GRIN Related Disorders
Patient journey

First symptom

Timeline: From the 1st day of life up to 1 year old.

Clinical Presentation / Symptoms

Seizures

• 80% of cases present with seizures in the 1st year of life, with neonatal-onset seizures in about half.
• Seizure onset at a later age has been reported.
• Seizure types at onset are mainly focal motor/tonic, epileptic spasms, clonic, focal-to-bilateral tonic-clonic.
• Seizures may occur in clusters.

Developmental delay

• Present in all individuals and usually observed within the 1st year of life.
• May be the presenting symptom in patients with no or later onset seizures.
• Extreme irritability in approximately 50% of patients in the first months.
• Gastrointestinal issues (irritability associated with feeds).
• Poor sleep cycles.

Identifying Patient Needs

• Parents need counselling and professional help.
• Parents need information about epilepsy and epileptic seizures.
• Parents need to have clear instructions and a plan for managing epileptic seizures.
• Parents need information and a clear plan for prescription medications, their side effects and long-term monitoring.
• Medical advice on non-epileptic symptoms, especially related to severe motor and cognitive impairment.
• Counselling for other family members, like siblings of the affected individual.
• Identify potential treatment options for behavioural issues.

Ideal Outcome / support

• Families' concerns are taken seriously and are given reassurance.
• Regular consultations with a healthcare professional are provided.
• Parents receive clear instructions on managing seizures.
• Information on medication side effects and monitoring are provided to parents.
• Treatment strategy for non-epileptic symptoms is provided.
• A multidisciplinary team works with the patient on physical, communication, and occupational domains, with the rehabilitation plan provided and adjusted based on patient's needs.

Diagnosis

Timeline: Usually < age of 2 years, depending on the availability of genetic testing.

Clinical Presentation / Symptoms

Seizures

• Different types of epileptic seizures can be present: focal or generalized motor seizures are most frequent, but absences and focal seizures with impaired awareness can occur later. Status Epilepticus can occur.
• About 1/3 of patients become seizure-free in the first years of life; 2/3 develop drug-resistant epilepsy. Prolonged periods of seizure remission with later relapse can occur.

Developmental delay

• Present in all patients and usually observed within the 1st year of life.
• Developmental trajectories differ on an individual basis, but delayed speech and motor development is usually clear from an early age.
• Periods of developmental stagnation or regression can occur at different ages and do not always correlate with epileptic activity.
• Developmental outcomes differ significantly between individuals: some need a wheelchair, others can walk independently; language is severely impaired in up to 80% of individuals.
• Intellectual disability is present in all individuals, ranging from mild-moderate to profound.
• Behavioural problems, including autistic features, are seen in more than half of the patients.
• Movement disorders are frequent, including tremor and ataxia.
• Other recurrent comorbidities are gastrointestinal problems, sensory integration (cortical vision impairment, etc.) and orthopaedic issues.
• People with the syndrome will be life-long partially or totally dependent.

Identifying Patient Needs

• Parents need to be offered genetic testing and counselling.
• Parents need an explanation of the diagnosis and possible prognosis, with psychological support.
• Parents should understand that developmental and epilepsy outcomes are different from child to child.
• Parents need to be trained on how to keep the child safe (falls, prolonged seizures, fever etc.).
• Parents need access to early rehabilitation within a multidisciplinary team to maximize development potential and reduce comorbidities.
• Parents should be informed about family groups and associations in their country and worldwide for support, networking, and information.
• Parents need advice on pre-school/school/aid.
• Parents need to know what social assistance is available from the government.

Ideal Outcome / support

• Genetic diagnosis and consultancy are provided, with an explanation of causes and recurrence risk.
• Professional support is offered to help parents cope with the diagnosis and the family is directed to the parent support group and/or association.
• Families receive clear instructions, emergency protocols, explanation of risks, and how to minimize them.
• Up-to-date information is available to parents at any time, including research initiatives.
• Emphasis on the importance of education and rehabilitation for the child's development which are closely monitored.
• Families receive support for finding a school/daily assistance and care.
• Families receive a document summarizing available social benefits available in their country/region.

Treatment

Timeline: Life long.

Clinical Presentation / symptoms

Seizures

• Epileptic seizures are often difficult to treat. No specific anti-seizure treatment has been proven superior and treatment needs to be individualized.
• Ketogenic diet has been reported to maintain seizure freedom in some.
• Epilepsy surgery should not be excluded, especially in the presence of clear focality and intractable seizures.
• Treatments should aim at controlling seizures and reducing side effects, especially in infancy and childhood when seizures can contribute to developmental impairment.
• Seizures resolve in childhood in about one-third of individuals. Seizure recurrence at a later age is possible and needs to be monitored.

Developmental delay

• An early multidisciplinary rehabilitation plan, including physiotherapy, speech therapy, occupational therapy, and behavioural therapy, is important to maximize developmental potential and needs to be tailored to the individual patient.

Non-epileptic symptoms

• Addressing behavioural problems is very important to the overall effect this has on the quality of life of the patient and his/her family.
• Addressing gastrointestinal issues is necessary because of the overall health issues that can limit the life of the patients affected. Decreased appetite and weight loss are major issues impacting the quality of life of these patients.
• Addressing psychiatric issues that may arise.

Identifying Patient Needs

• Parents need evidence-based information on additional symptoms and comorbidities that may arise.
• Needs and expectations change over time and need to be re-evaluated and discussed.
• Parents need information and a clear plan for prescription medications, their side effects and long-term monitoring.
• Parents need access to clinical trials for new treatment opportunities, where their child is eligible.
• Parents need information on other possible treatments for epilepsy such as Ketogenic Dietary Treatment and Vagal Nerve Stimulation, and for movement disorders like Deep Brain Stimulation.
• Parents need information on evidence-based therapies (psychomotricity, speech therapy, postural re-education, behavioural therapy) that need to be tailored to the individual patient's needs and age.
• Siblings' and parents' wellbeing and needs must be evaluated and discussed, and support provided.

Ideal Outcome / support

• Patient is regularly monitored and, if possible, offered a treatment for mentioned issues.
• Parents receive information about possible clinical studies in which their child can participate with in-depth information on risk and benefits.
• Families' needs and expectations are discussed, and treatment strategies are planned and defined.
• A rehabilitation program (psychomotricity, speech therapy, postural re-education, behavioural therapy) tailored to individual patient's needs and age is defined.
• Siblings' and parents' needs are adequately addressed.

Follow-up

Timeline: Lifelong.

Clinical Presentation / symptoms:

Childhood

• Epileptic seizures may be intractable, may be in remission, or may have relapsed.
• Behavioural problems may manifest.
• Movement disorders may manifest, such as tremor and ataxia.
• Sleep disturbances can be present.
• Orthopaedic issues may occur.

Adulthood

• In adult patients, epileptic seizures may also be intractable, may have remitted, or may have relapsed.
• Behavioural problems may change.
• Movement disorders are present.
• Sleep disturbances can be present.
• Orthopaedic issues are common.
• Adolescents and adults with GRIN disorder are partially or totally dependent for activities of daily living and need continuous support.
• When reaching adulthood, legal issues such as a legal guardian for when the patients become of age should be discussed.
• The transition from paediatric to adult care may cause a lack of appropriate support for the patient and the caregivers.

Identifying Patient Needs

• Patient needs regular follow up and monitoring.
• Parents need counselling and support in the transition to adulthood.
• Monitoring and treating comorbidities and new symptoms that may arise, which needs to be continued in adults as well.
• Parents need additional support when caring for an adult person.
• Possibilities of daycare or residential care need to be discussed with the parents.

Ideal Outcome / support

• Transition process from child to adult specialist is planned and well defined.
• Rehabilitation plan for maintenance and prevention of comorbidities is defined.
• Patient is provided with occupational therapy/day-care centres/residential centres.
• Availability of home and/or institutional care at the highest level.
• Family's needs and concerns are re-evaluated.
• Support and advice on later stages of adulthood and in case the primary caregivers become unable to provide is offered.