

Lennox Gustaut Syndrome: A Case Report

Dr Siddharth Shah, Dr Hetal Pandya, Dr Kaushik Rana

Abstract: *Background and literature review: Lennox-Gastaut syndrome (LGS) is one of the catastrophic childhood epilepsies. It is defined by a triad of symptoms. 1) Multiple types of generalized seizures, which are difficult to control. 2) Slowness of intellectual growth, often accompanied by mental retardation and behavioral problems. 3) A specific electroencephalogram (EEG) pattern called a slow spike-and-wave pattern (< 2.5 Hz), which is present when the child is awake [1-4]. Seizures most often present between the second and sixth year of life, however; they can start a little earlier or later. They rarely start after the age of eight [2,3]. William Lennox described the clinical features of the syndrome in 1930s, and then Lennox and Davis reported the symptomatic triad of the syndrome. Later, Gastaut expanded on the original observations of Lennox and Davis [5,6]. The diagnostic criteria of the syndrome have been refined by researchers, but the basic characteristics of the syndrome remained unchanged since Lennox and Davis [7-11]. Distinguishing LGS syndrome from other epilepsy syndromes has been challenging as it is characterized by plethora of underlying causes, multiple types of seizures, and cognitive impairment. Seizures are classified according to the International League Against Epilepsy (ILAE) classification, and specific epilepsy syndromes of childhood are recorded when their essential diagnostic elements are fulfilled. It is now agreed that a number of individual syndromes, including LGS, form a spectrum of childhood epilepsies, each with differentiating criteria [12-14].*

Keywords: Lennox-Gustaut, Epilepsy Syndrome

1. Prevalence

The Lennox-Gastaut syndrome is uncommon but it is very serious. The mortality rate ranges from 3% to 7% [2,5].

Often the prevalence of LGS is described as a percentage of childhood epilepsy. The reported prevalence of LGS varies between studies but it is in the range of 3–10% of childhood epilepsy, and is more common in males than females [1-3].

Epilepsy is relatively common, but its prevalence varies widely affecting approximately 3.4/1000 of the population in Japan, 6/1000 in the United States, and 11.2/1000 in Mexico [15,16].

In South Africa, the prevalence of epilepsy (all ages) has been reported as 10 per 1,000 [17]. In rural South African children aged 2–9 years the prevalence of epilepsy was 0.73%. Out of the affected, 57.1% didn't receive medication, and 71.4% had developmental disability. These figures are slightly higher than those derived from other sub-Saharan African countries [15].

As LGS constitutes a fraction of childhood epilepsy it is overall rare. However, it is clinically prominent due to the frequent and difficult to treat seizures that persist into adulthood, as well as to the need for continuous medical attention [1].

Epidemiologic community based studies in the so-called developed countries revealed that the annual incidence of LGS in childhood was approximately 2 per 100,000 children, and the prevalence of LGS was 0.1–0.28 per 1000 in Europe [4]. Studies demonstrated that the figures of LGS are relatively consistent across the developed populations. For example, in Atlanta, USA, LGS accounts for 4% of patients with childhood epilepsy, with a reported incidence of 0.26 per 1000 live births [6]. The true incidence in different populations is not known, due to the disparity between parameters used to

define the disease, as well as to the variability of the predisposing factors to the disease among different populations.

2. Etiology

Etiology of LGS is variable; LGS does not usually run in families but genetic factors may play a role in the etiology [2,7]. In 20–50% of cases the child has previously had infantile spasms with underlying brain disorder (also known as symptomatic West syndrome) [3,5,7,18,19].

For about one third of the affected children a known cause cannot be identified. These cases are referred to as cryptogenic Lennox-Gastaut syndrome [2,3].

On the other side, many of the children who develop Lennox-Gastaut syndrome had a pre-existing brain disorder or injury. Causes identified include tuberous sclerosis, congenital infections, hereditary metabolic diseases, brain malformation, and brain damage (due to birth asphyxia or other birth injuries, encephalitis, meningitis or head injuries) [2,3].

These patients tend to have worse prognosis than those of cryptogenic etiology [2,3]. It was noted, however, that these potential causative factors are different in different populations, and that in developing countries LGS was mainly secondary to trauma and infections [17].

In developing countries, there is a high incidence of preterm and abnormal births. During infancy and early childhood, meningitis, tuberculosis, neurocysticercosis, and head trauma are common. This situation is expected to increase the prevalence of secondary (symptomatic) epilepsy and that of intellectual handicap in the child population [17].

In a study of childhood recurrent seizures in Red Cross memorial hospital in Cape Town, South Africa, 11% suffered from meningitis or encephalitis as a precipitating factor and 55% were intellectually handicapped [20]. Most patients who

had both grand mal and myoclonic seizures suffered from LGS [20].

In another study in Cape Town, It was found that 43% of childhood epilepsy was symptomatic (secondary) [17]. This figure is even higher than other figures found in studies conducted predominantly in tropical African countries [17].

Perinatal hypoxia, meningitis, granulomata (cysticercosis and tuberculosis), and trauma have high prevalence among the poor of the Western Cape, and it is expected that these conditions serve as precipitating factors of secondary epilepsy [17]. On the other hand diagnostic facilities are better in Cape Town than in the rest of the studied African cities, which is expected to reduce the number of overlooked cases, resulting in higher figures.

3. Clinical features

Typically, daily multiple seizure types that occur in LGS are of wide range, more than that of any other epileptic syndrome. The major kinds of seizures that usually occur in LGS are the tonic seizures, which are often nocturnal [3], the atonic seizures (involuntary losses of muscle tone that cause drop attacks) or atypical absences (child goes blank lasting up to a minute) [3]. Additionally, about 60% of children may have prolonged or repeated seizures very close together. This is called status epilepticus and is an emergency [5]. Some children also have other types of seizures, such as myoclonic, partial or tonic-clonic seizures [1,3].

Most children with the Lennox-Gastaut syndrome have a degree of intellectual impairment and learning disability that ranges from mild to severe. Behavioral problems and depression are also common, which can be attributed to the brain injury, the frequent seizures, the lack of normal social stimulation or as side effects of Anti Epileptic Drugs (AEDs) [5,21]. Children with Lennox-Gastaut syndrome are also more likely to have cerebral palsy, progressive decline in IQ and progressive gait disturbances [5].

Development of the child is frequently retarded at the onset of disease, depending on the etiopathogenesis of the underlying brain disease [14].

The syndrome is also characterized by an interictal (between-seizures) EEG disturbance called slow spike-wave pattern (< 2.5 Hz), often accompanied by a burst of fast rhythms of 10 to 12 Hz at night [1-3].

As a result of all these abnormalities, the child may look irritable, tired or bored. Many children fail to cope with school and need institutional care. The child's development is rarely normal, and often there is delayed development or other forms of epilepsy. The seizures can cause sudden falls and/or loss of balance, and patients are advised to wear a helmet to prevent head, face and teeth injuries.

The effects of LGS on the child and his family require a team of health care professionals to provide the best seizure control, the highest level of function with the least side effects, and the maximum quality of life possible for the child and to direct families to appropriate community resources. These children and their families need the combined support of services from healthcare workers, caregivers, friends, school and social workers as well as psychologists.

4. Treatment

LGS seizures are often treatment resistant. Basic treatment is pharmacological and some children may need more than one mode of treatment.

Pharmacological treatment consists mainly of one or multiple antiepileptic drugs (AED's). No single treatment regimen could be considered superior to the others, and management depends on the response of the patients. Medical treatment usually starts with valproates (valproic acid, sodium valproate and valproate semisodium) followed by adjunctive therapy with either lamotrigine or topiramate [5,21].

Controlled clinical trials demonstrated that felbamate was beneficial in patients with the LGS. However, since felbamate was associated with an increased risk of aplastic anemia and hepatotoxicity, it is used with extreme caution and requires regular monitoring of complete blood count and liver enzymes. It is reserved for children who are refractory to other therapies [22].

Benzodiazepines, (specifically clonazepam, nitrazepam, and clobazam) and Phenobarbiturates, are recommended as third-line choices in cases difficult to control or if standard treatment is intolerable [5,21].

Surgical options for treatment include:

- Vagus nerve stimulation: The procedure involves implantation of a battery-operated device with connecting wires to the left vagus nerve, which is programmed to deliver a current at variable frequencies, pulse widths, and times [23].
- Corpus callosotomy: an operation to cut the corpus callosum (the large bundle of nerve fibres connecting the two cerebral hemispheres) may be considered in the treatment of LGS [23].

Electrical stimulation of the centromedian thalamic nucleus (ESCM) was reported as being efficient in the control of generalized seizures and improvement of quality of life of the patients. The method involves stereotactic surgical implantation of electrodes to the centromedian nuclei of the thalamus. Electrodes are stimulated within set parameters. Patients are scheduled for follow-up visits for assessment of seizures and neurophysiologic tests. Main disadvantage was skin erosions that could not be controlled by plastic surgery procedures [24].

Ketogenic diet is a reportedly effective option for treatment. A ketogenic diet is a high fat, low protein, low carbohydrates diet that induces ketosis, a state in which there is an excessive amount of ketones in the body. It is very effective and is becoming increasingly popular for treatment of LGS [2].

5. Prognosis

The long term outcome is poor in terms of seizure control and intellectual development. Catastrophic disorders such as LGS are associated with morbidity and mortality [1]. Eighty percent of patients with Lennox-Gastaut syndrome continue to have seizures throughout childhood and into their adult life. The mortality rate ranges from 3 to 7% [2]. To the best of our knowledge this is the first report that documents the oral clinical and radiographic findings as well as the response to treatment in a patient with LGS.

6. Case Report

A twenty two year old male with longstanding seizure disorder presented to the casualty with multiple episodes of generalized seizures lasting more than 30 min. Seizures were well controlled with injectable benzodiazepine. The patient had a past history of Dengue viral encephalitis at the age of 13 years after which he developed the seizure episode with in between episodes of absence seizures for which the child was on regular dual antiepileptic medication. The child was mute and deaf since then with developmental retardation including intellectual abilities and autism.

On investigating the MRI showed atrophy of bilateral temporal lobes and posterior inferior aspect of bilateral parietal lobes as well as dilatation of bilateral lateral ventricle. EEG showed multifocal epileptiform abnormalities along with moderate degree of diffuse electrophysiological dysfunction over frontal regions bilaterally. Intermittent polymorphic 0.5-1 Hz, slow waves were noted over both hemispheres, more over the frontal area. Relatively symmetrical and synchronous 3-4Hz activity over both the posterior head regions were noted.

The patient despite being started on two antiepileptics (phenytoin and valproate) developed a seizure episode one day later during the stay and a third antiepileptic (Clobazam) was started. There was no other episode after that and the patient was discharged after 9 days.

7. Discussion

Lennox-Gastaut syndrome (LGS) is a catastrophic epileptic encephalopathy that consists of multiple types of generalized seizures which often vary in their frequency over a period of time. The syndrome is difficult to treat and many people receive multiple drugs (polypharmacy) without achieving satisfactory seizure control [23].

The long-term prognosis is poor; although the epilepsy often improves with time, complete control of seizures is rare and

with time the mental and behavioural disorders tend to worsen [23].

In managing patients with LGS the type of seizures, the level of seizure control, the intellectual activity of the patient and the possible drug reactions should all be considered [25].

The reported case is typical for LGS patients who may present for dental/oral health care. The patient experienced LGS and he was controlled on three drugs (Polypharmacy)

Seizures may occur several times every day, and patients suffering drop attacks might have fractures in the head and face region. Severe cases may interfere with school and social activities exacerbated by medications especially phenobarbiturates.

No history of trauma to the face or teeth was recorded but the patient had poor communication skills and he w

as dependant on her family.

Patients on AED's are subject to gingival overgrowth, mostly associated with using phenytoin. About half of the patients placed on phenytoin will show evidence of gingival enlargement, usually within 2 to 18 months after starting the medication [25]. The etiology is still unknown, but there appears to be an increase in the number of fibroblasts in the connective tissues [27]. Valproate is also associated with gingival hyperplasia but less than phenytoin [29]. Polypharmacy itself may predispose the patient to gingival enlargement [30].

8. Conclusion

The clinical findings in LGS could be associated with the syndrome itself or with the effects of pharmacological treatment, and it might include facial deformities, periodontitis and gingival swellings. Interdisciplinary treatment of these patients is fundamental.

9. Competing interests

The authors declare that they have no competing interests.

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