EpiCARE

Lennox-Gastaut Syndrome

Also known as: LGS

Overview

Lennox-Gastaut syndrome (LGS) is a rare epilepsy syndrome. No one is born with LGS, it may develop over time, within a particular neurodevelopmental period and mainly due to genetic and structural etiologies.

Children and adults with LGS share similar electroclinical features: a) seizures that start in childhood; b) more than one seizure type; c) slow spike-and-wave on EEG and developmental delay/cognitive impairment.

Incidence and prevalence

LGS constitutes between 3-4% of all children with epilepsy and 1-2% of overall people with epilepsy.

Diagnosis of LGS

Diagnosis of LGS is based on the core electroclinical features: more than one seizure type, tipically including tonic seizures during sleep; slow spike-wave discharges on EEG (in addition to paroxysmal fast activity during sleep) and developmental delay/cognitive impairment. Normally it presents with a drug resistant epilepsy.

Age of onset

LGS typically appears between the ages of 2-7 years, but it can be seen in older and younger children. It is established in the majority of children by 6 years of age. The presence of core features of LGS is not universal and stable, and they may evolve from and to other epilepsy syndromes.

Seizure types at presentation

Any and every seizure type can be seen in LGS. For accepted definitions of seizure types, see EpiCARE seizure types leaflet or www.epilepsydiagnosis.org. Seizure characteristic of Lennox-Gastaut syndrome and more common are:

- Tonic seizures:The body, arms, or legs become suddenly stiff or tense in extension posturing. They typically appear during non-REM sleep.

- Atonic/Drop seizures: Loss of muscle tone usually causing a person to drop, almost like a puppet without strings, to the floor. Can also be seen with the head which falls forward suddenly. They sometimes include a tonic component, being labelled as tonic-atonic seizures.

- Generalised Tonic-Clonic seizures: These can occur in isolation or evolve from other seizures. The person loses consciousness, the muscles stiffen (tonic phase) and jerking movements are seen afterwards (clonic phase). These types of seizures usually last 1 to 3 minutes and take longer for a person to recover.

- Atypical Absences: This means it is a different, unusual, or not typical absence seizure compared to typical absence seizures. The person is non-reactive and with behavioural arrest during few seconds. They last longer than typical seizures and may present other features, with EEG showing slow generalised spike-wave activity.

- Non-convulsive status epilepticus (NCSE): These are prolonged seizures (mainly with features of atypical absences) which may last many minutes, to hours, to even days in some cases.

- Myoclonic: Short sudden jerks of a muscle or group of muscles, usually on both sides of the body at the same time.

How do seizure types change over time?

Currently, there is no highly effective treatments for LGS. Seizures may go into remission but also may recur. Between 30-50% of children with Infantile spasms (also formerly known as West syndrome) will develop LGS and 80-90% of children with LGS will continue to have seizures into adulthood. Up to 70% of children with LGS will no longer show slow spike-and-wave over time. As the children get older, the types of seizures may change. However, nearly all adults with LGS have tonic seizures.

EEG features

Slow generalised spike-and-wave (<2.5-3Hz) on EEG. In comparison, generalized spike-and-wave activity is fast in idiopathic generalized epilepsies (>3Hz).

Most patients with LGS, at some point in their life, will show paroxysmal fast rhythms (10-20Hz) on EEG, mainly during non-REM sleep.

Work-up evaluation

Patients with LGS need a comprehensive and fast evaluation to establish the underlying etiology and precision treatments if possible, especially at the clinical onset. Most important diagnostic evaluations are genetic testing (preferably whole exome sequencing) and neuroimaging (high definition MRI with epilepsy protocol). In some specific cases, it may be

necessary to perform metabolic evaluations, as well as neuroimmunological studies.

Treatment

The prognosis, and therefore treatment options, can vary greatly from person to person. Complete recovery with freedom of seizures and normal development is unusual for a child with LGS. There are various treatment options, including antiseizure medications (ASMs), the Ketogenic Diet, as well as surgical treatments, such as Resective Surgery of the epileptogenic area (curative option in some cases), Vagal Nerve Stimulation, Deep Brain Stimulation and Corpus Callosotomy (palliative surgeries). In case of genetic etiologies, precision treatments targeted to the underlying genetic condition can be implemented in a proportion of patients.

Individual emergency protocols – seizure action plan

The clinician should advise particular treatment or protocol (seizure action plan) for emergency situations, as prolonged seizures. It is important that every person has an individualised treatment plan for emergencies. In case of cognitive worsening, it is important to re-evaluate the clinical situation, typically with prolonged video-EEG monitoring to exclude non-convulsive status epilepticus or other problems.

Comorbidities

70% of children will show cognitive impairment at diagnosis and more than 50% presents behavioural comorbidities, with hyperactivity, rage attacks or aggression. Other impactful comorbidities frequently present are sleep disturbances, gastrointestinal problems (mainly constipation), respiratory abnormalities (such us aspiration pneumonias), orthopaedic issues (such as scoliosis), motor comorbidities (such as cerebral paralysis) and autistic features, among others.

The mortality rate is 5%, and those with LGS are more likely to die prematurely. Premature death in LGS is often due to Sudden Unexpected Death in Epilepsy (SUDEP), status epilepticus, injury after drop seizures or the underlying brain disorder.

Review the impact of seizures, drugs & comorbidities on:

- Day-to-day activities
- Overall well-being
- Mental health
- Physical health
- Independence
- Sleep
- Biological and psychiatric health
- Behaviour

Provide patient and/or carer with:

- Safety advice especially for the 'confusional state' associated with episodes of NCSE
- A personalised rescue medication (seizure action plan) protocol for prolonged or cluster seizures.
- The side effects of medication particularly when changing treatment
- Etiological evaluation and genetic counselling if possible
- Liaison with school or college for support during education
- Patient, carer & employer support requirements including neuropsychological evaluation, guidance, potential psychiatric support
- Sudden Unexpected Death in Epilepsy (SUDEP) and drop risk management

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Lennox-Gastaut syndrome

Also known as: LGS

Overview

Lennox-Gastaut syndrome is a rare epilepsy syndrome. No one is born with LGS, it may develop over time from different causes, mainly brain structural anormalities or genetic conditions.

Children and adults with LGS share similar features: seizures that start in childhood; more than one seizure type; slow spike-and-wave on EEG and developmental delay/cognitive impairment. Although around 70% have this at the diagnosis of LGS, it is not necessary for the diagnosis to be made.

How common is LGS?

LGS constitutes between 3-4% of all children with epilepsy and 1-2% of all people with epilepsy.

When do symptoms first appear?

LGS typically appears between the ages of 2-7 years, but it can be seen in older and younger children. It is established in the majority of children by 6 years of age.

What are the type of seizures seen in LGS?

Any and every seizure type can be seen in LGS. For accepted definitions of seizure types, see EpiCARE seizure types leaflet or www.epilepsydiagnosis.org

Seizures characteristic of Lennox-Gastaut syndrome and more common are:

Tonic seizures- The body, arms, or legs become suddenly stiff or tense

Atonic/Drop seizures- Loss of muscle tone usually causing a person to drop, almost like a puppet without strings, to the floor. These can also be seen with the head, which falls forward suddenly.

Generalised Tonic-Clonic- These can occur in isolation or evolve from other seizures. The person loses consciousness, the muscles stiffen (tonic) and jerking movements are seen (clonic). These types of seizures usually last 1 to 3 minutes and take longer for a person to recover.

Atypical Absence- This means it is different, unusual, or not typical compared to typical absence seizures. They are a type of generalised onset seizure, which means they start in both sides of the brain.

Non-convulsive status epilepticus- These are prolonged generalised seizures with impairment of awareness, which may last many minutes, to hours, to even days in some cases. These seizures cannot be excluded without prolonged video-EEG monitoring, preferable 12 to 24h registers.

Myoclonic- Short sudden jerks of a muscle or group of muscles, usually on both sides of the body at the same time

Is LGS linked to underlying brain disorders?

LGS is caused by many different causes, mainly structural (malformations of cortical development or perinatal injuries, among others) or genetic (CDKL5, CHD2, dup15, among many others). It is of relevance to perform a fast diagnostic evaluation of patients after the onset, to try to discover the cause and start a targeted treatment (precision treatments or surgeries) if possible. In addition, LGS may be and evolution from other epilepsy syndromes, particularly epileptic spasms (formerly called West syndrome).

How frequent are seizures in LGS?

Seizures can become very frequent with multiple types and events every day.

How may seizures and EEG change over time?

Seizures may go into remission but also may recur in some cases. Between 30-50% of children with Infantile Spasms will develop LGS and 80-90% of children with LGS will continue to have seizures into adulthood. Up to 70% of children with LGS will no longer show slow spike-and-wave (<3Hz) on EEG in adulthood.

Most people with LGS, at some point in their life, will show paroxysmal fast rhythms (10-20Hz) on EEG, mainly during non-REM sleep. As the children grow older the types of seizures may change. Nearly all adults with LGS have tonic seizures.

What other problems apart from epilepsy, affect people with LGS?

70% of children will show cognitive impairment at diagnosis and more than 50% presents behavioural comorbidities, with hyperactivity, rage attacks or aggression. Other impactful

comorbidities frequently present are sleep disturbances, gastrointestinal problems (mainly constipation), respiratory abnormalities (such us aspiration pneumonias), orthopaedic issues (such as scoliosis), motor comorbidities (such as cerebral paralysis) and autistic features, among others.

The mortality rate is 5%, and those with LGS are more likely to die prematurely. Premature death in LGS is often due to Sudden Unexpected Death in Epilepsy (SUDEP), status epilepticus, injury after drop seizures or the underlying brain disorder.

What are the treatment options for LGS?

The prognosis, and therefore treatment options, can vary greatly from person to person. Complete recovery with freedom of seizures and normal development is unusual for a child with LGS. There are various treatment options, including antiseizure medications (ASMs), the Ketogenic Diet, as well as surgical treatments, such as Resective Surgery of the epileptogenic area (curative option in some cases), Vagal Nerve Stimulation, Deep Brain Stimulation and Corpus Callosotomy (palliative surgeries). In case of genetic etiologies, precision treatments targeted to the underlying genetic condition can be implemented in a proportion of patients.

What is the emergency protocol for seizures?

Your doctor should advise particular treatments or protocols (seizure action plan) for emergency situations, as prolonged seizures. It is important that every person has an individualised treatment plan for emergencies. In case of cognitive worsening, it is important to re-evaluate the clinical situation, typically with prolonged video-EEG monitoring to exclude non-convulsive status epilepticus or other problems.

What could I ask my doctor about?

- Safety advice especially regarding the 'confusional state' associated with episodes of NCSE
- A personalised rescue medication plan for prolonged or cluster seizures.
- The side effects of medication particularly when changing treatment
- Genetic counselling
- Liaison with school or college for support during education
- Patient, carer & employer support requirements including neuropsychological evaluation, guidance, potential psychiatric support
- Sudden Unexpected Death in Epilepsy (SUDEP) and drop risk management

For patient support, contact

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