Ring Chromosome 20 Syndrome - r(20) syndrome

Allison Watson
Ring20 Research and Support UK CIO

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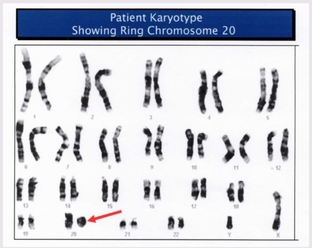
Causes of the Condition

Ring Chromosome 20 Syndrome, also known as r(20), 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 r(20) 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 a subset of cells (mosaicism). These variables will impact the clinical features associated with the ring. Almost all cases which have been reported are sporadic with no family history.



r(20) syndrome is likely under-reported and under-diagnosed.

r(20) was first reported in 1976; since then we counted 138 cases reported in literature, although as a patient support group we are aware of significantly more cases.
To date there is still no published data on the incidence and prevalence of r(20) syndrome.
This disorder appears to be pan-ethnic and non-gender specific. Cases of this syndrome have been reported from many different parts of the world involving different ethnicities.
Finding the cause of a patient's epilepsy is enormously helpful to physicians to guide treatment, identify other clinical problems that patients may be at risk for, and provide prognostic information.

Diagnosing r(20):
Since chromosomal analysis or karyotype testing is not a routine investigation when epilepsy first presents, the diagnosis of r(20) may be delayed or go unrecognized. Therefore the physician 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 r(20) can present as a mosaic with the ring in only a small number of cells, a minimum of 100 cells must be analysed. Newer 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

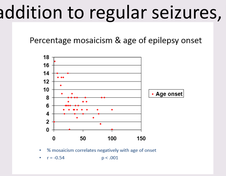
Symptoms and Treatments

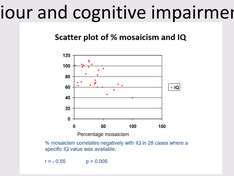
- ❑ This syndrome is characterized by medically intractable (difficult to treat) epilepsy, nocturnal subtle seizures, behavioural problems and intellectual disability (usually mild). Unlike other chromosomal abnormalities, dysmorphism is rarely reported.

Key symptoms:

- ❑ In most of the cases normal childhood development until onset of epilepsy
- ❑ Predominantly focal impaired awareness seizures
- ❑ Medically refractory epilepsy with long lasting focal seizures with impaired awareness with normal neuroimaging
- ❑ Frequent nocturnal seizures (in most of the cases subtle and of frontal lobe origin)
- ❑ Interictal EEG with characteristic appearance with log trains of theta waves, with a peak at 5 Hz and a sharply contoured 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

There are two distinct forms of r(20): mosaic and non-mosaic, with the latter being where all chromosome 20 in the body are formed in the ring. Non-mosaic cases of r(20) have the earliest reported age of onset of seizures (which are generally of a higher frequency and severity) can experience significant cognitive decline and regressed development. Mosaic cases have a later age of onset of seizures (typically between age 4-8) for which there is quite a broad spectrum of impact including loss of function such as mobility, ability to feed themselves and/or continence issues in addition to regular seizures, behaviour and cognitive impairment.





There are currently no recommended treatments for r(20) 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, cannabidiols and/or ketogenic dietary therapy – the latter with some significant success in a number 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.

Impact of the Condition

The main impact of living with r(20) 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 r(20) 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 NCSE is common.

Seizure triggers include:

- ❑ Tiredness
- ❑ Stress
- ❑ Exercise
- ❑ Bathing/showering
- ❑ Change in temperature (hot/cold)

Seizure control vs side effects
Balance = **QUALITY OF LIFE**

Failure to control seizures adequately can lead to cognitive decline.

Due to the nature of the seizures patients are prescribed emergency rescue medication (which some use daily) however many are admitted to A&E for seizures that cannot be stopped. One patient has been placed in an induced coma to let her body heal from a prolonged seizure.
These incessant seizures (and some of the side effects of the medications) take a toll on the body and mind, making the patient physically tired. Constant 'background activity' or non-clinical seizure activity i.e. that which you cannot see, affects concentration and the brain's ability to process information.

This has an impact on education and learning as well as an adult's ability to gain/maintain employment.
Families report behavioural issues with their children, including aggressive outbursts, impulsivity and obsessive behaviour. Many are said to be on the autistic spectrum.
Some r(20) patients require 24hr care, whereas other can lead a relatively independent life, albeit often with a degree of support.
These combination of symptoms can impact the individual's ability to socialise, friends and family may shy away and most individual's can't travel independently.

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 r(20) amongst neurologists, paediatricians, epilepsy specialist nurses - to understand when and how to test for r(20 . Better information for test laboratories, to influence test requests where r(20) is suspected, to ensure appropriate testing is carried out to improve overall diagnostic rates.

Recognition of the importance of confirming a diagnosis for an r(20) 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 r(20) and to ensure patients have the opportunity to be involved in appropriate clinical trials for potential treatments and to better characterize the syndromic features enlarging 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 r(20)? 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.

r(20) 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 r(20) 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?**

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