Original Article

Clinical profile of children with West syndrome: A retrospective chart review

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Abstract

Background: This study was intended to document the clinical profile and treatment outcome of West syndrome in children attending a tertiary care centre in Northern India. **Methods:** Data were collected by a retrospective chart review of children diagnosed with West syndrome between January 2017 to January 2018. Information was recorded pertaining to the age at onset and presentation, etiology, and associated co-morbidities; results of electroencephalography (EEG) and neuroimaging; treatment given; and final outcome. The following drugs were used for treatment: ACTH (n = 7), prednisolone (n = 17), vigabatrin (n = 25), sodium valproate (n = 28), clonazepam (n = 30), and levetiracetam (n = 13) and modified Atkins diet (n = 7). The response was categorized as spasm cessation, partial improvement (>50% improvement), or no improvement. **Results:** Records of 30 children (21 boys) were analyzed. The median (IQR) age at onset was 4 (3, 6.5) months. The median (IQR) lag time to treatment was 5 (2,14) months. Eight (26%) were premature, 2 (7%) were small for gestational age, birth asphyxia in 56%, neonatal encephalopathy in 62%. EEG findings were hypsarrhythmia in 13 (43.3%) children and modified hypsarrhythmia in 9 (30%) children. MRI finding was periventricular leukomalacia (54.1%), cystic encephalomalacia (13.8%), normal MRI (20.7%) and one had arrested hydrocephalus. There was no improvement with valproate (93%), clonazepam (89%), levetiracetam (78%). Cessation of spasm was achieved with vigabatrin (28%), prednisolone (38.2%), ACTH (42.8%). Hypsarrhythmia resolved with improvement in of background and other epileptiform abnormalities in 17 children. **Conclusion:** The present research highlights favourable response of West syndrome to oral steroids, vigabatrin and ACTH with limited role of conventional antiepileptic drugs like sodium valporate, levetiracetam and clonazepam. Primary care physician plays a vital role in early recognition and treatment of epileptic spasm.

Keywords: Developmental delay, epileptic spasms, hypsarrhythmia, infantile spasms

Introduction

West syndrome is an epileptic encephalopathy of childhood manifested by presence of epileptic spasm, developmental delay and EEG showing evidence of Hypsarrhythmia.[1] The clinical spasms are characterized by brief movements of head, trunk or limbs alone or their synchronized movements which may be flexor, extensor or a mixture of both lasting approximately one second, the most subtle being a head nod.

Classical age of west syndrome is from the age of 4 months to 2 years but can extend well beyond 2 years of age. Children with west syndrome have a poor outcome when left untreated.[2] Etiologically, IS (Infantile Spasm) can be classified into the categories of cryptogenic and symptomatic.[3] Etiology in majority of children with west syndrome includes perinatal insults including perinatal asphyxia, prematurity, kernicterus, hypoxic ischemic encephalopathy and intracranial haemorrhage.

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Treatment of West syndrome includes ACTH and oral steroids.[4] The second line treatment includes vigabatrin.[5-9] Other drugs that are known to be effective in west syndrome includes sodium valproate, levetiracetam, topiramate, clonazepam and zonisamide. Modified Atkins diet and ketogenic diet are useful among those who fail primary treatment.[10] The efficacy of various drugs is variable in children with west syndrome. The present study was designed to describe the etiology and treatment outcome of children diagnosed with West syndrome.

Methods

This retrospective study was conducted in a tertiary care teaching hospital of North India. An institutional ethical committee clearance was obtained prior to commencement of study. The records of children aged 6 months to 5 years with clinical diagnosis of west syndrome were retrieved. Children were considered to have west syndrome when there was presence of epileptic spasms, with or without electroencephalographic evidence of Hypsarrhythmia with or without presence of developmental delay. Children who had a minimum follow up of 6 months were recruited in the study. Records of patients from January 2017 to January 2018 were retrieved for the purpose of study.

All children were subjected to detailed clinical history which includes age at the onset of spasm, frequency of epileptic spasm, number of spasms per cluster, number of clusters per day, presence or absence of developmental delay. Spasm type, frequency, age at onset, age at diagnosis, frequency of spasm, perinatal details, family history, developmental status and treatment history were noted. Number and nature of antiepileptic medications and their doses were recorded in case record form. Written informed consent were taken from parents. All the clinical details were recorded in the file. A detailed examination including presence of any neurocutaneous markers, any evidence of spasticity, dystonia was recorded. Head circumference was also recorded and its percentile to age norms were compared.

All children were subjected to minimum of 1.5 Tesla magnetic resonance imaging of brain. Their findings were recorded in the sheet. Similarly, children were also subjected to electroencephalography (EEG). The EEG was recorded using standard 10-20 system with 21 electrodes. EEG would be repeated after clinical cessation of spasm to document resolution of Hypsarrhythmia.

All children with symptomatic west syndrome were subjected to Mantoux, chest X-ray to rule out latent tuberculosis. Following screening for latent tuberculosis, children were administered either of oral prednisolone or ACTH. If there was failure of both the drugs, then vigabatrin was initiated. Those who failed steroids and vigabatrin, trial of valproate, clonazepam was provided. Children were offered modified Atkins diet for those who failed either of the above options. The treatment outcome was determined in terms of spasm cessation which was defined as absence of spasm for consecutive 28 days within 14 days of commencement of treatment.

All data collected were entered in Microsoft Excel (MS Excel). Data were analysed using SPSS 21.0 version. All categorical variables were expressed in Numbers (percentage), all continuous variables were expressed as Mean (SD) or Median (IQR). Categorical variables were compared using Chi Square Test or Fischer Exact Test. Continuous variables were compared between cases and controls using Student 't' test or Wilcoxon Rank Sum test.

Results

Records of 30 children with west syndrome who completed a minimum of six months follow up were retrieved for analysis. Majority of them were males [21 (70%)]. They had prior developmental delay [28 (93.2%)]. Motor disability in the form of cerebral palsy was present in 20 (66.7%) children. Microcephaly was also detected in majority of enrolled children [16 (53.3%)] [Table 1].

Age at onset of spasm as elicited by history was 4 months whereas, age at diagnosis was 12 months resulting in lag time of around 5 months. Majority of the children had cluster of epileptic spasms, with median (IQR) number of spasms per cluster being around 5 [4, 6] [Table 1]. Etiology of West syndrome was birth asphyxia [n = 16] in majority of patients. Other aetiologies included cryptogenic, metabolic cause, neonatal meningitis, perinatal stroke and postnatal meningoencephalitis [Figure 1].

Treatment response was favourable in nearly one third of children who received oral prednisolone or vigabatrin [Table 2]. There was nearly no response to sodium valproate or clonazepam. Two children were attempted on pulse methylprednisolone resulting spasm cessation in one and partial response in another child. Hypsarrhythmia or modified Hypsarrhythmia resolved with improvement in background and other epileptiform abnormalities in 17 children (57%).

Discussion

The present study revealed that steroids and vigabatrin remain the mainstay of treatment with more than 50% showing complete or partial response. Owing to logistic and financial constraints, ACTH could not be attempted in more than two-third of enrolled children. The present study also highlighted that conventional antiepileptic drugs like sodium valproate, and clonazepam does not result in clinical resolution of epileptic spasms.

Spasms may be subtle, brief, and sudden, the most subtle being a head nod or tonic eye rolling, which may be easily missed; they also show great variability in frequency.[11] Typically, the spasms involve brief symmetrical contractions of musculature of the neck, trunk and extremities lasting for up to 5 seconds and occurring in clusters.[12] In most cases there is an initial phasic component

Table 1: Clinical characteristics of children with West syndrome

Parameter	Number (Percentage)
Proportion of Male	21 (70%)
Developmental delay prior to onset	28 (93.2%)
Microcephaly	16 (53.3%)
Cerebral palsy	20 (66.7%)
Parameter	**Median (IQR)**
Age at onset (months)	4 (3,6.5)
Age at diagnosis (months)	12 (6,21)
Time lag (months)	5 (2,14)
Number of clusters per day	9 (6,12)
Number of spasms per cluster	5 (4,6)

Table 2: Treatment response of children with west syndrome

Drugs	Complete response	Partial response	No response	Not attempted
Pyridoxine	0	0	2 (6.6%)	28 (93.3%)
Levetiracetam	1 (3.4%)	11 (36.6%)	2 (6.7%)	16 (53.3%)
Valproate	0	3 (10%)	25 (83.3%)	2 (6.7%)
Vigabatrin	7 (23.3%)	7 (23.3%)	11 (36.6%)	5 (16.7%)
Prednisolone	7 (23.3%)	9 (30%)	2 (6.7%)	12 (40%)
Methyl pred	1 (3.3%)	1 (3.3%)	0	28 (93.3%)
ACTH	3 (10%)	3 (10%)	1 (3.3%)	23 (76.6%)

lasting less than 1 to 2 seconds, followed by a less intense but generally more sustained tonic contraction, which could last up to about 10 seconds. Majority of our enrolled patients in present study had 5-8 clusters per day and around 5 spasms per cluster.

EEG record in all patients revealed Hypsarrhythmia or modified Hypsarrhythmia. Hypsarrhythmia is defined as chaotic, nonrhythmic, asynchronous, disorganized, high-voltage spike activity and slow-wave activity. The hypsarrhythmic pattern is most frequent during stages 2/3 of non-rapid eye movement (non-REM) sleep and it does not occur or is greatly reduced during REM sleep.Variation of the prototype pattern (modified hypsarrythmia) include hypsarrhythmia with increased interhemispheric synchronization, asymmetrical hypsarrhythmia, hypsarrythmia with a consistent focus of abnormal discharge, hypsarrythmia with episodes ofattenuation, and hypsarrhythmia comprising primarily high voltage slow activity with little sharp-wave or spike activity.

The diagnosis of infantile spasms is made by a combination of the typical epileptic spasms with a typical EEG. Etiology of west syndrome includes focal-cortical dysplasia, other brain malformation, tuberous sclerosis complex, other neurocutaneous diseases, hypoxic ischemic encephalopathy, intraventricular hemorrhage, and other acquired injuries. In our cohort, majority of them resulted from perinatal asphyxia.

The drugs effective in west syndrome include ACTH, Vigabatrin, and Corticosteroids.[4,13-16] Owing to logistic reasons and high

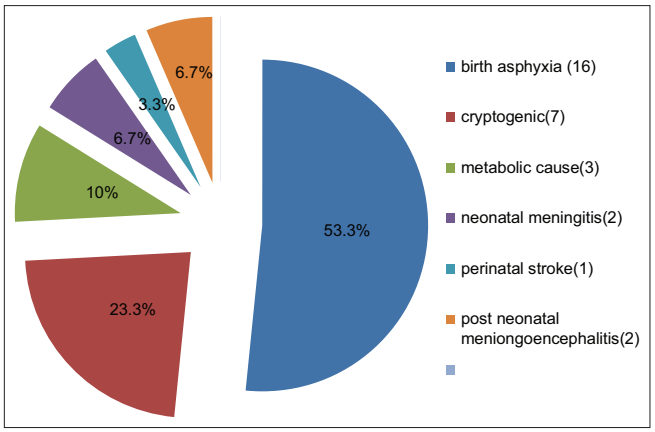

Figure 1: Figure showing etiology of children with west syndrome

cost of ACTH, majority of our enrolled patients could not afford ACTH. Evaluation of treatment effectiveness for infantile spasms includes cessation of spasms and normalization of the EEG in cryptogenic cases and a resolution of hypsarrhythmia on the EEG in symptomatic cases. More than 50% of patients in our cohort achieved spasm cessation with ACTH or steroids or Vigabatrin. However, conventional antiepileptic drugs like sodium valproate and clonazepam did not work for children with west syndrome. Hence, it is essential to reach clinical diagnosis early and treat them with oral steroids or ACTH and vigabatrin if they fail to achieve spasm cessation.

Delay in diagnosis of West syndrome was evident in majority of our enrolled patients. Parents typically bring the child to the paediatrician for episodes that may be mistaken for colic or gastroesophageal reflux.[3] Home video recordings of infant spasms may assist with the clinical evaluation. Consultation with a pediatric neurologist is warranted as early as possible if the events on video are suspicious.[2] Early diagnosis and treatment of infantile spasms is associated with potential benefits of improved neurodevelopment. Here comes the role of primary care physicians to identify and refer such patients to the higher center as early as possible so that timely treatment can be initiated.

Moreover, during the current ongoing COVID-19 pandemic, referral of IS patients may be hampered by the restrictions in travel as well as fear of exposure to the virus. One solution to this problem could be that the primary care physicians can share home video recordings of spasm events and the same can be analysed by the teleconsultation team. The role of telemedicine is being emphasized to prevent the increase in diagnostic and treatment lag.[17-19]

Conclusion

The present study concludes that main etiology for west syndrome is perinatal asphyxia. Steroids and vigabatrin achieves cessation of epileptic spasm in more than 50% of patients. Conventional antiepileptic drugs like sodium valproate and clonazepam are not effective in achieving reduction of epileptic

spasm. Timely identification, teleconsultation and referral by the primary care physicians is crucial in preventing delay in treatment and improving the neurodevelopmental outcome.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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