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Clinical profile of patients with infantile spasms

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Abstract

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 of onset and presentation, details of seizure , family history of epilepsy, significant pre-/peri/post-natal insults, neuro imaging evaluation , detailed neurological and neuro developmental ,assessment were done by. Broad categories of possible etiologies were used the results were recorded for further study.

Results: Age of onset of infantile spasm 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%) were 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 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

Keyword: infantile spasm , seizures , epilepsy

Introduction

Infantile spasms represent a seizure disorder with unique clinical and electroencephalographic features and a poor prognosis including chronic intractable epilepsy and psychomotor retardation.; the incidence of infantile spasms is considered to be 0.16 to 42 per 1000 live births (***Cowan and Hudson; 1991***) , it associated with the particular EEG pattern, hypsarrhythmia (***Shields ; 2006***)

Early diagnosis with a careful diagnostic evaluation and proper therapy can obtain a normal development or a much improved situation in some cases (***Dreifuss 1981***) ,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 EEG characteristics. Focal seizures as well as focal lesions can also be present (***Dulac et al , 1994***)

Epileptic spasms (ES) 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 (***Fusco and Vigevano , 1993***) 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 (***Gobbi , 1987***)although late onset up to seven to eight years of age has been reported in rare cases (***Riikonen , 2001***)

Although the epileptogenic mechanisms of infantile spasms is not well understood, an etiologic diagnosis can be identified in more than 70% of cases (***Rantala , 1999***), 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 at regular visit at pediatric neurology clinic or admitted to neurological department of queen rania hospital for children , focused on age of onset , type of seizure , associated neurological deficits and the etiology .

Patients and Methods

Subjects included in this study were fifty infants suffering infantile spasm, who attended pediatric neurology clinic or from the in-patient services of neurological department of queen rania hospital for children in Jordan , the following data were collected : sex, age of onset , age of presentation to our center , details of seizure, , family history of epileptic disorders (1st and 2nd degree relatives), significant pre-/peri/post-natal insults .

Detailed neurological, medical, neurodevelopment 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 atrophy was diagnosed when ventricular dilatation with widening of the sulci is present.

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

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

Neuroimaging MRI/CT 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.

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 spasms were 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), and MRI findings at onset [6].

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 infantile spasm 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. 44% infants have other types of seizures these were focal (16%), generalized (20%) and others (8%). In 96% of cases IS where classically maxi-mum on awakening from sleep;. History of birth asphyxia was obtained in 48%, , The etiology of infantile spasm in this study showed in ***Table 1***. Among the 50 patients, 3 (6%) had a first- degree relative clinical profile is seen in ***Table II.***

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 III***

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 ***Figures 2, 3,4 and 5***

Symptomatic patients were 78% and 22 % as cryptogenic.

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 (***Bednarek, 1998***) . 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 , frost and hrachovy reported an excess of female subjects with this disorder (***Frost and Hrachovy, 2003***). 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 (***Brna et al., 2001***).

Spasms can be of the flexor or extension or mixed flexor extension types of the neck, trunk, arms and legs (***Chugani ,2002***) , among the clinically observed types of spasms, flexor types were most frequent which is similar to other reports (***Lombroso ,1983 ,Dulac 1997***). Most infants with this disorder have more than one type of spasm (***92%, Kellaway et al., 1979; 100%, King et al., 1985***) while in this study it forms 44% .

Seizures may occur before the onset of infantile spasms (***Yamamoto etal 1988 , Velez et al 1990***) Approximately one third to one half of patients with epileptic spasms have other seizure types preceding or accompanying the onset of the spasms (***Lombroso ,1983***) . 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 pre-dates the onset of spasms in about 70% of children.(***Arzimanoglou et al 2004***) Disappearance of social smile, loss of visual attention,(***Kramer , 1997***) or autistic withdrawal are often observed with the onset of spasms.

For some patients with spasms, psychomotor retardation was present from birth and epilepsy began several months later, and the question of the real age of onset of the epilepsy is raised, and the question of the contribution of hypsarrhythmia overlooked during a long period of time to the generation of psychomotor delay has to be addressed (***Villeneuve , 1998***) . On the other hand, some patients do not experience deterioration, and seem to continue developing. However, in these cases, treatment effective on the spasms and the EEG abnormalities soon shows that development velocity before treatment was not as good as following it.

The percentage of cases having a positive family history for epilepsy of any type has ranged from none (***Liou et al., 2001***) to 33% (***Druckman and Chao, 1955***). However, when only larger series (studies with more than 100 patients) are analyzed, the range is much lower: 1% to 7% (; ***Lombroso, 1983***) which is consist with our finding , true familial occurrence of infantile spasms has been documented in a number of families, and various underlying causes, including some neurologic syndromes with a genetic basis, have been identified (***Howitz, 1980; Sugaiet al., 2001***).

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 (***Trasmonte and Barron ,1998***)

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 (***Matsumoto et al , 1981***) As seen in our study more recent studies have consistently classified 70-80% of patients into the symptomatic group (***Rantala and Putkonen , 1999***)

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 ***(Van et al 1993***)

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 (***Kurokawa et al 1980***) which is consistent with our study , although perinatal causes have been reported to be on the rise (***Watanabe , 1998***)

Regarding the neurological co morbidities 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 IS (***Koul et al 2001***). Visual impairment has been found in approximately 25% of cases (***Koul et al 2001***) which is closed to our finding

(***Aydinli et al 1998***) a study on neuroradiological aspects of IS in patients also reported normal CT scans in 17% and normal MR scans in 18% , while in our study it was abnormal in3 6 % . MRI is more informative than CT scan 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 (***Juhasz et al , 2001***)

Prognosis depends more on the cause than on treatment. Bad prognostic factors include symptomaticity, early onset (younger than 3 months), pre-existing seizures other than spasms, asymmetric EEG, And relapse after initial response to treatment ***(Saltik et al 2002***) . 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 (***Kivity , 2004***)

Conclusion and recommendations;

The results of this study proposed the need for long-term population epidemiological outcome studies. The pattern of infantile spasm in our country do not differ from that of developed countries, preventive measurements regarding birth asphyxia should be initiated

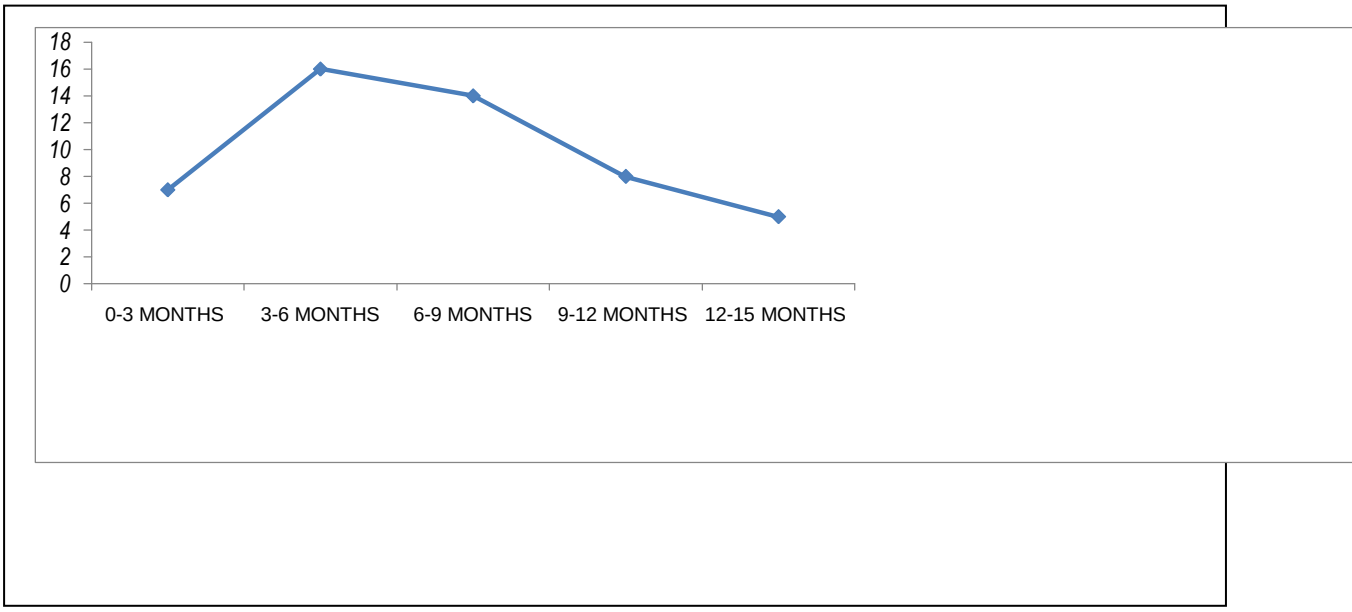

Fig (1) Distribution of infantile spasm according to age of onset

Etiology	**No**	**Percent**
Cryptogenic	11	22%
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 Female	37 13	74% 26%
Positive Family history	3	6%
Seizure pattern Flexor Extensor Mixed	 21 11 18	 42% 22% 36%
Number of spasm / day 5 5-10 More than 10	 12 18 20	 24% 36% 40%
Associated seizures Generalized seizure Focal seizure Others	 10 8 4	 20% 16% 8%
Symptomatic Cryptogenic	39 11	78% 22%
Reponses to treatment Complete Transient	 15 35	 30% 70%
Radiological finding Normal Abnormal Not done	 27 18 5	 54% 36% 10 %

Table II: Clinical profile of studied cases

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 III : Associated neurological disorders

FINDING	NO	PERCENT
Abnormal	27	54%
Cerebral atrophy	8	16%
Stroke	4	8%
Malformation	3	6%
White matter disorders	2	4%
Calcifications	1	2%

Table IV: Brain imaging finding in patient with IS

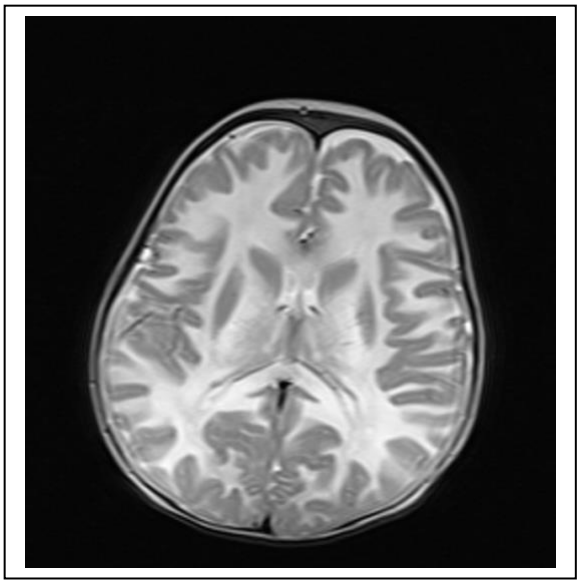

figure (3) : Brain MRI : extensive periventricular hyperintense signal suggestive of leuckodystrophy

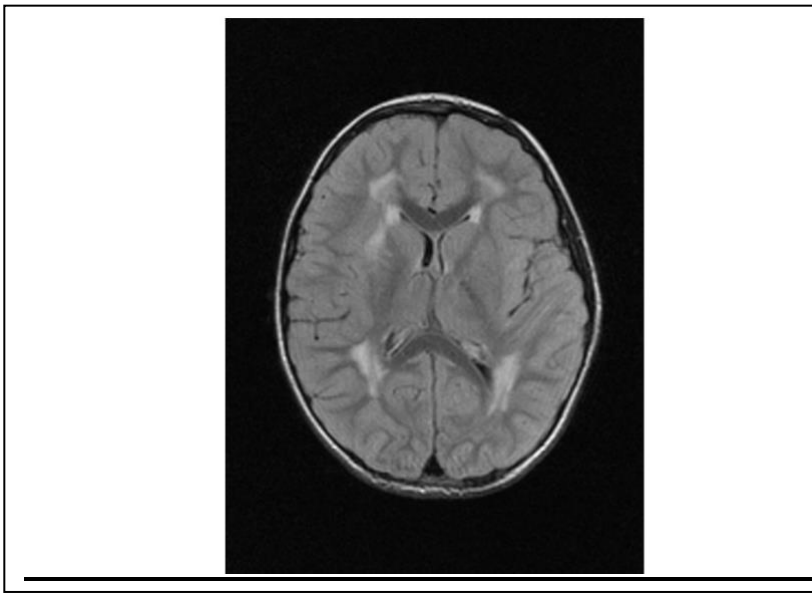

figure (2): White matter hyperintense suggestive of leuckodystrophy

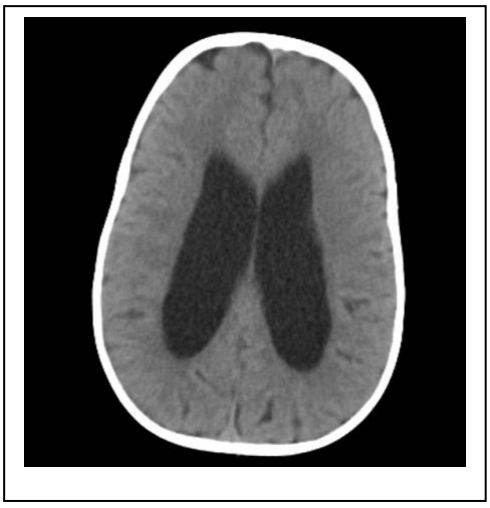

Figure (5) :Brain CT scan: dilated ventricular system with loss of white motor core result of birth asphyxia

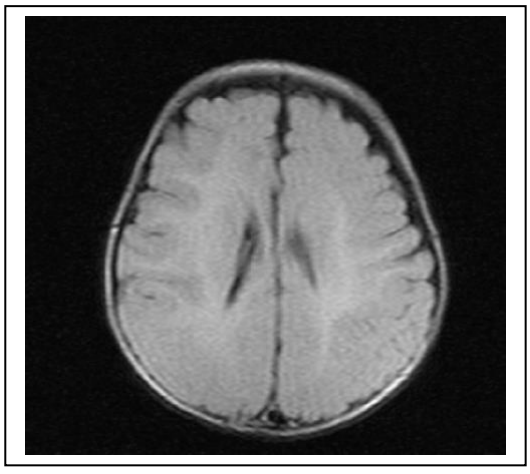

Figure (4): Atrophic changes involved bitemporal area

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الملف السريري للمرضى الذين يعانون من تشنجات الرضع

وائل خريسات
أخصائي أعصاب الأطفال مستشفى الملكة رانيا للأطفال / الأردن

الهدف :
تهدف هذه الدراسة الى إجراء مسح أولي للمرضى الذين يعانون من تشنجات الرضع والأمراض العصبية المرتبطة بها .

الطرق والإعداد :
تشمل هذه الدراسة على 50 حالة تشنج رضع يراجعون عيادة الأعصاب في مستشفى الملكة رانيا للأطفال ، الأردن .
أخذت منهم المعلومات التالية : الجنس ، العمر ، بدء الحالة ، تفاصيل التشنج ، الصرع العائلي ، الفحص السريري العام والعصبي وتقييم النمو والتطور باحثاً عن السبب ، جمعت النتائج للدراسة .

النتائج :
يبدأ تشنجات الرضع من الشهر الأول ولغاية السنة و 6 أشهر (المعدل 4.8 شهر) 74% ذكور ، 52 % تشنجات ثنية وأكثرها شيوعاً ، 44% تشنجات من نوع آخر ، 6% صرع عائلي ، تاخر في التطور والنمو قبل بدأ الحالة 52% ، صغر حجم الرأس أكثر الأمراض المرتبطة 78% من المرضى يوجد سبب لمرضهم ، الصور الدماغية غير طبيعية في 18 حالة

الإستنتاجات والتوصيات :
حالة تشنجات الرضع في الأردن مشابهة لغيرها من البلدان ، وضع أساليب لوقاية من تعسر الولادة متطلب .

مفتاح الكلمات :
تشنجات الرضع ، التشنج ، الصرع .