

## Epilepsy in Chromosomal Disorders

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### Editorial

Epilepsies are frequently reported in chromosomal diseases. Certain chromosomal disorders are particularly associated with epilepsy, showing a specific electro-clinical pattern such as 1p36 deletion syndrome, 4P deletion syndrome, ring 20 chromosome, Miller-Dieker syndrome and Down syndrome. Other chromosomal anomalies have no specific pattern of seizures such as ring 14 chromosome, fragile-X syndrome and Klinefelter syndrome. Many of their seizures onsets during the neonatal period or the infancy. Close watching for the seizure occurrence is mandatory for those diagnosed chromosomal disorders through their life.

Seizures may be the presenting symptom in many chromosomal disorders [1]. The dysmorphic facial appearance in conjunction with specific physical findings often lead to recognition of a chromosomal disorder which can be verified through karyotyping, and many new advanced molecular cytogenetic techniques. This overview will focus on seizure entities of common chromosomal diseases.

#### 1p36 deletion syndrome

1p36 deletion syndrome is associated with terminal deletions in the 1p36 region. In addition to the characteristic craniofacial features, all patients have developmental delay. Seizures are noted in up to 75% of cases, with onset at early age. Different seizure types have been observed with a spectrum of EEG abnormalities ranged from hypersarrhythmia to focal slow wave activity. Epilepsy is easy to control with conventional anti-epileptic drugs (AEDs), but some are refractory [2].

#### 4p deletion (Wolf-Hirschhorn) syndrome

Wolf-Hirschhorn syndrome is due to deletion of chromosome 4p16.3. Distinct craniofacial findings are often suggestive of the disease entity. Seizure rate are overall high, typically presenting within the first two years of life as clonic, tonic, focal and/or generalized seizures from the onset. They are often triggered by fever, and tend to occur in the early years. Seizures are effectively controlled by AEDs for the generalized types of seizures. The long term prognosis for seizure control is good, as they tend to disappear with age [3].

#### Ring chromosome 14 syndrome

The seizure incidence in patients with ring chromosome 14 is nearly 100%, with onset mostly in infancy. A recognizable phenotype includes psychomotor delay, cognitive impairment, growth retardation and microcephaly. Distinct facial features are also characteristic. Various seizure types have been reported, most are intractable [4] including generalized tonic-clonic, myoclonic, minor motor seizures, complex partial seizures with secondary generalization, and status epilepticus.

EEG findings are also varied from normal to multifocal epileptiform discharges.

#### Inv dup 15 syndrome

Inverted duplication of chromosome 15 [Inv dup (15)] is quite common, reported with an incidence of 1:30,000 at birth. This rearrangement results in tetrasomy 15p and partial tetrasomy 15q. Common clinical features include moderate to profound intellectual disability, severe epilepsy, diffuse hypotonia and autistic behavior [5]. Dysmorphic features may or may not be present. Most affected individuals have refractory seizures with poor outcome.

#### 17p13.3 del (Miller Dieker) syndrome

Miller Dieker syndrome with large deletions of chromosome 17p region is characterized by distinct facial features, lissencephaly, severe cognitive impairment, microcephaly, and epilepsy. Seizures begin in the early life and many individuals have infantile spasms and other seizure types. Prognosis is generally poor and seizures are refractory to AEDs [6].

#### Ring chromosome 20 syndrome

Seizures occur in most affected individuals with ring chromosome 20. Chromosomal mosaicism is often noted. This kind of patients may have no any dysmorphic features in the early life, resulting in delayed diagnosis. The seizure features include non-convulsive status followed by a long confusional state and focal seizures associated with orolimentary automatisms [7]. These seizures may be mistaken as behavioral abnormalities, especially in children. Seizures onset from infancy to adolescence, and tend to be refractory to AEDs [8].

#### Down syndrome

Down syndrome, or trisomy 21, is the most common chromosomal disorder in children. The combination of mental impairment and distinct clinical features usually leads to the diagnosis. Seizures occur in about 6% of individuals with Down syndrome [9]. All major seizure types have been reported, though infantile spasms and reflex epilepsies appear to be the most often seen. Their seizure treatments are guarded according to clinical responses.

#### Sex chromosome anomalies

Sex chromosome anomalies belong to a group of genetic conditions caused or affected by the loss, dysfunction or addition of the sex chromosomes. Among these, Fragile-X syndrome (Fra-X) is relatively common with the appearance of epilepsy ranging from 14% to 44% [10]. The seizures varied from benign childhood epilepsy to severe refractory one. Both epilepsy and EEG improve with age. Klinefelter

syndrome and Turner syndrome are rarely reported with epilepsy [11,12]. The electro-clinical spectrum is heterogenous and outcome with AED treatment is variable.

In conclusion, some of the chromosomal disorders show a peculiar epileptic and EEG pattern. The prognosis of seizure treatment is variable from benign nature to intractable entity. Further studies are needed to understand the true mechanism of epilepsy associated with chromosomal abnormalities.

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