Epilepsy syndromes of childhood and adolescence

Amy McTague

Abstract

Epilepsy syndromes are defined as distinctive disorders identifiable on the basis of a typical age of onset, specific EEG characteristics, seizure types, and other features. A wide range of epilepsy syndromes present throughout infancy, childhood and adolescence from benign self-limiting syndromes to severe epileptic encephalopathies. Accurate recognition and diagnosis of these syndromes is essential to ensure appropriate investigation and treatment. Recent revisions to the classification of childhood epilepsy and recent scientific, particularly genetic, discoveries have had an impact on our understanding of the childhood epilepsies. In this review we consider the role of syndromic diagnosis and describe the typical features and presentation of the most important epilepsy syndromes of childhood and adolescence.

Keywords child; epilepsy; epilepsy syndrome; epileptic encephalopathies; focal epilepsy; generalized epilepsy

Introduction

Epilepsy is defined as a tendency to have recurrent epileptic seizures. It is the commonest neurological condition of childhood, affecting 51,500 of the population under 16 years of age or 1 in 240 children. A recent national audit of epilepsy care revealed that only 37% of children had appropriate classification of their epilepsy syndrome and 11% of children with an initial diagnosis of epilepsy had this diagnosis withdrawn. Although children with epilepsy should be looked after by a paediatrician with expertise in this area, it is vital that all those caring for children have a working knowledge of the differing presentations of epilepsy throughout childhood and adolescence. In this article, an overview of the presenting features of the more common and important epilepsy syndromes is provided. For guidance on treatment of specific epilepsy syndromes, see further reading.

What is an epilepsy syndrome?

The International League against Epilepsy defines an electro-clinical syndrome as a distinctive disorder identifiable on the basis of a typical age of onset, specific EEG characteristics, seizure types, and other features. A number of electro-clinical syndromes are recognized by the ILAE and are listed in Table 1. A useful way to organize these is by age of onset.

Why is it important to diagnose epilepsy syndromes?

The first step in making a diagnosis of epilepsy is to ask — is this really epilepsy? There is a wide age-dependent differential diagnosis of paroxysmal episodes in adolescence and childhood (see further reading). Making this distinction depends on taking an accurate history from the child and any eyewitnesses and reviewing a video recording of the event if possible- now made much easier by the availability of mobile phone cameras.

The second step is to attempt to classify the type/s of seizures that the child or young person is experiencing. This will be important as if a syndromic diagnosis is not possible it may direct treatment choice and will certainly direct investigation. The ILAE recently revised the classification of seizure types (Table 2), reflecting advances in knowledge such as the increasing awareness of the importance of discrete epilepsy networks in generalized epilepsies. In addition the terms "simple partial" and "complex partial" were felt to be misleading and have been replaced. A complex partial seizure might now be described as a focal dyscognitive seizure with further description of the aura, motor and other components using the glossary of ictal semiology (see further reading).

An attempt should then be made to classify the epilepsy and make a syndromic diagnosis where possible. This is important for several reasons. Firstly, it enables the clinician to consider which investigations will be relevant. For example, a history consistent with benign rolandic epilepsy of childhood (see below) may reassure the clinician that further investigation of these focal seizures is not required. Secondly, it may direct treatment choice and allow one to avoid medications which are known to exacerbate the seizures in those patients. A common example of this is the incorrect use of carbamazepine in childhood absence epilepsy, where inaccurate recognition of seizure type and epilepsy syndrome may precipitate absence status epilepticus. Lastly and most importantly a syndromic diagnosis allows prognostication and an adequate explanation of the likely future course of the epilepsy to the child and family.

There are several caveats to this. Firstly, it may not be possible to ascribe a syndromic diagnosis and this should not justify an inaccurate diagnosis as this could lead to harm. If this is the case an attempt should be made to classify the seizures with consideration given to aetiology. In the past children not "fitting" a specific epilepsy syndrome would be described as having idiopathic, symptomatic or cryptogenic epilepsy. The most recent revision of the organization of the epilepsies has replaced these terms with Genetic, Structural, Metabolic or Unknown. In addition it may take time for the syndromic diagnosis to become clear. A useful approach is to describe the epilepsy as "epilepsy characterised by…" with an accurate seizure description.

Even where a syndromic diagnosis is made, it is good practice to ensure that the diagnosis is reviewed at every clinic visit. For example a young person with presumed juvenile myoclonic epilepsy who does not respond to medication and begins to display loss of cognitive skills should be investigated for causes of progressive myoclonic epilepsy including neurodegenerative conditions.

Severe epilepsy syndromes of infancy and early childhood

Many of the severe epilepsy syndromes which present in the first two years of life can be described as epileptic encephalopathies, defined by the ILAE as a condition where the epileptic activity itself

Amy McTague *MBChB MRCPCH Neuroscience Unit, UCL-Institute of Child Health, London, UK.*

ILAE-recognized electro-clinical syndromes organized by age

- Neonatal period
  - Benign familial neonatal epilepsy (BFNE)
  - Early myoclonic encephalopathy (EME)
  - Ohtahara syndrome
- Infancy
  - Epilepsy of infancy with migrating focal seizures
  - West syndrome
  - Myoclonic epilepsy in infancy (MEI)
  - Benign infantile epilepsy
  - Benign familial infantile epilepsy
  - Dravet syndrome
  - Myoclonic encephalopathy in non-progressive disorders
- Childhood
  - Febrile seizures plus (FS+) (can start in infancy)
  - Panayiotopoulos syndrome
  - Epilepsy with myoclonic atonic (previously astatic) seizures
  - Benign epilepsy with centrotemporal spikes (BECTS)
  - Autosomal-dominant nocturnal frontal lobe epilepsy (ADNFLE)
  - Late onset childhood occipital epilepsy (Gastaut type)
  - Epilepsy with myoclonic absences
  - Lennox—Gastaut syndrome
  - Epileptic encephalopathy with continuous spike-and-wave During sleep (CSWS)
  - Landau—Kleffner syndrome (LKS)
  - Childhood absence epilepsy (CAE)
- Adolescence — Adult
  - Juvenile absence epilepsy (JAE)
  - Juvenile myoclonic epilepsy (JME)
  - Epilepsy with generalized tonic—clonic seizures alone
  - Progressive myoclonus epilepsies (PME)
  - Autosomal dominant epilepsy with auditory features (ADEAF)
  - Other familial temporal lobe epilepsies
- Less specific age relationship
  - Familial focal epilepsy with variable foci (childhood to adult)
  - Reflex epilepsies

Adapted from Berg et al, Epilepsia, 51(4):676—685, 2010.

Table 1

Classification of seizure types

Generalized seizures: (Arising within and rapidly engaging bilaterally distributed networks)	Tonic—clonic Absence: Typical Atypical Absence with special features: myoclonic absence, eyelid myoclonia Clonic Tonic Atonic Myoclonic: myoclonic, myoclonic—atonic, myoclonic-tonic
Focal seizures: (Originating within networks limited to one hemisphere)	Characterized by one or more features: Aura Motor Autonomic Awareness/responsiveness: altered (dyscogntive) or retained
Unknown	Epileptic spasms

Adapted from Berg et al, Epilepsia, 51(4):676—685, 2010.

Table 2

may contribute to the severe neurological and cognitive impairment seen in severe epilepsy, over and above that which would be expected from the underlying pathology alone. Although there is some controversy around this term, it is certainly true that these syndromes are associated with developmental delay or regression, are resistant to treatment and carry a poor prognosis.

Ohtahara syndrome

This syndrome is characterized by frequent tonic spasms commencing in the neonatal or early infantile period. Other seizure types include focal motor and generalized tonic seizures and infants show a marked lack of developmental progress or delay with hypotonia. There is a characteristic inter-ictal EEG with burst suppression consisting of high amplitude slow waves and polyspikes interspersed with isoelectric phases. Causes of Ohtahara syndrome include structural brain abnormalities such as hemimegalencephaly or less commonly metabolic disorders. Recently mutations in the *STXBP1* and *ARX* genes have been identified in some cases. Many babies with Ohtahara syndrome will evolve into having West syndrome (see below) or will continue to have intractable epilepsy.

Early myoclonic epileptic encephalopathy

This syndrome presents at a similar age to Ohtahara syndrome and also with burst suppression on the inter-ictal EEG but infants display frequent myoclonic seizures and later develop tonic spasms and other seizure types. They also have marked developmental delay and the seizures are resistant to treatment. The aetiology tends to be more metabolic with causes such as pyridoxine dependency, non-ketotic hyperglycinaemia or organic acidaemias. Some rare cases with mutations in *SLC25A22* have been described.

Epilepsy of infancy with migrating focal seizures

This rare syndrome is characterized by the onset of frequent focal seizures in the first 6 months of life associated with autonomic features, developmental stagnation or delay and a characteristic ictal migrating pattern on EEG. The response to treatment is poor. Initially the aetiology was unclear but mutations in a variety of genes including *SCN1A, PLCB1, SLC25A22* and *KCNT1* have now been reported in a small number of cases.

West syndrome

West syndrome is a triad of infantile spasms, developmental delay and a characteristic inter-ictal EEG pattern of hypsarrhythmia. Infants present in the first year of life with clusters of infantile spasms which may be flexor, extensor or a combination. Onset of