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Clinical Profile of Infants with Hypsarrhythmia

Wael Hayel Khreisat
Queen Rania hospital for children, King Hussein medical center, Royal medical services, Amman. Jordan

Original paper
SUMMARY
Objective: The present study was done in order to obtain a baseline profile of infantile spasms and associated neurological disorders. **Patient and methods**:. The study included 50 patients with infantile spasm in Queen Rania Hospital for children in Jordan. The following data were obtained: sex, age at onset of spasms, details of seizure, family history of epilepsy, significant pre-/peri/post-natal insults, Electroencephalography and detailed neuro imaging evaluation , detailed neurological, neuro developmental ,assessment were done by. Broad categories of possible etiologies were used the results were recorded for further study. R**esults**: Age of onset of infantile spasms ranged from 1month to 1 year and 6 months , (mean 4.8 months). The mean time of presentation was 9.4 months . A male preponderance was noted (74 %). flexor spasms (52%) was the commonest . Other types of seizures also accompanied infantile spasm in 44% children . (84%) were born of normal delivery, History of birth asphyxia was obtained in 48%, 3 (6%) had positive family history Developmental delay was recognized prior to onset of spasms in 52%, microcephaly was the commonest associated problem, Imaging studies of the brain revealed abnormality in 18 patients. 78% patients were classified as symptomatic and 22 % as cryptogenic. **Conclusion**: the pattern of infantile spasm in our country do not differ from that of developed countries, further researches is required to prevent both chronic epilepsy and psychomotor retardation and .preventive measurement to prevent birth asphyxia is recommended
Key words: infantile spasm, epilepsy, hypsarrhythmia.

1. INRODUCTION

Infantile spasms represent a seizure disorder with unique clinical and electroencephalographic (hypsarrhythmia) features and a poor prognosis including chronic intractable epilepsy and psychomotor retardation, incidence is considered to be 0 16-0-42 per 1000 live births (1).

Infantile spasms (IS) is "one of the catastrophic childhood epilepsies" due to the difficulty of controlling seizures and the association with mental retardation. Early diagnosis with a careful diagnostic evaluation and proper therapy can obtain a normal development or a much improved situation in some cases (2)- This spasm is also referred in literature as massive spasms, Salaam tics, infantile myoclonic seizures, It has been classified in the category of generalized seizures with specific electroencephalographic characteristics. Focal seizures as well as focal lesions can also be present (3).

Epileptic spasms are define as seizures characterized by brief axial contraction, in flexion, extension or mixed, symmetric or asymmetric, lasting from a fraction of a second to 1-2 s (4) it occurs almost exclusively during the first year of life, mostly between four and seven months of age. It may be present in clusters do not appear generally after one to two years of age (*5*) although late onset up to seven to eight years of age has been reported in rare cases (*6*). Although the epileptogenic mechanisms of infantile spasms is not well understood, an etiologic diagnosis can be identified in more than 70% of cases (7), which may lead to a specific therapy that can have a dramatic influence on the outcome of the patient

The present study was done to obtain a baseline profile of infantile spasms who are of regular visit at pediatric neurology clinic or admitted to neurological department of Queen Rania AL-Abdullah hospital for children. Focused on age of onset, associated neurological deficits electroencephalography findings, imaging and various therapeutic aspects.

2. PATIENTS AND METHODS

Subjects included in this study were infants suffering infantile spasm, who attended pediatric neurology clinic or from the in-patient services of neurology department Queen Rania Hospital for Children in Jordan. We evaluated 50 patients diagnosed as having IS, with electroencephalographic features of hypsarrhythmia or modified hypsarrhythmia. the following data were collected: sex, age at onset of spasms, age at presentation to our center details of seizure, mode of delivary, family history of epilepsy (1st and 2nd degree relatives), significant pre-/peri/post-natal insults, lead- time to clinical diagnosis (defined as the time from the initial observation of spasms to the clinical diagnosis).

Electroencephalography and detailed neuroimaging computerized tomography (CT) or magnetic resonance imaging (MRI) evaluation was done and a detailed neurological, medical, neuro developmental, assessment was done by pediatric neurologist. Broad categories of possible etiologies were used. The diagnosis of birth asphyxia required the documentation of moderate to severe encephalopathy. Brain atro-

phy was diagnosed when ventricular dilatation with widening of the sulci is present.

Acquired brain insult included patients with birth asphyxia, intracranial hemorrhagie, trauma, vascular etiology, toxins (kernicterus) and infectious or immunologic causes.

An infectious etiology required objective cerebrospinal fluid finding or immunological evidence of intrauterine infection.

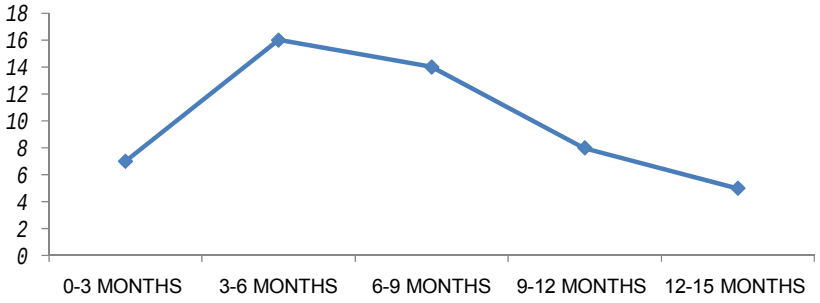

Figure 1. Distribution of infantile spasm according to age of onset

Etiology	No	Percent
Cryptogenic	11	22%
Symptomatic	39	74%
CNS infection	3	6%
Birth asphyxia	24	48%
Neuro metabolic	2	4%
Birth trauma	2	4%
Congenital anomaly of the brain	6	12%
Neuro coetaneous	1	2%
TORCH	1	2%

Table 1. The etiology of infantile spasm

Characteristic	no	Percent
Male	37	74%
Female	13	26%
Norma vaginal	42	84%
Cesserian section	5	10%
Vacuum	1	2%
Forceps	2	4%
Positive Family history	3	6%
Seizure pattern		
Flexor	21	42%
Extensor	11	22%
Mixed	18	36%
Asymmetrical	5	10%
Number of spasm / day		
5	12	24%
5-10	18	36%
More than 10	20	40%
Associated seizure	22	44%
Generalized	10	20%
Focal	8	16%
Others	4	8%
Symptomatic	39	78%
Cryptogenic	11	22%
Reponses to treatment		
Complete	15	30%
Transient	35	70%
Radiological finding		
Normal	27	54%
Abnormal	18	36%

Table 2. Clinical profile of studied cases

For all patients we did complete blood count, liver function tests, kidney function tests, serum uric acid, screen for intrauterine infection (TORCHs titer) and thyroid function tests. Specific laboratory tests like screening for inborn error of metabolism, chromosomal analysis were done when needed. Neuroimaging tomography (CT) or magnetic resonance imaging (MRI) or both were done for more than 90% of patients. Magnetic resonance imaging was the preferred investigation but those who could not tolerate it because of their medical condition; a computerized tomography scan was done instead.

Patients had their Electroencephalography which was carried out at the Neurophysiologic Department and the neuroimmaging, results were recorded for further study. The response to treatment was classified as follows: complete (no relapse observed after last spasm for the entire follow-up period), transient (relapse of spasms after at least a 7-day spasm free period) and no response

Infantile spasm was classified into symptomatic and cryptogenic groups. Cryptogenic group is characterized by (1) normal pregnancy and birth, (2) normal development before the onset of spasm and absence of neurological abnormalities at the onset of spasm, (3) absence of any other types of seizure before the onset of spasm, and (4) normal laboratory, computerized tomography (CT) or magnetic resonance imaging (MRI) findings at onset (6).

3. RESULTS

Age of onset of infantile spasm ranged from 1month to 1 year and 6months, (mean 4.8 months). The age at the time of presentation ranged from 1.5 months to 4.5 years (mean 9.4 months). Distribution of epileptic children according to age of onset Figure 1. A male preponderance was noted (74 %). Clinical seizure pattern was typical in most with majority presenting with flexor spasms (52%). Most of them more than 10 times per a day. Other types of seizures also accompanied IS in 44% children these were focal (16%), generalized tonic clonic (20%) and others (8%). In 96% of cases infantile spasm where classically maximum on awakening from sleep. Most children (84%) were born of normal\ delivery, 10% by caesarean section and 6% by forceps or vacuum; 96% were term babies; History of birth asphyxia was obtained in 48%. The etiology of infantile spasm in this study showen in Table 1. Among the 50 patients, 3 (6%) had a first- degree relative

Developmental delay was recognized prior to onset of spasms in 52% and after the onset of spasms in 34%. Associated problems like microcephaly, visual abnormalities and hearing problems were shown in Table 3.

Imaging studies of the brain - computerized tomography (CT) or magnetic resonance imaging (MRI)) were done in 45 patients and revealed abnormality in 18 patients. The findings are shown in Table 4. and 78% patients were classified as symptomatic and 22 %as cryptogenic.

Neurological disorder	No	Percent
Microcephaly	26	52%
Hypotonic	12	24%
Spastic	18	36%
Visual defect	15	30%
Deafness	12	24%
Dysmorphic	2	4%
Developmental delayed	26	52%
Developmental regression	17	34%
Hypo pigmentation	2	2%

Table 3. Associated neurological disorders

FINDING	NO	PERCENT
NORMAL	18	36%
Brain ct scan	5	10%
Brain mri	13	26%
Cerebral atrophy	8	16%
Stroke	4	8%
Malformation	3	6%
White matter disorders	2	4%
Calcifications	1	2%

Table 4. Brain imaging finding in patient with IS

4. DISCUSSION

On the basis of records from pediatric neurology clinic and department, this study has provided important baseline information on the etiology, clinical presentation and associated developmental problems with infantile spasm.

Infantile spasm onset in our series occurs mainly in infancy with the mean age of 3.4 months although it was reported that the peak of age of onset is in the middle of the first year of life, onset may be delayed to after the age of 1 year in 2% of the patients, from the newborn period to the age of 4 years (***8***). The reason for the late onset in some patients appears clearly when the patient has a postnatal lesion, but is less clear when the patient has a congenital brain lesion. In addition, the location of the lesion in the cortex determines in part the age of onset, and lesions affecting the posterior half of the brain often generate earlier onset of seizures than those affecting the anterior half.

Although many studies have reported a male preponderance of infantile spasms as seen in the present study male to female ratio 2.8 to 1, this figure is highly variable.. It has been suggested that the observed male predominance observed in some studies may simply reflect a larger proportion of male patients in the referral population (9).

Spasms can be of the flexor or extension or mixed flexor extension types of the neck, trunk, arms and legs (10), among the clinically observed types of spasms, flexor types were most frequent which is similar to other reports (11). most infants with this disorder have more than one type of spasm ranged from 92 % to 100 % (12) while in this study it forms 44% .

Seizures may occur before the onset of infantile spasms (13). Approximately one third to one half of patients with epileptic spasms have other seizure types preceding or accompanying the onset of the spasms (13). In this studied group, 36 % had other types of seizures prior to the onset of infantile spasms with focal or generalized seizure, delay in giving specific diagnosis and treatment occurred which might be one of the contributing factors for poor outcomes in some patients.

Developmental delay was recognized prior to onset of spasms in 52% and after the onset of spasms in 34 %. Developmental delay predates the onset of spasms in about 70% of children, disappearance of social smile, loss of visual attention or autistic withdrawal are often observed with the onset of spasms (14).)

Concerning the genetics of infantile spasms, cogent information is sparse. The percentage of cases having a positive family history for epilepsy of any type has ranged from none (15) to 33% (16). However, when only larger series (studies with more than 100 patients) are analyzed, the range is much lower: 1% to 7% (11) while in the prsente study it showed 3%.

Although the list of specific diseases potentially causing infantile spasms is enormous, diagnostic evaluation does not necessarily have to be exhaustive. A recent study examined the effectiveness of using a staged diagnostic evaluation for infantile spasms (17).

It is therefore important to establish a protocol management of patients in order to obtain a precise etiology, The reported percentage of total infantile spasms cases classified as symptomatic has risen over the years as etiologies have become identified more readily. In the early 1980s, most studies found identified symptomatic etiologies in approximately 45-60% of patients (18). As seen in our study more recent studies have consistently classified 70-80% of patients into the symptomatic group (8).

This trend can be attributed mostly to the improved sensitivity of diagnostic testing, especially neuroimaging studies. Magnetic resonance imaging has a higher sensitivity for detecting focal abnormalities in West syndrome patients compared with computed tomography (19).

Within the symptomatic group the etiologies for infantile spasms have traditionally been divided into prenatal, perinatal, and postnatal causes. As seen in recent study most studies identify prenatal etiologies as the most common, accounting for almost 50% of symptomatic cases (20) which is consistent with our study.

Regarding the neurological comorbidities associated with infantile spasm microcephaly was the commonest associated finding present in almost 50% of our cases. In other studies also this has been a significant clinical abnormality, it has been suggested that it denotes the involvement of brain parenchyma even before the onset of infantile spasm (21). Visual impairment has been found in approximately 25% of cases (21) which is closed to our finding

A study on neuroradiological aspects of infantile spasm in patients also reported normal computerized tomography (CT) in 17% and normal magnetic resonance imaging (MRI) in 18% (22), while in our study it was abnormal in3 6 %. Magnetic resonance imaging (MRI) is more informative than tomogra-

phy (CT) as it demonstrates focal cortical and subcortical lesions and white matter lesions better and may also help in prognostication of motor outcome in these cases (23).

Prognosis depends more on the cause than on treatment. Unfavourable prognostic factors include symptomaticity, early onset (younger than 3 months), pre-existing seizures other than spasms, asymmetric electroencephalographic, And relapse after initial response to treatment (24). Good prognostic indicators include cryptogenicity, normal brain MRI, typical hypsarrhythmia, rapid response to treatment, and no regression after onset of spasms or its short duration (25).

5. CONCLUSION

The pattern of infantile spasm in our country do not differ from that of developed countries The results of this study proposed the need for long-term population epidemiological outcome studies aimed to clarify the prevalence of infantile spasm. Preventive measures by raising the standard of health education system to prevent birth asphyxia

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Corresponding author: Wael khreisat, MD. P.O .box 211133. Amman 11121. Jordan. Phone office : 00962-6-5804804-66411. Wael_khreisat@yahoo.com