Infantile Spasms–A Clinical and Follow up Study

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Research Article

Abstract: Infantile spasms (IS; West syndrome) is a severe form of encephalopathy that typically affects infants younger than 2 years old. Information about infantile spasms in Indian literature is very sparse. Educating pediatricians and general pediatric health care providers about infantile spasms may be especially important as a recent Infantile Spasm working group (ISWG) of pediatric neurologists reviewed the literature and determined that early recognition of infantile spasm and prompt treatment are mandatory and may improve developmental and cognitive outcomes in some patients.

Introduction

Infantile spasms (IS; West syndrome) is a severe form of encephalopathy that typically affects infants younger than 2 years old. Infantile spasms commonly known as West syndrome following the first clinical description of the illness by Dr. WJ. West in 1841 based on his observations of his own son.[1] Although IS was first described over 160 years ago, its diagnosis, evaluation, and management continue to pose many challenges to health care professionals and affected families. The incidence of IS ranges from 2 to 3.5/10,000 live births, with onset during the first year of life in 90% of those affected.[2] The peak age of onset is between 3 and 7 months; onset after 18 months is rare, though onset up to 4 years of age has been reported.[3] IS presents with myoclonic-tonic seizures (spasms) that may be characterized by flexor, extensor, or mixed movements, a distinct electroencephalogram (EEG) pattern of hypsarrhythmia, and psychomotor delay/arrest.[4] The etiologic classification of IS includes the categories of cryptogenic and symptomatic. The cryptogenic form of IS occurs in 10% to 40% of IS patients. Within symptomatic IS, a defined underlying cause is present, usually with developmental delay at onset of spasms. The percentage of IS cases classified as symptomatic has increased over time due to improved diagnostic techniques, such as metabolic and genetic testing and neuroimaging.[5] Outcome is often poor with severe neurocognitive impairment and evolution into other types of seizures.[6] Information about infantile spasms in Indian literature is very sparse. Educating pediatricians and general pediatric health care providers about IS may be especially important as a recent IS working group (ISWG) of pediatric neurologists reviewed the literature and determined that early recognition of IS and prompt treatment are mandatory and may improve developmental and cognitive outcomes in some patients.[7] Hence the present study was aimed at reevaluating the clinical spectrum of this disease and study the response to the standard treatment. Further an attempt was made to follow –up these patients to assess the outcome as far as developmental behavior and seizure activity was concerned.

Materials and Methods

In the present study 20 cases which presented to our hospital, Krishna institute of Medical sciences, Karad between 2011-2013 were studid.11 of these cases were followed up for one and a half years. In all 20 cases a detailed history regarding time of onset and type of spasm, psychomotor development prior to the onset of spasms, any treatment taken before presenting and response to it was taken. Family history of similar convulsions or any other type of convulsions, early deaths, mental retardation or skin lesions was also elicited, details of pregnancy and birth events and any other history, suggestive of CNS infections were inquired into. A detailed clinical examination was done for all the patients. Stigmata of intrauterine infections, neurocutaneous markers and dysmorphic features were looked for. In 18 cases EEG and CT scan of brain both were done. All the 20 cases were subjected to neuroophthalmic examination and the urine was screened for inborn errors of metabolism. The diagnosis was essentially made by observing the type of spasm and cases were classified into symptomatic or cryptogenic depending on the presence or absence of abnormal EEG, CT findings and psychomotor retardation. Patients were treated with anti-epileptic drugs like clonazepam, sodium valproate and phenobarbitone along with ACTH /steroid and high dose Vit B6. 11 patients were followed up for one and a half years, 4 patients for 1 year and the remaining for 4-6 months.1 patietn was lost during follow-up. During the follow up, response to treatment and evaluation of psychomotor development was done. All of the data was reviewed and analyzed.

Observations and Results

20 patients were enrolled in our study. The age of onset in all of the 20 cases studied was less than 1 year, with

maximum number of patients (65 %) falling in the 3-8 months group. The mean age of onset was 6 months. There was a preponderance of males to females in the ratio 2.3:1. All 20 cases in our study were classified as symptomatic with prenatal causes accounting for 60 %. None of the patients in the study were under the cryptogenic group. Table 1 showing the various etiologies of IS in the patients.

Table 1: Showing the various etiologies in symptomatic infantile spasm

Sr. No.	Etiology	No of cases (n=20)	Percentage
	Prenatal	12	60%
1.	Intrauterine infection	7	35 %
2.	Brain malformation	2	10 %
3.	Tuberous Sclerosis	2	10 %
4.	Hypomelanosis of Ito	1	5 %
	Perinatal		
1.	Birth asphyxia	6	30 %
	Postnatal		
1.	Post encephalitis	2	10 %

The only external congenital anomaly seen was micrcephaly in 4 patients (20 %). Hypomelanotic ash-leaf naevi were seen in the 2 cases diagnosed to have tuberous sclerosis. Hypomelanotic linear nevi were seen in 1 patient with hypomelanosis of Ito. Flexor type of spasms were seen in 14 (70 %) and was the commonest, followed by mixed in 4 (20 %) and extensor in 2 (10 %) of the patients. Only 1 patient had associated partial seizures. While abnormal psychomotor development was seen in 16 (75 %) prior to the onset of seizures. Regression of milestones was observed in 8 (40 %) of the patients after the onset of seizures. Neurological deficit seen were hypotonia in 6 cases and cerebral palsy in 1 case. EEG was done in 18 cases. Only 4 (20 %) of the patients had normal EEG recordings while 14 (80 %) had abnormalities. Table 2 presents the EEG findings in the patients with IS.

Table 2: EEG findings in the patients with Infantile spasms..

Sr. No.	EEG findings	No of cases	Percentage
1	Classical hypsarrhythmia	6	30
2.	Modified hypsarrhythmia	1	5
3.	Generalised seizure discharges	7	35
4.	Normal EEG	4	20
	Total	**18**	**100**

None of the cases showed inborn errors of metabolism or abnormal fundoscopy. CT scan study of the brain was done in 18 of the cases.83.3 % of the cases showed abnormalities on CT study. Only 3 cases (16.7 %) had normal CT scans. Table 3 demonstrates the CT findings of the patients

Table 3: CT findings in patients with infantile spasm

Sr. No.	CT diagnosis	No of Cases	Percentage
1	Brainstem and cerebral cortical atrophy	1	55 %
2	Diffuse cortical and subcortical atrophy	34	16.7%
3	Diffuse cerebral atrophy	1	22.2%
4	Cerebral and cerebellar atrophy	2	5.5%
5	Tuberous scelosis	1	11.1%
6	Cerebellar, cerebral and brainstem atrophy	1	5.5 %
7	Infarct of middle cerebral atrophy territory with cerebral atrophy	1	5.5%
8	Partial agenesis of corpus callosum	1	5.5%
9	Dysgenesis of corpus callosum with Dandy Walker malformation	1	5.5%
10	CT normal	3	16.7%
	Total	**46**	**149%**

Of the 12 patients who received the first course of Inj ACTH only 2 responded,8 out of the10 remaining patients received a second course, at the end of which only 4 responded.8 out of the 20 patients received only anti-epileptic drug, 3 of whom responded. Follow –up results in our study showed that1 child had a relapse, 1 developed tonic-clonic seizure and 4 remained refractory to treatment. Outcome in these children was poor as all 20 developed mental retardation. 8 showed autistic features, 4 became hyperkinetic, 2 showed mild improvements in mental status and 1 child developed generalized tonic-clonic seizures.

Discussion

Infantile spasms is an age specific generalized epileptic syndrome. In 90 %of the cases the spasms appear in the first year of life with maximum frequency occurring between 3 and 7 months. Though onset up to 4 years of age has been reported. [3] In this study too all 20 children presented with spasms in the 1st year of life. The mean age of onset of spasms was 6 months which compares well with other studies.[3, 10.] 11 children had onset of spasm before 6 months points to a prenatal etiology with diffuse brain damage or malformations of the brain. [9] The prognosis is poor in this group. Infantile spasms is known to occur more frequently in males. A preponderance of males over females up to 2:1 has been reported by some authors. We noticed a similar preponderance in our study.[9, 10] Patients are traditionally separated into two categories, Symptomatic and cryptogenic. with newer imaging techniques like CT,MRI,SPECT the proportion of symptomatic group has increased while that of cryptogenic group has decreased (30 to 10 %).[9,10] It is interesting to note that in this study all cases came under the symptomatic group. Evidence of brain damage, either clinical and /or radiological was found in all the 20 cases. The etiological factors in the symptomatic group could be prenatal, perinatal or postnatal. Prenatal causes represent 50 % of the cases, brain malformations, tuberous sclerosis and intrauterine infections being the common causes.[11, 12] in the present study prenatal causes constituted 60 % of the cases with brain malformations representing 10 %, tuberous sclerosis (10 %) and probable intrauterine infections in 35 % of the cases. Thus intrauterine infections constituted the major group in this study. With proper antenatal care and good hygiene the percentage of this group can be brought down. In single gene defect disorders like tuberous sclerosis and hypomelanosis of Ito, recognition of the disorder in family members help in proper genetic counseling. In this study birth asphyxia was the only perinatal cause for infantile spasms amounting to 30% of the cases. With better intrapartum care this figure can be brought down. Flexor type of spasms is considered to be the most characteristic type and represents 34-42 % of the cases.[10, 11]. Our findings were similar as majority of the children (70 5) had flexor spasm in our study. A delay in psychomotor retardation with the onset of spasm is seen in 65-85% [9.10.13]of the cases. Psychomotor development was abnormal prior to onset of spasm I 80 % of the cases. The recommended approach to EEG evaluation, during the diagnostic evaluation and during follow-up to determine treatment effectiveness, is an overnight inpatient 24-hour video EEG to capture both hypsarrhythmia and spasms. It will allow the exclusion of other movements that may mimic IS and allow the investigation of other seizure types that may be occurring. If Hypsarrythmia in EEG studies is seen in 50-60 % of the cases and is not the sole EEG pattern associate with infantile spasm.[10, 11] in the present study only 30 % showed classical hypsarrthymia. Our results are comparable with other studies. With the advent of neuroimaging techniques more and more cases with brain abnormalities are being detected. It is therefore advisable that all children presenting with IS undergo CT scan of the brain. Recently, an IS consensus group reviewed the most recent practice guidelines from the American Academy of Neurology and the Child Neurology Society for the medical treatment of Infantile spasms and outlined goals for improving outcomes in IS. The IS consensus group goals for improving IS outcomes include early detection and diagnosis of IS, short-duration treatment with first-line therapy (agreed upon as either ACTH or vigabatrin), timely EEG evaluation of treatment effectiveness, and, if indicated, prompt treatment modification. [14] Short term effects of ACTH treatment on spasms and EEG abnormalities in the first 2 weeks is seen in 50 -8 0% of cases.[10] the present study compares well with this observation. The prognosis for mental outcome is poor in infantile spasm. For the symptomatic group it is uniformly bad. In our study all cases belonged to the symptomatic group, 80% had severe mental retardation and 20 % mild to moderate mental retardation.

Conclusion

IS imposes a significant ongoing challenge to the child's family and caregivers, as well as to health care professionals. Early detection and referral to a pediatric neurologist for clinical evaluation and prompt effective treatment is strongly recommended as it may improve prognosis. Thus, the goal of therapy is to achieve control as soon as possible, especially for children who may have the potential for normal intellectual development.

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