuromental development of patients.

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