Ring Chromosome 20 Syndrome - r(20) syndrome

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Causes of the Condition

Ring Chromosome 20 Syndrome, also known as (r20), is a rare chromosomal anomaly resulting from a break on each arm of chromosome 20 resulting in ring formation. It is one of the more commonly seen ring chromosomes. There are several different forms of the (r20) syndrome, with potential differences among individuals in the size of the chromosomal deletions and differences in the percentage of cells with the ring. The ring can be associated with deletions at one or both ends and may occur when the fusion takes place; these deletions can be of different sizes, with more or less genes deleted. Additionally, the ring can be in every cell of an individual or it can be present in only one or a subset of cells (mosaicism). These variations will impact the clinical features associated with this syndrome. Almost all cases which have been reported are sporadic with no family history.

Symptoms and Treatments

This syndrome is characterized by medically intractable (difficult to treat) epilepsy, nocturnal subtle seizures, behavioural problems and intellectual disability (usually mild). Unlike other chromosomal abnormalities, dysmorphism is rarely reported.

Key symptoms:
- In most of the cases normal childhood development until onset of epilepsy
- Predominantly focal impaired awareness seizures
- Seizures without a clear focal origin or with secondary generalisation
- Frequent nocturnal seizures (in most of the cases subtle and of frontal lobe origin)
- Intercalary EEG with characteristic appearance with log trains of theta waves, with a peak at 5 Hz and a sharply contour or notchy appearance
- Epilepsy (often onset between 4 and 11 yrs), may be associated with cognitive difficulties (epileptic encephalopathy) and with non convulsive status epilepticus
- Lack of dysmorphism or other congenital malformations
- Cognitive impairment/learning difficulties very often after the onset of epilepsy

Failure to control seizures adequately can lead to cognitive decline.

Impact of the Condition

The main impact of living with (r20) syndrome is managing the regular (often daily) seizures. Seizures can occur anytime 24/7 usually without warning and are often worse and/or more frequent at night, affecting quality of sleep and putting the patient at risk of Sudden Unexpected Death in Epilepsy (SUDEP). We know of at least 2 cases of loss of life due to uncontrolled seizures in (r20) patients. At its worst, a patient can have having anything up to 100 seizures per day, comprising a mixture of focal, tonic clonic and myoclonic (jerks). Seizures have a tendency to be prolonged and NCS is common.

Seizure triggers include:
- Tiredness
- Stress
- Fatigue
- Bathing/showering
- Change in temperature (hot/cold)

Since chromosomal analysis or karyotyping testing is not a routine examination when epilepsy first presents, the diagnosis of (r20) may be delayed or gone unrecognized. Therefore the patient must be aware of the signs and symptoms first, in order to request appropriate cytogenetic (chromosomal) testing. The ring 20 has been seen in as few as 5% of cells, and it is recommended to request a screen for chromosomal mosaicism. Since (r20) can present as a mosaic with the ring in only a small number of cells, a minimum of 50 cells must be analysed. Lower array technology (CGH or SNP arrays) will not detect the ring chromosome and standard metaphase chromosome analysis is recommended especially in the mosaic cases where no deletions or duplications have been detected in the reported cases.

Diagnosing (r20):

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There are currently no recommended treatments for (r20) syndrome.

No consistent response to treatment has been reported in any group of patients. Many patients report being on multiple AEDs with associated side effects yet limited control over their seizures. AEDs may prevent secondary generalised tonic clonic seizures, but do not influence the epilepsy. Patients have also tried VNS, cannabinoids and/or ketogenic dietary therapy – the latter with some significant success in a number of patients (though no published data exists to support this). Interestingly, due to the behaviour phenotype, the majority of French patients see a psychiatrist before they see a neurologist.

Hopes and Aspirations for the Future

At Ring20 Research and Support UK CIO, we and our member families would like the following:

Increased awareness of the signs and symptoms of (r20) amongst neurologists, paediatricians, epilepsy specialist nurses - to understand when and how to test for (r20). Better information for test laboratories, to influence test requests where (r20) is suspected, to ensure appropriate testing is carried out to improve overall diagnostic rates.

Recognition of the importance of confirming a diagnosis for an (r20) patient in terms of future treatment and prognosis, especially in adults, where the cause of their epilepsy is unknown due to historic lack of availability/knowledge around genetic testing. Increased understanding of the associated comorbidities of the syndrome e.g. on cognition/behaviour.

Creation of a patient registry to determine the rate of incidence of (r20) and to ensure patients have the opportunity to be involved in appropriate clinical trials for potential treatments and to better characterize the syndrome specific features emerging in the number of cases studied.

More targeted treatment options to improve seizure control and lessen side effects, or indeed lessen the impact of cognitive decline if introduced early enough to prevent seizures. In the short term by evaluating response to existing treatment options; longer-term through studying gene expression of the ring and/or clinical trials for new innovative treatment options.

Availability of prognostic information – what does the future hold for a patient with (r20)? How will the disease progress and how will this impact their lives?

We are hopeful that the introduction of the new EPiCARE ERN for rare and complex epilepsies will begin to address some of the above, but we also want to progress these ourselves.

(r20) is a unique epileptic encephalopathy which is ripe for a multitude of research studies to better understand the disease and ultimately improve outcomes for patients. Indeed by studying the cognitive and behavioural impact of (r20) we may unlock information about how to treat other epilepsies. The appetite amongst researchers to unlock these mysteries exists today, however this vital work can only be realised through available funding for clinical and/or genetic research. As a relatively small patient support group we have limited capacity to achieve this goal alone. There is an opportunity for medical professionals, multi-disciplinary teams and scientists to recognise opportunities in studying this rare disease. Could you help us raise funds or awareness?