Lennox-Gastaut syndrome

Synonyms: childhood epileptic encephalopathy

What is Lennox-Gastaut syndrome?

The Lennox-Gastaut syndrome is characterised by multiple types of epileptic seizures, a characteristic electroencephalogram (EEG) with generalised slow spike-and-wave discharges, psychomotor delay and behavioural disorders.

The onset is usually before the age of 8, with a peak between the ages of 3 and 5 years. Late cases occurring in adolescence and early adulthood have rarely been reported.[1]

- The most common seizure types are tonic-axial, atonic, and absence seizures; however, myoclonic, generalised tonic-clonic, and partial seizures may also occur.
- Drop attacks are a frequently recognisable seizure type and also the most dangerous physically, severely limiting quality of life.[2]
- Seizures are often resistant to treatment.
- Lennox-Gastaut syndrome can be classified as either idiopathic (25% of the total) or symptomatic (75%).
- In idiopathic, normal psychomotor development occurs prior to the onset of symptoms and no neurological or neuroradiological abnormalities are found.
- Symptomatic cases are due to diverse cerebral conditions, which are usually bilateral, diffuse, or multifocal, involving cerebral grey matter.[3]

- Examples of underlying disorders responsible for symptomatic Lennox-Gastaut syndrome include encephalitis, meningitis, tuberous sclerosis, brain malformations, birth injury, frontal lobe lesions and trauma.

How common is Lennox-Gastaut syndrome? (Epidemiology)[1]

- Lennox-Gastaut syndrome represents approximately 3% to 5% of all childhood onset epilepsies. In population-based childhood epilepsy incidence cohorts, only up to 0.9% of patients are identified with Lennox-Gastaut syndrome when epilepsy is diagnosed.
- Other defining characteristics such as multiple seizure types and EEG features evolve over time.
- The prevalence of Lennox-Gastaut syndrome was estimated at 26 per 100,000 in a regional US study.

Lennox-Gastaut syndrome symptoms (presentation)[4]

Language is frequently affected, with both slowness in ideation and expression in addition to difficulties of motor dysfunction. Severe behavioural disorders (eg, hyperactivity, aggressiveness and autistic tendencies) and personality disorders are nearly always present. There is also a tendency for psychosis to develop with time.

The tonic type of seizure is seen in all patients but may not be present at the time of its onset. Atypical absence seizures (with gradual onset and termination) are the second-most common type of epileptic activity, but is difficult to diagnose clinically in patients with diminished cognition. Prolonged atypical absences are seen in 66% of the patients with altered consciousness, which is periodically interrupted by episodes of tonic seizures. These non-convulsive episodes may last for hours to weeks in severe cases (non-convulsive status epilepticus).

Atonic and myoclonic seizures have also been recorded. Drop attacks are also common (more than 50%), but not a pathognomonic clinical manifestation. Other types of seizures more commonly seen in later stages of the disease include focal seizures, generalized tonic-clonic seizures, or unilateral clonic seizures.

There is an increased risk of intellectual disability with a history of non-convulsive status epilepticus, a diagnosed case of West syndrome, any identifiable aetiology, and early age of onset. Cognitive decline is secondary to epilepsy itself, like all other epileptic encephalopathies or may be due to abnormal neuronal connections and the side effects of medications.

Differential diagnosis

- Other epileptic encephalopathies.[5]
- Epilepsy with general learning disability.
- Infantile spasms.
- Juvenile myoclonic epilepsy.
- Myoclonic-astatic epilepsy.[6]

Investigations

- Blood tests to exclude a metabolic cause.
- Magnetic resonance imaging of the brain.
- Electroencephalogram.
- Genotyping.

Lennox-Gastaut syndrome treatment and management

The majority of cases remain refractory to medical management and require polytherapy, and only 10% of cases are estimated to undergo full seizure remission with available therapies.[7]

Randomised controlled trials of monotherapy and comparison of add-on anti-seizure medications are currently lacking. However, a Cochrane review found high-certainty evidence for overall seizure reduction with add-on lamotrigine and rufinamide.[1]

The National Institute for Health and Care Excellence (NICE) guidance[8]

Ensure that people with Lennox–Gastaut syndrome have an adult or paediatric neurologist with expertise in epilepsy involved in their care.

First-line treatment:

- Consider sodium valproate as first-line treatment. Sodium valproate should be used with caution in women and girls, but it is recommended as first-line treatment for Lennox–Gastaut syndrome because of the severity of the syndrome and the lack of evidence for other effective first-line treatment options.
- Take into account the likelihood of pregnancy and put in place a pregnancy prevention programme, if appropriate.

Second-line treatment:
If first-line treatment is unsuccessful, consider lamotrigine as a second-line monotherapy or add-on treatment for people with Lennox–Gastaut syndrome.

Third-line treatment:
If second-line treatment is unsuccessful, consider the following as third-line add-on treatment options for people with Lennox–Gastaut syndrome: cannabidiol in combination with clobazam (if the child is over 2 years), clobazam, rufinamide, or topiramate.

Further treatment options

- If seizures continue with third-line treatments, consider a ketogenic diet as an add-on treatment under the supervision of a ketogenic diet team.
- If all other treatment options for Lennox–Gastaut syndrome are unsuccessful, consider felbamate as add-on treatment under the supervision of a neurologist with expertise in epilepsy.

Other treatment considerations
The following medications may exacerbate seizures in people with Lennox–Gastaut syndrome: carbamazepine, gabapentin, lacosamide, oxcarbazepine, phenobarbital, pregabalin, tiagabine, vigabatrin.

Surgical[4]
Surgical options for Lennox-Gastaut syndrome include corpus callosotomy, vagus nerve stimulation, and focal cortical resection.

- Corpus callosotomy: the resection of the anterior 4/5th is sufficient to produce effective results, but a 10% lower response rate as compared to those with total resection of the corpus callosum.
- Vagus nerve stimulation: reserved for patients with medically refractory seizures where surgery is not the option. It is effective in all types of seizures and adverse effects are much less as compared to corpus callosotomy. The most common side effects are hoarseness of voice, dysphagia, dyspneoa, and coughing.
- Cortectomy/lobar dissection: selective dissection of the cortex.
- Other options are gamma knife callosotomy, deep brain stimulation, and multiple subpial transactions.

Complications
- General learning disability.
- Behavioural disturbances.
- Injuries or death resulting from a seizure.
- Renal, cardiac, or metabolic complications resulting from a ketogenic diet.

Prognosis[4]

- Features of typical Lennox-Gastaut syndrome will evolve over time.
- The variety and frequency of seizures decrease over time, and so does their severity.
- Generalised paroxysmal fast activity on EEG will typically persist into adulthood, while slow spike-wave complexes will remain in a minority of cases.
- Cognitive and behavioural disturbances will remain as an adult in most with Lennox-Gastaut syndrome .
- The long-term outcome is variable, from normally functioning individuals to severe learning difficulties and treatment-resistant seizures in 47%-76% of cases, and these will need special home or institutional care.

Further reading

- Amrutkar C, Riel-Romero RM; Lennox Gastaut Syndrome. StatPearls, July 2023.

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