Seizure in a newborn – common defect and uncommon effect

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Abstract

Background Neonatal seizures are a common problem faced in a neonatal unit. While most of them have a common cause and a predictable course, an unusual case presents itself off and on.

Case presentation A 17-days-old growing preterm, admitted for feed assessment following parental concern about nasal regurgitation of feeds, developed recurrent seizures requiring multiple antiepileptic drugs. After the common causes were ruled out, exome sequencing was done. 22q11 deletion conclusive of DiGeorge syndrome was diagnosed.

Conclusion Genetic epilepsy, though unusual, should be considered when seizure is resistant to usual drugs or when seizures do not conform to known pattern:

Keywords Neonatal sezures, hypocalcaemia, DiGeorge syndrome

Background

Neonatal seizures are a common problem faced in any neonatal unit. Common causes include hypoxic ischemic encephalopathy, transient metabolic disorders, intracranial infection, intraventricular haemorrhage and congenital brain malformations **[1]**. Genetic epilepsy is a rare cause, but when seizure is unresponsive to multiple antiepileptic drugs or when seizure don't conform to known patterns, genetic epilepsy should be considered. The authors present a case where the final diagnosis was far from what was expected, though in retrospect was not that 'unobvious'.

Case Presentation

A 17-days-old, 36 weeks' preterm female baby delivered by caesarean section, birth weight 2.8 kg, was referred to our institute with rapid breathing and nasal regurgitation of feeds for one day. There was no significant perinatal history. On probing, mother felt that there was nasal regurgitation of feeds since birth. Systemic examination was unremarkable.

Infant was admitted in new born intensive care unit (NICU) for feed assessment. She was started on direct breastfeeds and additional oral feeds. Sixteen hours after admission, she had tonic seizure following nasal regurgitation, requiring phenobarbitone and phenytoin. Aspiration of feed was suspected as there was intermittent grunting. Chest x-ray taken showed no parenchymal abnormality. As infant continued to have refractory seizures, she was given levetiracetam and clonazepam.

Initial workup including blood counts, calcium, septic screen, Cerebrospinal fluid analysis and MRI brain were normal. Genetic epilepsy, myopathy associated epilepsy and inborn errors of metabolism were considered as differentials. EEG showed bilateral spike and wave discharges. CPK was normal. Complete metabolic screening and genetic workup were sent. ECHO showed PDA of 1.7 mm.

Carbamazepine was given as there was strong suspicion of genetic epilepsy. Infant responded well and was seizure free. Other antiepileptic drugs were withdrawn gradually. Minimal orogastric feeds were initiated and graded slowly to full feeds. ENT surgeon opinion was sought and laryngomalacia was confirmed. As there was no seizure and her nasal regurgitation reduced, she was discharged with carbamazepine and other oral supplements.

- On review, she was seizure free and tolerating feeds. Metabolic screening was negative.
- Clinical exome sequencing report showed heterozygous deletion of 1.18 Mb at the 22q11.2 location conclusive of DiGeorge syndrome. Chest x-ray was reviewed again and there was no significant thymic shadow.
- Further investigation showed low ionised calcium with normal phosphorus, ALP and PTH levels. Immunological workup showed low CD4 count with normal CD8 level. Parents were explained about the course of the disease, neurological outcome and prognosis.

Discussion

DiGeorge syndrome is the most common chromosomal microdeletion syndrome. 90% will have 22q11.2 microdeletion. The most common deletion is 3 Mb seen in approximately 70–

80% of patients. This deletion is prevalent in patients with epileptic seizures and epilepsy **[2]**. The estimated prevalence is 1/2000 in general population. The 22q11 deletion syndrome is among the most clinically variable syndrome with more than 180 features associated with the deletion **[3]** Symptoms may vary from hypocalcaemia to congenital cardiac anomalies. It has a wide spectrum of presentation at various age group **(Table 1) [4]**.

Table 1 Clinical presentations with frequency of occurrence.

Clinical presentation	Frequency of occurrence (%)
Palatal anomalies	69–100
Speech delay	79–90
Learning disabilities	45–90
Cardiac abnormalities	49–83
Developmental delay	75
Ophthalmological abnormalities	7–70
Hypocalcemia	17–60
Psychiatric disorders	9–60
Skeletal abnormalities	17–45
Renal abnormalities	31–37
Short stature	20
Neurologic	8
Dental	2.5

Neonatal seizures associated with hypocalcaemia is a common feature in these infants. Infants with impaired T-cell immunity causing recurrent infections and congenital cardiac defects are at high risk of mortality. Seizures in DiGeorge syndrome most often will respond to carbamazepine and calcium in case of hypocalcaemia.

However, there are reports of seizures with no associated hypocalcaemia, like this infant, responding well to carbamazepine **[4]**.

Live vaccines are generally contraindicated in DiGeorge syndrome. Rotavirus vaccine may cause diarrhoea. MMR vaccine should be deferred and given after one year.

Conclusion

Seizure in the new born is a manifestation of a transient disorder usually. However, prognosis is guarded when it is secondary to structural abnormalities, congenital or acquired. Genetic causes need to be considered as they can guide therapy and counselling, when identified. Exome sequencing is a useful tool in making a diagnosis in such cases.

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Competing interests

The authors have no competing interest to declare.

Author contributions

All authors were involved in the diagnosis and management of the infant. The authors Meganathan Pachamuthu and Suresh Chelliah were prepared and edited the manuscript. Suresh Chelliah will act as guarantor for this paper

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