Journal of Health Science Research, *Vol 7(2), 2022, 7-11*
ISSN (Online) : 2456-2688
DOI: https://doi.org/10.7324/jhsr.2022.722

Retrospective Evaluation of Patients with Infantile Spasm Diagnosis

Mahmut Aslan[1]*, Serdal Gungor[2]

[1]Department of Pediatric Neurology, VM Medical Park Mersin Hospital, Mersin, Turkey, [2]Department of Pediatric Neurology, Faculty of Medicine, Inonu University, Malatya, Turkey
Email: dr_mahmut_21@hotmail.com

Abstract

Introduction: Infantile spasm (IS) (West Syndrome) is an age-dependent epileptic encephalopathy clinic specific to the first 2 years of life. IS is the most known epileptic syndrome of infancy with typical seizures in the form of spasm, psychomotor retardation, and hypsarrhythmia on electroencephalography. Typical spasms are in the form of flexor/extensor contractions that last for about 2–5 s, which usually symmetrically involves all muscle groups in the body. **Materials and Methods:** In this study, the data of patients, who were followed up with the diagnosis of "infantile spasm" in the Pediatric Neurology Clinic of Mersin City Training and Research Hospital between 2020 and 2022, were retrospectively analyzed. Demographic characteristics, clinical, EEG, and MRI findings of the patients were analyzed. **Results:** Eighteen patients were included in the study. Ten (55.5%) of our patients were male and 8 (44.5%) were female. The mean age of patients was 7.22 ± 6.44 years. Eleven (61.1%) patients were in the symptomatic group, 5 (27.7%) patients were in the cryptogenic group, and 2 (11.1%) patients were in the idiopathic group. At the time of diagnosis, there were flexor spasm, extensor spasm, mixt spasm, tonic seizure, myoclonic seizure in 5 (27.7%), 4 (22.2%), 4 (22.2%), 3 (16.6%), and 2 (11.1%) patients, respectively. Hypsarrhythmia, suppression-burst pattern, focal epileptic abnormality, and generalized epileptic abnormality were observed in 8 (44.4%), 4 (22.2%), 3 (16.6%), and 3 (16.6%) patients, respectively. Of the 14 patients who were first diagnosed, 8 (57.1%) were treated with ACTH, 4 (28.6%) with phenobarbital, and 2 (14.3%) with vigabatrin. **Conclusion:** IS is an important age-related encephalopathy with severe neurological sequelae, resistant seizures, and high morbidity and mortality all over the world and in our country. Spasms cause further damage to the central nervous system, which continues to develop. For this reason, a positive contribution can be made in terms of prognosis with the early and appropriate treatment.

Keywords: Infantile spasm, Diagnosis, Treatment

1. Introduction

Infantile spasm (IS) (West Syndrome) is an age-dependent epileptic encephalopathy clinic specific to the first 2 years of life. It was first described by Dr. West in 1841 after observing spasms in his son. The term infantile spasm (IC) is used to describe both the seizure type and the epileptic syndrome. IS is the most known epileptic syndrome of infancy with typical seizures in the form of spasm, psychomotor retardation, and hypsarrhythmia on electroencephalography[1]. IS occurs most frequently between the 4th and 8th months. Its incidence has been reported to be approximately 1 in 3000 live births[2]. It is slightly more common in male patients. Its pathophysiology is not yet clear. Typical spasms are in the form of flexor/extensor contractions that last for about 2–5 s, which usually symmetrically involves all muscle groups in the body. Spasms are usually seen in series at intervals of 5–30 s. Ongoing spasms have serious effects on the developing brain, causing treatment-resistant epilepsy, motor and mental retardation, sensory, and psychiatric problems. The etiology of IS may be due to various

*Author for correspondence

How to cite this article: Aslan M, Gungor S. Retrospective Evaluation of Patients with Infantile Spasm Diagnosis. J Health Sci Res 2022;7(2):7-11.

reasons. It is divided into three groups according to the etiology as cryptogenic, idiopathic, and symptomatic. Approximately 75% of the patients are in the symptomatic group. While prenatal causes are the most common etiology in developed countries, perinatal and postnatal causes are more common in developing countries. While the underlying cause could not be revealed in the cryptogenic IS group, the psychomotor development of the patients before the seizure onset is normal in idiopathic IS[1,3]. Although the course of the disease varies according to the underlying cause, varying degrees of cognitive impairment develop in approximately 80% of patients[3]. A better clinical course is observed in patients in the idiopathic group. Apart from typical spasms, other seizure types can be seen in some of the patients. Lennox–Gastaut Syndrome with tonic seizures may develop with advancing age in some patients. Delay in diagnosis or treatment is one of the most important factors that negatively affect the psychomotor development[3]. Although there is no standard recommendation in the treatment of IS, corticosteroids and vigabatrin are preferred as the first-line choice in the treatment of IS[4].

2. Materials and Methods

In this study, the data of patients, who were followed up with the diagnosis of "infantile spasm" in the Pediatric Neurology Clinic of Mersin City Training and Research Hospital between 2020 and 2022, were retrospectively analyzed. Gender, detailed prenatal, natal, and postnatal histories, systemic and neurological examinations, findings accompanying spasms, and neuromotor developmental stages before spasms were recorded. The duration and frequency of seizures, the presence of seizures before the spasm, and the development of other seizure types after IS were examined. Types of spasm were examined in three main groups as flexor, extensor, and mixed (flexor-extensor). Brain MRI and/or CT, EEG, and laboratory findings of the patients were examined. Basic hematological and biochemical parameters, metabolic disease scans, cerebrospinal fluid examinations, and genetic test results were also recorded.

Sleep and wakefulness EEG examinations were performed with a 16-channel electroencephalogram device according to the international 10–20 system. Basal activity in EEG was classified into three groups as irregularity and slowing down, asymmetry, and normal. The EEG findings of the patients were analyzed in four main groups: Hypsarrhythmia, focal epileptic activity, generalized epileptic activity, and suppression burst pattern. For the diagnosis of IS, the triad, consisting of typical seizures, pause/regression in mental and motor development, and characteristic EEG findings, was used. The presence of at least two findings was sufficient for diagnosis[5,6]. The patients were divided into three main groups as idiopathic, cryptogenic, and symptomatic in terms of etiology. Patients with no neurological disorder or etiologic cause, leading to IS, and patients with normal neuromotor development before the onset of symptoms, are considered idiopathic IS group. On the other hand, patients with suspected but unclear etiology were included in the cryptogenic IS group and patients with a definite etiological cause were considered as symptomatic IS group[7].

3. Results

Eighteen patients were included in the study. Ten (55.5%) of our patients were male and 8 (44.5%) were female. The age range of the patients was 1–24 months. The mean age of patients was 7.22 ± 6.44 years. Fourteen of our patients (77.7%) were diagnosed for the 1st time, the other 4 (22.3%) had been diagnosed before. At the first examination, the neurological examination of 12 (66.6%) patients was abnormal and 6 (33.4%) patients were normal. The follow-up period of our patients was 3–14 months, the mean follow-up duration was 8.61 ± 2.87 months (Table 1). Seizures of 16 (88.8%) patients were started before 1 year of age. Four (22.2%) patients had other seizures before IS. Eleven (61.1%) patients were in the symptomatic group, 5 (27.7%) patients were in the cryptogenic group, and 2 (11.1%) patients were in the idiopathic group. In the symptomatic group that includes 11 patients, five patients, two patients, two patients, one patient, and one patient were followed up with cerebral palsy (27.7%), CNS developmental anomaly (11.1%), tuberous sclerosis (11.1%), Down syndrome (5.55%), and non-ketotic hyperglycinemia (5.55%), respectively (Table 2). Cranial MRI was taken in all our patients. Cranial MRI findings of 5 (27.7%) patients were normal. Of these five patients, two were symptomatic, two were idiopathic, and one were cryptogenic. Cranial MRI findings of the other 13 (72.3%) patients were abnormal according to their etiology.

At the time of diagnosis, there were flexor spasm, extensor spasm, mixt spasm, tonic seizure, myoclonic

seizure in 5 (27.7%), 4 (22.2%), 4 (22.2%), 3 (16.6%), and 2 (11.1%) patients, respectively. We performed EEG for all our patients at the first examination. Basal irregularities were observed in 13 (72.2%) patients. Basal rhythm was normal in 4 (22.2%) patients, and asymmetrical basal rhythm was observed in 1 (5.5%) patient. Hypsarrhythmia, suppression-burst pattern, focal epileptic abnormality, and generalized epileptic abnormality were observed in 8 (44.4%), 4 (22.2%), 3 (16.6%), and 3 (16.6%) patients, respectively (Table 3). Of the 14 patients who were first diagnosed, 8 (57.1%) were treated with ACTH, 4 (28.6%) with phenobarbital, and 2 (14.3%) with vigabatrin. We performed a control EEG 3 months later in 12 of the 14 patients with whom we started the new treatment, and all of the patients showed improvement compared to the previous traces. At the same time, seizures ceased completely in 8 (66.6%) of 12 patients, and more than 50% reduction in seizures was observed in 4 (33.3%) patients.

Table 1. Demographic characteristics of patients

Age	
Mean (months)	7.22±6.44
Range (months)	1–24
Gender	
Male (*n*/%)	10 (55.5)
Female (*n*/%)	8 (44.5)
Neurological examination	
Normal (n/%)	6 (33.4)
Abnormal (n/%)	12 (66.6)
Follow-up duration	
Mean (months)	8.61±2.87
Range (months)	3–14

Table 2. Etiological classification of patients

Classification	**(*n*/%)**
Symptomatic	11 (61.1)
Cerebral palsy	5 (27.7)
Central nervous system developmental anomaly	2 (11.1)
Tuberous sclerosis	2 (11.1)
Down syndrome	1 (5.5)
Non-ketotic hyperglycinemia	1 (5.5)
Cryptogenic	5 (27.7)
Idiopathic	2 (11.1)

Table 3. Seizure types and EEG findings of the patients

Type of seizure (*n*/%)	
Flexor spasm	5 (27.7)
Extensor spasm	4 (22.2)
Mix	4 (22.2)
Tonic seizure	3 (16.6)
Myoclonic seizure	2 (11.1)
Basal rhythm in EEG (*n*/%)	
Irregularity in basal rhythm	13 (72.2)
Asymmetry in basal rhythm	1 (5.5)
Normal	4 (22.2)
EEG findings (*n*/%)	
Hypsarrhythmia	8 (44.4)
Suppression-burst	4 (22.2)
Focal epileptic abnormality	3 (16.6)
Generalized epileptic abnormality	3 (16.6)

3.1. Statistical analysis

The IBM SPSS Statistics 22 (IBM SPSS, Turkey) software program was used for the statistical analysis of the study results. In the assessment of the study data, descriptive statistical methods (average, standard deviation, and frequency) and the Chi-square test, the Fisher Freeman Halton test, and Fisher's Exact test were used to compare the qualitative data.

4. Discussion

The incidence of IS is similar all around the world and has been reported as 1/3000[2]. Although there seems to be no difference between male and female patients in terms of the incidence of IS, it is slightly more common in male patients. Male/female ratio is 1.2/1[8]. In our study, the male/female ratio was found to be 1.25. Although spasms usually start between the 4th and 8th months of life, most commonly begins in the 6th month[9]. In our study, seizures started before the age of 1 in 88.8% of the patients. While the most common prenatal causes such as developmental malformations, genetic and metabolic diseases are found in the etiology of IS in developed countries; perinatal and postnatal causes, especially hypoxic birth, are most common in developing countries[10,11]. In our study, the most common group was symptomatic (61.1%) and the most common etiology was cerebral palsy (27.7%). Down syndrome is the most common chromosomal abnormality in symptomatic etiology. In a study, it was reported that IS was common in Down syndrome cases and had a later onset compared to the cryptogenic group[12]. In our study, Down syndrome was detected in one patient with chromosomal anomaly. The association between more than 25 metabolic disorders and IS was reported in the literature[13]. One of our cases was being followed up with non-ketotic hyperglycinemia.

Three main types of motor spasm have been described in patients with IS. These types include flexor, extensor, and mixed spasms (flexor-extensor). Mixed spasm was reported most frequently (42–50%) in different series, followed by flexor spasm with a rate of 32–42% and extensor spasm with a rate of 19–23%, respectively[14]. In a study of Yilmaz, flexor spasm was reported in 79% of the cases, extensor spasm in 16%, and mixed spasm in the remainder[15]. In our study, the rates of spasm were consistent with the literature. Other motor seizure types apart from spasms with focal onset or generalized onset may precede or accompany spasms in 12–42% of patients with IS[16]. In our study, there were other seizure types before spasm at a rate of 22.2%.

The classical interictal EEG finding in IS is hypsarrhythmia and is among the diagnostic criteria. Knupp *et al*. reported classical hypsarrhythmia in 47% of patients in their multicenter, prospective study[17]. In our study, a hypsarrhythmia pattern was observed in 44.4% of the patients. Although many studies have been conducted on the treatment of IS, a standard treatment approach has not been established yet. First-line treatments can be counted as ACTH, vigabatrin, prednisolone, and pyridoxine. Studies have also been conducted on the ketogenic diet as an alternative treatment option[18]. In our study, 8 (57.1%), 4 (28.6%), and 2 (14.3%) of the 14 patients who were first diagnosed were treated with ACTH, phenobarbital, and vigabatrin, respectively. Among 14 patients with whom we started new treatment, improvement in EEG was observed in 12, seizures stopped completely in 8 (66.6%), and seizures decreased more than 50% in 4 (33.3%) patients.

5. Conclusion

IS is an important age-related encephalopathy with severe neurological sequelae, resistant seizures, and high morbidity and mortality all over the world and in our country. Etiology is one of the most important factors that determine the prognosis. Spasms cause more damage to the central nervous system, which continues to develop, and a positive contribution can be made to prognosis with the early and appropriate treatment.

6. References

1. Hrachovy RA, Frost JD. Infantile epileptic encephalopathy with hypsarrhytmia (infantile spasms/West syndrome). J Clin Neurophysiol 2003;6:408-25.
2. Swaiman KF, Ashwal S, Ferriero DM. Swaiman's Pediatric Neurology. 5th ed. Netherlands: Elsevier Health Sciences; 2012. p. 781-9.
3. Ohtsuka Y, Kobayashi K, Ogino T, Oka E. Spasms in clusters in epilepsies other than typical West syndrome. Brain Dev 2001;23:473-81.
4. Eling P, Renier WO, Pomper J, Baram TZ. The mystery of the Doctor's son, or the riddle of West syndrome. Neurology 2002;58:953-5.
5. Commission on classification and terminology of the

International League against Epilepsy. Proposal for revised classification of epilepsies and epileptic syndromes. Epilepsia 1989;30:389-99.
6. Engel J. Report of the ILAE classification core group. Epilepsia 2006;47:1558-68.
7. Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J, Guilhoto L, *et al*. ILAE classification of the epilepsies: Position paper of the ILAE commission for classification and terminology. Epilepsia 2017;58:512-21.
8. Apak S. Konvülziyonlar. İn: Neyzi O, Ertuğrul T, editor. Pediyatri 4. Baskı, İstanbul: Nobel Tıp Kitabevi; 2010. p. 1678.
9. Hrachovy RA, Frost JD Jr. Severe encephalopathic epilepsy infants: İnfantile spasms (West syndrome). In: Pellock JM, Bourgeois BF, Dodson WE, editors. Pediatric Epilepsy: Diagnosis and Therapy. 3rd ed. New York: Demos; 2008. p. 249-68.
10. Osborne JP, Lux AL, Edwards SW, Hancock E, Johnson AL, Kennedy CR, *et al*. The underlying etiology of infantile spasms (West syndrome): Information from the United Kingdom infantile spasms study (UKISS) on contemporary causes and their classification. Epilepsia 2010;51:2168-74.
11. İbrahim S, Gulab S, Ishaque S, Saleem T. Clinical profile and treatment of infantile spasms using vigabatrin and ACTH-a developing country perspective. BMC Pediatr 2010;10:1.
12. Marandi E, Kumar A, Kaddurah A, Chugani H. Infantile Spasms in Children with Down Syndrome: Detroit Experience. J Int Child Neurol Assoc 2017;1:116.
13. Glaze DG, Nordli DR Jr., Dashe JF. Etiology and pathogenesis of infantile spasms. United States: UpToDate; 2017.
14. Glauser TA, Kao A. Infantile Spasm (West Syndrome). United States: Medscape; 2017.
15. Yılmaz Ü. West sendromu: Klinik özellikleri ve kısa dönem prognozu. J Clin Exp Investig 2014;5:1.
16. Özmen M. Yenidoğan ve Bebeklik Dönemi Epilepsi Sendromları. In: Gökçay E, Sönmez FM, Topaloğlu H, Tekgül H, Gürer YK, editor. Türkiye Çocuk Nöroloji Derneği Çocuk Nörolojisi. Ankara: Anıl Grup Matbaacılık; 2010. p. 289-92.
17. Knupp KG, Leister E, Coryell J, Nickels KC, Ryan N, Juarez-Colunga E, *et al*. Response to second treatment after initial failed treatment in a multicenter prospective infantile spasms cohort. Epilepsia 2016;57:1834-42.
18. Taghdiri MM, Nemati H. Infantile spasm: A review article. Iran J Child Neurol 2014;8:1.