Recent Trends in Management of Childhood Epilepsy

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ABSTRACT

Epilepsy is a disorder characterized by the occurrence of at least 2 or more unprovoked seizures. Epilepsy is a common brain disease affecting 1-2% of the population, and 4% of children. In 1989, the International League Against Epilepsy (ILAE) developed a classification of epileptic syndromes revising its own previous classification of 1981 which is based on the age of epilepsy onset, EEG features, imaging studies, response to treatment and prognosis of the patients. The diagnosis of epilepsy and assigning it to a class is a very vital part of management; ideally, physicians would classify the seizures of their patients, using the classification for seizures type, and if possible, make a syndromatic diagnosis for proper management. Because childhood period most affected with epilepsy and epileptic syndromes, proper management is very crucial to forestall long-term morbidity, mortality, mental and physical handicap in this age group.

INTRODUCTION

Epilepsy is a disorder characterized by the occurrence of at least 2 or more unprovoked seizures. Seizures are the manifestation of abnormal hypersynchronous discharges of cortical neurons. The clinical signs or symptoms of seizures depend upon the location and extent of the propagation of the discharging cortical neurons. Epilepsy is a common brain disease affecting 1-2% of the population, and 4% of children. The lifetime likelihood of experiencing at least one epileptic seizure is about 2-5% of general population, and point prevalence is 4-8 per 1000.

CLASSIFICATION OF EPILEPTIC SEIZURES

Classification of Epileptic Seizures remains always a contentious issue because of ever-increasing clinical spectrum and advanced newer investigations in this field. In 1989, the International League Against Epilepsy (ILAE) developed a classification of epileptic syndromes revising its own previous classification of 1981, because since that time much have been changed in brain imaging technology and newer concept have been developed. The newer ILAE classification is based on the age of epilepsy onset, EEG features, imaging studies, response to treatment and prognosis of the patients, which were not given due consideration in previous classifications. The current system comprises 2 major categories: localization-related syndromes and generalized-onset syndromes. This is as follows:-

APPROACH TO CHILDHOOD EPILEPSY

The diagnosis of epilepsy and assigning it to a class is a very vital part of management, as with approach to the other medical problems, which is carried out by a good detailed medical history, family history and complete systemic examination including neurological examination, backed up by proper investigations, because comprehensive treatment and prognosis will totally depend on the type of epilepsy. Many type of epileptic events are self-evident by their mode and pattern of presentation. Ideally, physicians would classify the seizures of their patients, using the classification for seizures type, and if possible, make a syndromatic diagnosis for proper management. There should be high priority to search of treatable cause of seizure, like intracranial tumors, infections (bacterial, fungal, viral or parasitic) etc. It is very important to exclude, possibly by judicious use of investigations, those medical conditions which can mimic seizure disorder to avoid not so pleasant course of long term pills and of course stigmatizing child. Main differential diagnosis of epilepsy is:

INVESTIGATIONS

Along with routine investigations, one should not hesitate to go for more advanced investigations to establish possible type and etiology of epilepsy and protocol should be followed by clinical situation of patient and discretion of physician. Two cornerstone investigations are:

Electroencephalogram (EEG)

This is simple, harmless and inexpensive diagnostic tool, being an indispensable in correct syndromic diagnosis of epilepsy. Its advanced form, the Video-EEG has revolutionised it further, it has very important role in differentiating pseudo seizures
Table 1: International classification of epilepsies and epileptic syndromes (Commission on Classification and Terminology (ILAE, 1989).

<table>
<thead>
<tr>
<th>Class Classification</th>
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<tbody>
<tr>
<td>1. Localization-related (focal, local, partial)</td>
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<tr>
<td>1.1 Idiopathic (with age-related onset)</td>
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<tr>
<td>Benign childhood epilepsy with centrotemporal spikes</td>
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<td>Childhood epilepsy with occipital paroxysm Primary reading epilepsy</td>
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<td>1.2 Symptomatic</td>
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<tr>
<td>Chronic progressive epilepsy partialis continua of childhood</td>
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<td>1.3 Cryptogenic</td>
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<tr>
<td>The symptomatic and cryptogenic categories comprise syndromes of great individual variability that are based on:</td>
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<tr>
<td>Seizure types (according to the International Classification of Epileptic Seizures)</td>
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<tr>
<td>Anatomic localization: Temporal, frontal, parietal, and occipital lobe epilepsies</td>
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<tr>
<td>Bi-and multilobar epilepsies</td>
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<tr>
<td>Etiology (in symptomatic epilepsies) Specific modes of precipitation</td>
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<tr>
<td>2. Generalized</td>
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<tr>
<td>2.1 Idiopathic (with age-related onset, in order of age) Benign neonatal familial convulsions Benign neonatal convulsions Benign myoclonic epilepsy of infancy Childhood absence epilepsy (pyknolepsy) Juvenile absence epilepsy Juvenile myoclonus epilepsy (impulsive petit mal) Epilepsy with grand mal (GTC) seizures on awaking Other idiopathic generalized epilepsies not defined above Epilepsies with seizure precipitated by specific modes of activation</td>
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<tr>
<td>2.2 Symptomatic</td>
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<tr>
<td>2.3.1 Nonspecific etiology, Early myoclonic encephalopathy Early infantile epileptic encephalopathy with suppression-burst, Other symptomatic generalized epilepsies not defined above</td>
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<tr>
<td>2.3.2 Specific syndromes</td>
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<tr>
<td>3. Epilepsies and syndromes undetermined whether focal or generalized</td>
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<tr>
<td>3.1 With both generalized and focal seizures Neonatal seizures. Severe myoclonic epilepsy of infancy Epilepsy with continuous spike-waves during sleep. Acquired epileptic aphasia (Landau-Kleffner syndrome) Other undetermined epilepsies not defined above</td>
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<tr>
<td>3.2 Without unequivocal generalized or focal features (e.g. many cases of sleep-grandmal)</td>
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<tr>
<td>4. Special syndromes</td>
</tr>
<tr>
<td>4.1 Situation-related seizures (Gelegenheitsanfälle) Febrile convulsions Isolated seizures or isolated status epilepticus. Seizures due to acute metabolic or toxic factors such as alcohol, drugs, eclampsia.</td>
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Table 2: Disorders that may Mimic Childhood Epilepsy

<table>
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<tr>
<th>Confused With Generalized Tonic Clonic Seizures</th>
<th>Confused With Absence Seizures</th>
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<tbody>
<tr>
<td>• Breath holding spells</td>
<td>• Behavioral staring</td>
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<tr>
<td>• Syncope</td>
<td>• Tic disorder</td>
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<tr>
<td>• Cataplex</td>
<td></td>
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<tr>
<td>• Pseudo-seizures</td>
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<tr>
<th>Confused With Complex Partial Seizures</th>
<th>Confused With Epileptic Myoclonus</th>
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<tr>
<td>• Stereotype and self stimulatory behavior</td>
<td>• Benign infantile sleep myoclonus</td>
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<td>• sleep walking</td>
<td>• Physiologic hypnagogic myoclonus</td>
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<tr>
<td>• Confusional arousals</td>
<td>• Hyperekplexia (Startle disease)</td>
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<tr>
<td>• Temper tantrums and rage attacks benign paroxysmal vertigo</td>
<td></td>
</tr>
<tr>
<td>• Migraine related disorders</td>
<td></td>
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<tr>
<td>• Panic attacks</td>
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from epilepsy, localizing the site of lesion, and pre-operative evaluation of epilepsy surgery of the patients. EEG done in a sleep deprived child (yield is high) or if condition needs during deep sleep which may be natural or drug induced to assess certain type of seizures which electrophysiologically manifest mostly during deep sleep [e.g. Landau Kleffner syndrome, Lennox Gastaut syndrome, continuous spike and waves in slow wave sleep (CSWS)]

Brain Imaging
Imaging of the brain by CT scan or MRI study opened a gateway to brain to diagnose treatable or nontreatable etiology of epilepsy, which now became routine investigation of any seizure disorder. MRI brain for epilepsy is done with special sequences ($T_1$, $T_2$, flair and PD image with axial and coronal sections) and it is also very important for epilepsy surgery protocol to localize the site of lesion. Neuroimaging may show the presence of a lesion not suspected on clinical or EEG grounds and help
in formulating syndromic and etiological diagnosis to give to patients an physician an accurate prognosis. MRI detects mesial temporal sclerosis and neuronal migration related abnormalities accurately. Newer modalities, like PET and SPECT delineate abnormal areas of cortical dysplasia even invisible to MRI.

**SPECIAL PEDIATRIC EPILEPSY AND EPILEPTIC SYNDROMES**

**Benign Childhood Epilepsy**
The various types of epilepsy differ in many aspects, including (1) age of onset, (2) semiology, (3) EEG findings, and (4) outcome. Freeman et al reported that most children with generalized tonic-clonic (GTC) seizures have a "benign developmental disorder" that reduces their seizure threshold and will be outgrown. This disorder has been termed “benign childhood epilepsy” and is thought to be secondary to CNS immaturity. These are:

**Idiopathic Generalized Epilepsies**
These type of seizures are sometimes inherited condition with normal development and intellect, no brain structural abnormality, EEG shows normal background, easy to control seizures with good prognosis. These are:

**Juvenile myoclonic epilepsy**
It is an idiopathic generalized epileptic syndrome characterized by myoclonic jerks, generalized tonic-clonic seizures (GTCs), and sometimes absence seizures. Although patients usually require lifelong treatment with anticonvulsants, overall prognosis is generally very good. The seizures usually occur shortly after awakening and are often precipitated by sleep deprivation. Interictal and ictal EEG have rapid, generalized, often irregular spike-waves (SW) and polyspike-waves. Frequently the patients are photosensitive. Response to appropriate drugs is good. Myoclonic jerks, GTCs, and absence seizures all have an age-related onset in JME. If absence seizures are a feature, they usually begin between the ages of 5 years and 16 years; myoclonic jerks may follow 1-9 years later, usually around the age of 15 years; GTCs typically appear a few years later than myoclonic jerks. Management includes avoidance of precipitating factors and drugs of choice are valproic acid, lamotrigine, clobazam and clonazepam.

**Childhood absence epilepsy (Pyknolepsy)**
Seizures are brief, most commonly lasting 5-10 seconds, start and end suddenly, frequently occurring 10-100 times a day, occur spontaneously but may be precipitated by multiple factors including emotional, intellectual, or metabolic (e.g. hypoglycemia, hyperventilation). The main feature of absence seizures is loss of responsiveness with cessation of ongoing activity. GTC seizures develop in about 40%. They are infrequent, easily controlled, and generally occur 5-10 years after the onset of absences. Juvenile myoclonic epilepsy (JME) is reported to occur in 44% of patients who failed to have remission of their seizures. Problems with cognition, social adaptation, or behavior are not uncommon. Such difficulties may occur in one third of patients. 3Hz Spike and wave complexes is the typical EEG abnormality. They respond very well to valproic acid and ethosuximide.

**Juvenile absence epilepsy**
Children with JAE usually are neurologically normal. Absence seizures occur in all cases. Compared to childhood absence epilepsy, however, absence seizures in JAE have the features of: relatively infrequent with only a few episodes daily Longer in duration. A tonic-clonic seizure can be the presenting feature, occurring shortly after awakening. This type of seizure occurs in 80% of patients. Myoclonic seizures occur in about 15% of patients. Background EEG activity is usually normal. Characteristic features are the ictal and interictal generalized symmetric spike-and-wave discharges with frontal accentuation. Valproic acid is the drug of choice, as it controls absences and the other associated seizure types in about 80% of cases.

**Symptomatic generalized epilepsies**
Children with these type of epilepsy are developmentally delayed, may have a structural brain abnormality. They have intractable seizures, poor long term outcome even if treated. These are:

**West’s syndrome (Infantile Spasms)**
Applied to the triad of hypsarrhythmia in EEG, mental retardation and infantile spasms, refers to brief atonia followed by tonic contraction of the axial and proximal limb muscles, onset before the age of 1 year (max. 4-7 months). Infantile spasms show good response to steroids (especially to ACTH), benzodiazepines specially clonazepam, valproic acid and immunoglobulins.

**Lennox Gastaut syndrome (LGS)**
This label is often used loosely for intractable epilepsy in childhood, key components are: specific seizure types are tonic and atypical absence seizures which are difficult to control, specific interictal and ictal EEG abnormalities 2-3 Hz, slow or multifocal independent sharp waves and diffuse cognitive dysfunction, typical EEG pattern, may not be seen till 3 or 4 years of age, mental retardation may evolve with time. These patients respond poorly to valproic acid and benzodiazepins, and have overall poor prognosis.

**Progressive myoclonus epilepsies**
This is a rare group of inherited, neurodegenerative conditions where myoclonus occurs in association with one or more of the associated conditions like progressive deterioration in cognitive function, ataxia, visual loss and skin changes. Common type of syndromes is:

**Uvverricht-Lundborg Disease**
Mean onset of generalized seizures and myoclonus is at 11 years of age (range, 6 to 15 years). The jerks interfere with gait, swallowing, speech and, after approximately 5 years, leave the patient incapacitated and eventually, intention tremor, dysarthria, ataxia, and dementia develop.

**Lafora’s Disease**
This homogeneous autosomal recessive disease is the most common form of progressive myoclonus epilepsies in the Middle East including India. It manifests between ages 10 and 18 years, and patients die within a decade of the initial symptoms.
Generalized tonic-clonic seizures, absences, or drop attacks are the first manifestation, followed soon after by stimulus-sensitive myoclonic jerks. A rapidly progressive dementia with apraxia and visual loss ensues. Diagnosis is established by the presence of the periodic acid-Schiff-positive cytoplasmic inclusion bodies in the brain, striated muscle, liver, and skin.

**Neuronal Ceroid Lipofuscinoses**

Neuronal ceroid lipofuscinoses (NCL), are a group of neurodegenerative disorders characterized by accumulation of autofluorescent lipopigments (ceroid and lipofuscin) in neurons and other cell types. Onset is between 1 and 4 years of age and is characterized by impaired motor development, ataxia, speech impediments, and slow cognitive development. Myoclonic, generalized tonic-clonic, atonic, and atypical absence seizures appear after neurologic signs.

**Juvenile Gaucher's Disease**

It is inherited in an autosomal recessive trait. Myoclonic, generalized tonic-clonic, atonic, and atypical absence seizures appear after neurologic signs. Intellectual loss, optic atrophy, and blindness are present at 5 years of age. Spasticity and ataxia lead to a decorticate state and death between ages 3 and 10 years.

**Sialidosis Type I (Cherry-Red Spot-Myoclonus Syndrome or Guazzi Syndrome)**

This is rare, chronic neuronal storage disorder begins between the ages of 8 and 15 years with progressive myoclonus, macular cherry-red spots with visual failure, and generalized tonic-clonic seizures without dementia.

**Myoclonus Epilepsy and Ragged-Red Fibers (MERRF)**

The disease starts in early childhood or as late as 65 years of age. Ataxia and myoclonus are constant features together with generalized tonic-clonic seizures. Dementia, dysarthria, short stature, hearing loss, optic atrophy, neuropathy, hyperventilation, and migraine may also be present. Muscle biopsy reveals subsarcolemmal aggregates of mitochondria, the so-called ragged-red fibers. MERRF has been reported to be benefited by coenzyme Q with valproic acid in some studies.

Progressive myoclonus epilepsies has overall rapidly downhill course but seizures are partly responsive to valproic acid, clonazepam, and lamotrigine and worsened by phenytoin and gabapentin.

**Subacute sclerosing panencephalitis (SSPE)**

It is a rare chronic progressive demyelinating disease of the central nervous system associated with a chronic noninfectious infection of brain tissue with measles virus. Children usually present with poor performance in study and learning with mood and personality changes. In advanced stage there is profound intellectual deterioration, focal and generalized seizures, myoclonus and ataxia. Death may occur within weeks of onset; about half die within a year and most die with in two years. About 4% can achieve remission. Typical EEG changes includes characteristic periodic pattern with burst every 3-8 seconds of high-voltage, sharp slow waves, followed by periods of attenuated background. CSF is acellular with mildly elevated protein level with marked increase in γ-globulin. CT and MRI show evidence of multifocal white matter lesion and cortical atrophy. No definitive treatment available for SSPE, though intraventricular / intrathecal Interferon α along with a newer drug Isoprinosine (100 mg/kg/day) have been reported to prolong survival and clinical improvement. Valproic acid can be used for control of myoclonic seizures.

**Localization related epilepsies**

As described by the ILAE classification. Localization related epilepsies and syndrome are epileptic disorders in which seizure semiology or findings at investigation disclose a localized origin of the seizure. These are:

**Benign focal epilepsy with occipital paroxysms (Benign Occipital Epilepsy)**

Clinical semiology is complex and is characterized by ictal and postictal Visual symptoms with complex partial seizures with automatisms hemiclonic convulsions or generalized clonic seizures. Onset in children aged 3-7 years, associated with a good prognosis, disappears by adolescence. Carbamazepine may be the drug of choice, although almost all of the classic anticonvulsants are effective.

**Benign focal epilepsy with centrotemporal spikes (Benign Rolandic Epilepsy)**

This epileptic syndrome is characterized by brief, simple, partial, and hemifacial motor seizures with associated somatosensory symptoms with salivation and speech arrest, which have a tendency to evolve into GTC seizures. EEG shows high-voltage centrotemporal spikes often followed by a slow wave being the most common epilepsy syndrome in childhood. The syndrome is termed “rolandic” epilepsy because of the characteristic features of partial seizures involving the region around the lower portion of the central gyrus of Roland. The typical interictal EEG shows centrotemporal spikes or SW, which is either unifocal or bifocal. Carbamazepine is often the first medication to be tried. Seizures generally show a good response to treatment.

**Mesial temporal lobe epilepsy (MTLE)**

Most common syndrome associated with complex partial seizure and there is strong association with febrile seizures, onset in childhood, 6-10 years, two thirds have complex partial seizures from the onset; a third have generalized seizures as presenting seizures, auras are very common (>80% have) commonest aura is an abdominal aura (60%). MRI findings are small hippocampus with increased signal on T2-weighted sequences, small temporal lobe and enlarged temporal horn collectively known as mesial temporal sclerosis. EEG will show unilateral or bilateral anterior temporal spikes. Management is essentially surgical resection of affected part of temporal lobe by transcortical-transventricular approach to amygdalohippocampectomy by various methods.

**Special Syndromes and Syndromes undetermined as to whether they are focal or generalized**

In this type of seizure patient usually experience both focal and generalized seizure together or in succession and have both focal
and generalized EEG seizure discharge. So this becomes very difficult to assign them into one of these classes. These are:

**Febrile seizures**
This is the commonest seizure disorder seen in childhood period, occurring in 2-5% of the population. Most frequently from the age of 12-18 months with peak incidence between 18-24 months. These convulsions occur early in rising phase of infectious febrile illness. Girls younger than 18 months have relatively high risk in comparison with boys. **Simple Febrile Convulsions:** Solitary event that last for less than 15 minutes and lacks focal neurological deficit. **Complex Febrile seizures:** They are characterized by prolonged seizure duration more than 15 minutes, focal seizure manifestations, seizure recurrence within 24 hours, abnormal neurological status and afebrile seizures in sibling or parents. Approximately one third of patients with febrile seizure experience further attacks and between 1.5% to 4.6% of children develop later afebrile seizures. Management include prompt use of antipyretics and tepid sponge bathing to control fever, to treat underlying infection, use of intermittent clobazam and prophylactic anticonvulsants after weighing risk and benefit ratio.

**Landau Kleffner syndrome**
Age of onset ranges from 3 to 8 years, and boys are more frequently affected than girls. Acquired aphasia is the more prominent feature, since seizures are present in only 70% to 80% of the patients. The most common types of seizures are: eyelid myoclonia, eye blinking, atypical absences, head drops and tonic seizures in upper limbs, automatisms, and occasionally, partial motor seizures with secondary generalization. Waking EEG usually shows brief bursts of temporal or temporo-occipital spike and wave discharges, either symmetrical or asymmetrical. In fact, the most typical EEG findings appear during slow sleep as continuous 1.5 to 5 Hz spike and wave discharges.

**Epilepsy with continuous spike and waves in slow wave sleep (CSWS)**
The definition accepted by the ILAE was “epilepsy with CSWS results from the association of various seizure types, partial or generalized, occurring during sleep and atypical absences when awake”. Tonic seizures do not occur. The characteristic EEG pattern consists of continuous diffuse SW during slow wave sleep, which is noted after onset of seizures in most of the records. Despite the usually benign evolution of seizures, prognosis is guarded because of the appearance of neuropsychological disorders. Treatment of Landau Kleffner syndrome and Epilepsy with continuous spike and waves in slow wave sleep (CSWS) with standard antiepileptic drugs such as phenytoin, phenobarbital, and carbamazepine may be effective against seizures, but at present this treatment is not recommended because these drugs may worsen the EEG discharges and neuropsychological deficit. Instead, valproate, ethosuximide, and the benzodiazepines can be effective and deserve a trial before attempting treatments with higher risks. Treatment with high-dose corticosteroids was reported to yield the best results, and prolonged chronic or intermittent therapy may be necessary. In a recent report, in isolated cases, the use of intravenous immunoglobulins 2 g/kg showed excellent response; in both children the severe language and EEG abnormalities completely resolved.

**Rasmussen’s syndrome (chronic Focal Encephalitis)**
This rare syndrome in childhood due to postnatally acquired inflammatory cortical changes which may lead to severe focal epilepsy and progressive hemiparesis. Intellectual deterioration, of variable severity eventually plateaus, frequently leaving a neurologically devastated individual. EEG shows bilateral or multifocal abnormalities with unilateral predominance. MRI shows progressive unilateral hemispheric atrophy beginning in the perisylvian region. Management of this syndrome is very disappointing; with some improvement with high dose steroids and immunoglobulins if used early, while in advanced cases with hemiparesis classical treatment option is hemispherectomy or multiple subpial incisions.

**REFERENCES**


