

Rett syndrome

Also known as: RTT

Overview

Rett syndrome first appear in early childhood. Sudden regression is usual - it's days to weeks. The clinical criteria are regression in hand skills, acquired language, and then the development of hand streeotypies and gait abnormalities. Gastrointestinal problems, respiratory dysfunction such as hyperventilation, breathholding and apnoea, sleep disturbance, spinal curvature and epilepsy are common comorbidities. There is a wide variability in the rate of disease progression and severity. Patients have been reported to live into middle age and beyond.

Incidence and prevalence

Prevalence is 1 in 10,000 live female births. RTT is often lethal early in males - but a number do survive, with a variable phenotype, which sometimes follows a Rett syndrome course.

Aetiology

Pathogenic variants in the X-linked gene methyl CpG-binding protein 2 (MECP2; Xq28) are found in more than 95% of classic RTT cases.

Diagnosis

The clinical diagnosis of RTT is based on consensus clinical criteria. These include one necessary criteria i.e. presence of regression plus four main criteria that are absolutely required for the diagnosis of typical RTT that include (i) partial or complete loss of acquired purposeful hand skills, (ii) partial or complete loss of acquired spoken language, (iii) gait abnormalities, (iv) stereotypic hand movements. Genetic testing identifies variants in MECP2 in 95-97% of individuals with typical RTT, but is not mandatory for RTT diagnosis.

Age of onset

Symptoms first occur between 12-18 months, but can be earlier/later.

Seizure types at presentation

Almost every seizure type has been described in patients with RTT, but focal motor seizures, atypical absences, tonic seizures and bilateral tonico-clonic seizures are the most frequently reported. Very typically, patients have multiple non-epileptic events that can be confused with seizures.

How do seizure types change over time?

RTT patients may experience different seizure types during their development.

EEG features

Background activity is generally slower than attended for developmental age; paroxysmal abnormalities are frequently seen over the frontal and temporal regions and tend to spread to both hemispheres. A rhythmic theta activity can be recorded in the central regions. Can often progress to changes in sleep resembling ESES.

Treatment

ASMs can be prescribed in individuals with RTT on the basis of seizure type.

Co- morbidities

People with RTT may present several problems, such as scoliosis, disorders of tone, breathing disturbances, gastro-intestinal dysfunction, sleep problems, autonomic system alterations, nutritional deficits. Moreover, RTT patients have an increased risk of life-threatening arrhythmias associated with a prolonged QT interval, avoidance of a number of drugs is recommended.

Individualized emergency protocols

The emergency protocol is not disease specific - but person specific.

Review the impact of seizures, drugs & comorbidities on:

In some individuals, seizures may be drug-resistant and the association of several ASMs may be needed. As many ASMs have an impact on bone health, this issue should be monitored over time.

Provide patient and/or carer with:

- Information about epilepsy
- Information on QTs risks
- Seizure management
- Treatment options



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What causes Rett syndrome?

Pathogenic variants in the X-linked gene methyl CpG-binding protein 2 (MECP2; Xq28) are found in more than 95% of classic RTT cases.

When do symptoms first appear?

Generally, girls with RTT apparently develop normally during the first 6-18 months of life; thereafter developmental stagnation followed by rapid regression (days to weeks) mostly in hand skills. During the regression period, repetitive, stereotypic hand movements replace purposeful hand use.

What are the types of seizure(s) seen in Rett syndrome?

Almost every seizure type has been described in patients with RTT, but focal motor seizures, atypical absences, tonic seizures and bilateral tonico-clonic seizures are the most frequently reported. Very commonly, non-epileptic events which can be challenging to distinguish can happen. Also, not all children with RTT have seizures.

Is Rett syndrome linked to any other epilepsy syndromes?

In the classic form of RTT, no specific epilepsy syndrome can be identified.

How frequent are seizures typically in Rett syndrome?

There is a wide heterogeneity in seizure frequency in RTT, some girls may have daily seizures, and others present with seizure once a year.

How may seizures change over time?

RTT patients can show different seizure types during their development.

What other problems apart from epilepsy, affect people with Rett syndrome?

People with RTT may present several problems, such as scoliosis, disorders of tone, breathing disturbances, gastro-intestinal dysfunction, sleep problems, autonomic system alterations, nutritional deficits.

What are the treatment options for Rett syndrome?

Currently, treatment options remain symptomatic.

What types of surgery are available?

People with RTT do not show cerebral malformations and are not candidates for epilepsy surgery. Nevertheless, VNS implantation has been reported useful in some patients with RTT.

What is the emergency protocol for seizures?

The emergency protocol for seizures in RTT is identical to the one used for other patients with epilepsy and intervention with benzodiazepines is the first choice.

What could I ask my doctor or specialist epilepsy nurse about?

Seizures may respond to common anti-seizure medications (ASMs); in case of drug-resistant seizures a combination of ASMs should be prescribed, according to age of the patient and seizure types.

Who should be a part of the medical team?

Management of RTT needs a multidisciplinary approach, so the team should cover all the medical aspects of the syndrome (e.g. neurologist, pediatrician, speech therapist, physiotherapist, orthopedic,..)

Patient association

Rett Syndrome Europe

<https://www.rettsyndrome.eu/>



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