Lennox Gastaut In Pediatric : A Case Series

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Abstract: **Background**: Lennox-Gastaut syndrome (LGS) is a severe form of childhood epilepsy characterised by various types of generalised seizures, a noticeable deceleration in intellectual development, and a distinct EEG pattern. Those afflicted with LGS may have previously experienced infantile spasms or an underlying brain condition, though in some cases, the exact cause may be unknown (idiopathic). LGS seizures frequently resist conventional treatment, and the long-term prognosis is poor. **Case Presentation**: We present two Lennox-Gastaut syndrome cases. The first is a 3-year-old female who was diagnosed with brachycephaly at 3-months-old. Her initial EEG at 4-months-old revealed moderate right frontopolar hypofunction then a month later she underwent physiotherapy, and was prescribed valproic acid. At 2-year- old, the MRI displayed bilateral parieto-occipital cerebral atrophy and the EEG showed general slow-wave abnormalities in the left frontal region then the levetiracetam was added for her treatment. At the age of 2.5- year-old, levetiracetam was substituted by clobazam because the seizure didn't improve so that the patient got combination therapy of valproic acid and clobazam, and then the seizure decreased after the substitution therapy. The second case is a 3-year-old girl who was diagnosed with hypocalcaemia at the age of 2 weeks. Three months later, she was diagnosed with epilepsy and the brain CT scan showed encephalomalacia, microcephaly and cerebral atrophy. At the age of two she was eventually diagnosed with Lennox-Gastaut syndrome with a particular EEG showing general slow-wave abnormalities. Initially she was treated with valproic acid and phenobarbital. Since there was no improvement of the seizure frequency, levetiracetam was added and phenobarbital was substituted by clobazam, which fortunately cause better condition.
Discussion: The cases highlight the challenges of managing LGS, which tends to be drug-resistant and associated with developmental delays and cognitive impairment. They underscore the need for a multidisciplinary approach to optimize care and enhance the patient's quality of life. This report serves as a reminder of the complexity of LGS and the importance of customizing treatment strategies to meet the unique needs of each patient.

1 CASE

A 3-year-old girl diagnosed with brachycephaly at 3 months of age was admitted to the hospital due to seizures. Initially, she presented with generalized tonic-clonic convulsions, but over time, her seizures evolved to include myoclonic jerks, partial seizures, and absence seizures.

Despite attempts with various anti-epileptic medications such as valproic acid, levetiracetam, and physiotherapy, her condition did not respond positively. Diagnostic investigations revealed abnormal MRI findings in the brain, and the EEG displayed general slow waves (refer to Fig 1). Initial EEG at 4 months indicated moderate right frontopolar hypofunction. A month later, she underwent physiotherapy and was prescribed valproic acid. By

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the age of 2, the EEG revealed widespread slow-wave abnormalities in the left frontal area, and MRI showed bilateral parieto-occipital cerebral atrophy. Levetiracetam was then introduced to her treatment.

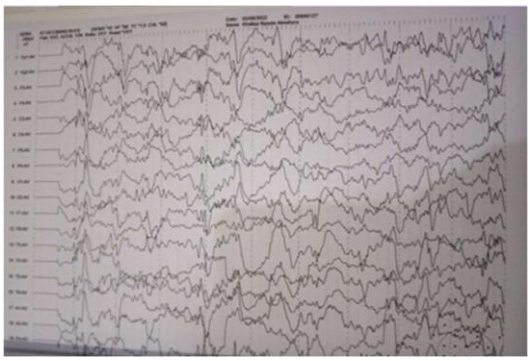

Fig. (1): EEG showed a slow wave of sharp spikes appears on F7 that spreads around

At 2.5 years old, clobazam replaced levetiracetam due to insufficient improvement in seizures. Combination therapy of valproic acid and clobazam resulted in a reduction of seizures after the substitution. The patient, born full-term at a clinic, had an unremarkable antenatal, perinatal, and postnatal history, with no dysmorphic features detected during examination. Despite several partial steps observed during examination, other general and systemic exams were normal. The diagnosis of Lennox-Gastaut Syndrome (LGS) was established based on her fulfillment of the three critical diagnostic criteria: various difficult-to-control generalized seizures, delayed intellectual progress, and distinctive EEG abnormalities.

Valproic acid was administered at a dose of 20 mg/kg, and clobazam at 0.15 mg/kg. Levetiracetam was discontinued and replaced with clobazam. At the time of discharge, the seizures were under control.

2 CASE

The second case involves a 3-year-old boy who was brought in for evaluation due to seizures that began at 3 months of age. He was diagnosed with hypocalcemia at 2 weeks old and later diagnosed with epilepsy at 3 months. A brain CT scan at that time revealed encephalomalacia, microcephaly, and cerebral atrophy. By the age of two, he received a diagnosis of Lennox-Gastaut syndrome, supported by a distinctive EEG showing general slow-wave abnormalities. Initially experiencing generalized tonic-clonic convulsions numerous times daily, over three years, he developed various seizure types, including myoclonic jerks, drop attacks, and absence seizures. Initial treatment with valproic acid and phenobarbital yielded no improvement in seizure frequency. Subsequently, levetiracetam was added, and phenobarbital was replaced with clobazam, resulting in a more favorable condition.

According to his detailed history, he was born full-term in a hospital, with insignificant antenatal, perinatal, and postnatal histories. No dysmorphic features were identified. Absence seizures were observed during the assessment, and apart from a stooping gait with short steps, other general and systemic exams were normal. He had limited speech that was difficult to understand, but his hearing and visual abilities were normal. Investigations revealed a normal fundus but an abnormal brain CT scan.

A recent brain CT scan at age 5 showed local atrophy in the upper right parietal lobe and a hypodense defect in the corresponding area. The latest EEG exhibited a general high-voltage slow-shaped wave, consistent with Lennox Gastaut's description. The diagnosis of Lennox-Gastaut Syndrome (LGS) was confirmed as he met the three key diagnostic criteria: various difficult-to-control generalized seizures, delayed intellectual progress, and distinctive EEG abnormalities.

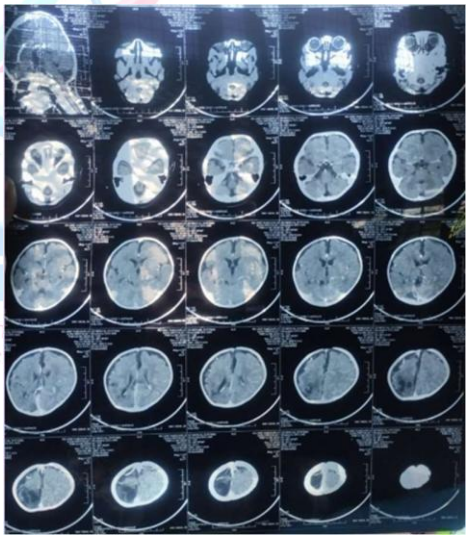

Fig. (2): Brain CT Scan showing local athrophy

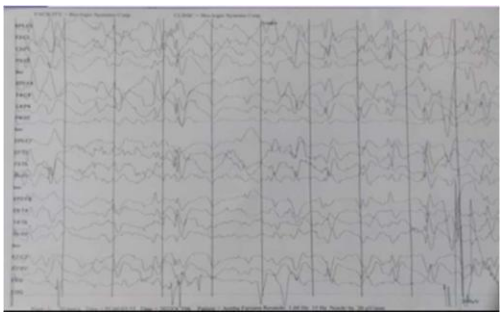

Fig. (3): EEG showed a general high voltage slow-shape wave appears

The prescribed medication dosages at discharge included 2 x 4 ml of valproate, 2 x 125mg of levetiracetam, and 2 x 2.5mg of clobazam, resulting in controlled seizures. Lennox-Gastaut Syndrome (LGS) stands out as one of the most severe forms of pediatric epilepsies, characterized by a triad of challenging-to-control multiple forms of generalized seizures, intellectual disability often coupled with mental retardation and behavioral challenges, as depicted in Fig. (3): EEG showing a general high-voltage slow-shaped wave.

DISSCUSSION

Lennox-Gastaut Syndrome (LGS) is a severe form of epileptic encephalopathy marked by a range of generalized seizures that exhibit varying frequencies over time. Although uncommon, this significant type of childhood epilepsy is distinguished by three primary attributes: challenging-to-manage generalized seizures, intellectual impairment often accompanied by mental retardation and behavioral challenges, and distinct electroencephalogram (EEG) patterns.[1-3]

Comprising around 2-5% of all pediatric epilepsies, LGS constitutes approximately 10% of epilepsy cases emerging before the age of five. In the 1930s, William Lennox first described the clinical symptoms of the condition, with Lennox and Davis later publishing the syndrome's symptomatic triad. Gastaut subsequently expanded on these initial findings. Furthermore, the International League Against Epilepsy's Commission on Classification and Terminology established specific criteria and frequencies for LGS, encompassing EEG diffuse slow spike waves (100%), tonic seizures (94%), atypical absences (80%), NREM sleep runs with fast spikes (approximately 70%), status epilepticus (60%), and atonic seizures (43%). Key characteristics of LGS include resistance to treatment and the persistent nature of epilepsy, with mental retardation affecting 90% of patients.[9,21]

Due to the challenging nature of treating the illness, many patients require multiple medications (polypharmacy) without achieving adequate seizure control. When managing patients with LGS, factors such as the patient's intellectual activity, seizure type, and the extent of seizure control should be carefully considered.[10]

Prevalence

LGS is predicted to affect 0.1 to 0.28 persons per 100.000 people. It is predicted to be 2 per 100,000 children. The total prevalence is around 26 persons per 100,000 people.[6] Males are more likely to develop LGS than females. There have been no reports of racial discrimination. Children with developmental and/or intellectual difficulties are more likely to be diagnosed with LGS because diffuse brain damage accounts for most cases.[7,21]

There have been no studies in this region, although V Karla et al observed that 3.5% of children attending the neurology department at AIIMS in India had epileptic encephalopathy, including LGS.[11,21]

Etiology

LGS exhibits diverse origins, with no typical familial pattern, although genetic factors may contribute to its development. In 20-50% of cases, infants previously experienced spasms associated with an underlying brain abnormality, known as symptomatic West syndrome. About one-third of affected children have an unidentified origin, termed cryptogenic LGS. Conversely, many LGS-affected children have pre-existing brain conditions such as tuberous sclerosis, congenital infections, inherited metabolic disorders, brain malformations, or injuries (resulting from birth complications, encephalitis, meningitis, or head trauma).[12]

Studies in developing nations reveal a heightened incidence of premature and abnormal births, with common occurrences of meningitis, TB, neurocysticercosis, and head trauma during infancy and early childhood. This trend is expected to contribute to an increased prevalence of secondary (symptomatic) epilepsy and intellectual impairment in children[5,21]

Clinical features

Lennox-Gastaut Syndrome (LGS) is characterized by a variety of daily seizures. The predominant seizure types in LGS include tonic seizures, often occurring during the night, atonic seizures (resulting in involuntary loss of muscle tone and drop attacks), and atypical absences (where the child goes blank for up to a minute). Additionally, nearly 60% of children with LGS may experience prolonged or repetitive seizures that happen in rapid succession, constituting a medical emergency known as status epilepticus. Some children may also encounter other seizure types like myoclonic, partial, or tonic-clonic seizures. The majority of individuals with Lennox-Gastaut syndrome exhibit mild to severe intellectual impairment and learning difficulties.[8-9]

Behavioral abnormalities and depression are common, potentially linked to brain damage, frequent seizures, a lack of typical social interaction, or as side effects of anti-epileptic drugs (AEDs). These children are also vulnerable to conditions such as cerebral palsy, progressive IQ decline, and worsening gait abnormalities. Developmental delays are typical in the early stages of the disease, contingent on the underlying brain condition's etiopathogenesis.[11]

As a consequence of these irregularities, affected children may appear irritable, fatigued, or disinterested. Many face challenges in academic settings and may require institutional care. Normal growth is rarely observed, and seizures can lead to unexpected falls and balance issues, prompting the recommendation for patients to wear helmets to safeguard their head, face, and teeth.[13]

The identification of LGS is based on clinical presentation and standard EEG findings, characterized by an interictal EEG disruption featuring a slow spike-wave pattern (< 2.5 Hz), often accompanied by bursts of rapid rhythms occurring predominantly at night (10–12 Hz).[10]

Treatment

The optimal treatment for Lennox-Gastaut syndrome remains uncertain. Antiepileptic medications (AEDs) play a central role in pharmacological therapy, with no single regimen proving superior, and treatment decisions are contingent on individual patient responses. Valproates (such as valproic acid, sodium valproate, and valproate semisodium) are typically the initial treatment, followed by the addition of lamotrigine or topiramate as adjunctive therapies.[14]

Felbamate has demonstrated benefits in controlled clinical studies for LGS patients; however, its use requires cautiousness due to an elevated risk of aplastic anemia and hepatotoxicity. Regular monitoring of complete blood count and liver enzymes is necessary, and felbamate is reserved for cases where previous therapies have not been effective.[16]

In instances of challenging seizure control or when standard treatments are intolerable, benzodiazepines (specifically clonazepam, nitrazepam, and clobazam) and phenobarbiturates are recommended as third-line options. Since the early 1980s, valproate has been widely considered a first-line drug for LGS, attributed to its efficacy against various seizure types, including partial and generalized seizures, lack of exacerbation of LGS-associated seizure types, relative absence of sedative side effects compared to barbiturates, and easier administration compared to the ketogenic diet.[19-20]

Treatment Objectives Goals

The main purpose of treatment is to educate parents or carers on the nature of the disease. Because children with LGS will never be seizure-free, the objective is to minimise seizures while remaining awake. Seizures that induce falls and injuries, as well as atypical absence seizures (which increase epileptic encephalopathy), should be the major treatment targets. Finally, relative remissions and exacerbations of seizure frequency that are frequently unconnected to any clear external variables; hasty decisions that result in the discontinuation of a medicine or the inclusion of an additional treatment may be regretted later. [13-14,20]

Prognosis

In general, the outlook for individuals diagnosed with Lennox-Gastaut syndrome (LGS) remains bleak. Both seizure control and intellectual development exhibit unfavorable long-term prognoses. LGS, along with other serious conditions, is associated with high levels of morbidity and mortality.[2]

Patients experiencing idiopathic LGS typically manifest less severe symptoms and subsequent impairment, while those with a history of infantile spasms or West syndrome tend to experience more challenging outcomes in terms of both seizure management and cognitive status. Approximately 80% of individuals with Lennox-Gastaut syndrome endure seizures from childhood into adulthood. Over an 8 to 10-year follow-up period, the mortality rate ranges from 3 to 7%.[3]

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