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Long-term outcomes in patients with West syndrome: An outpatient clinical study

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ABSTRACT

Purpose: Nearly half of all patients with seizure onset in the first year of life suffer from West syndrome (WS). The prognosis of epilepsy and psychosocial outcomes in children with WS are variable. This study was performed to examine the factors influencing the outcome of this patient population.
Methods: A total of 109 patients with WS followed up regularly for at least 3 years were included in the study. Relevant clinical, laboratory, and imaging data were collected.
Results: The male/female ratio was 65/44 (59.6%/40.4%). The mean age at onset of infantile spasm (IS) was 6 ± 6 (1–36) months. With regard to neuro-developmental and social conditions during the final evaluation, 29.4% of the patients were socially dependent on caregivers, 61.8% needed assistance, and 8.8% were normal. Among the patients, 5.9% were free of epilepsy and antiepileptic drugs (AED) for at least 2 years, 49.0% had no seizures with AEDs, and 45.1% had uncontrollable seizures. Parameters with significant negative effects on the long-term outcomes included symptomatic etiology, presence of developmental retardation before the onset of IS, persistence of active epilepsy, and male gender.
Conclusion: In this study, 37 (33.9%) patients had severe consequences as a result of WS. The majority of the rest could cope with daily life with varying degrees of assistance. Eight percent of the patients had a normal development. These results draw attention to the two-thirds of patients with WS who have the chance of an acceptable quality of life (QoL) with early diagnosis and therapeutic measures.

1. Introduction

West syndrome (WS) is the most frequently occurring infantile epileptic encephalopathy with a yearly incidence of 2–4.5/10,000 and a prevalence of 1.5–2/10,000 at 10 years of age or older [1]. Approximately 50% of patients with seizure onset before 12 months of age, excluding the neonatal period, suffer from WS characterized by infantile spasm (IS), psychomotor arrest or retardation, and hypsarrhythmia on electroencephalograms (EEG) [2–4]. Epileptic spasms most often show a temporal relationship with hypsarrhythmia, which is the typical interictal EEG activity in WS. Both spasms and focal seizures in WS are frequently intractable to conventional antiepileptic drug (AED) treatment, and in such cases, either polypharmacy and/or steroids are applied to suppress epileptic phenomena, although this has only been partially successful. There have been relatively few reports regarding the long-term prognosis of epilepsy and its impact on the daily life of patients with WS [4,5]. Both the prognosis of epilepsy and cognitive outcomes of WS are related to the etiological characteristics of the syndrome, as cryptogenic WS (cWS) has a more favorable outcome than symptomatic WS (sWS) [6–9]. Normal or subnormal cognitive development has been reported in approximately 25% of adult patients with previous WS [5]. The prognostic consequences of WS have been causally related to various additional parameters, such as premorbid developmental status, age at onset of WS, time and type of management [10–13]. The present study was performed to examine the long-term consequences of epilepsy and the psychosocial impacts of WS in the patient population under long-term follow-up in our center.

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2. Methods

Data belonging to a total of 109 patients with WS recruited since 1991 and followed up for at least 3 years in our WS outpatient clinic were included in the study. Last controls were completed in 2013. Patients with lack of recent information were called back and reevaluated to collect the missing data. Diagnosis of WS was confirmed by interviews, clinical observations, and analyses of video-EEGs. Patients were examined at least once a year until 6–7 years of age; regular follow-ups were once in 1–3 years later, if epilepsy was stabilized by then. Almost all patients underwent cranial magnetic resonance imaging (cMRI) and laboratory tests, including biochemical screening and tests for inborn metabolic diseases. Etiologically, patients were grouped as sWS, cWS, or idiopathic WS (iWS) according to the proposed ILAE classification scheme [14]. According to the neuro-developmental and social conditions during the final evaluation, the patients were divided into three categories: Group A, the "normal living group", patients with normal or subnormal motor and intellectual outcomes with favorable social status; Group B, the "assisted living group", ambulatory patients receiving special academic and/or physical support to cope with social needs; Group C, the "dependent living group", patients with severe motor and/or mental impairment with solely supervised living. Those groups were determined based on our neurological evaluations, interviews with the parents and on consultation reports of child-psychiatrists. Patients were grouped according to the status of epilepsy as follows: Group in remission, no epilepsy or treatment for at least 2 years; Group under control, epilepsy under control for a minimum of 2 years with AED treatment; Group active, persistent seizures despite AED treatment. The cMRI findings were classified as normal, diffuse cortical and/or subcortical involvement, or unilateral cortical and/or subcortical involvement.

The following parameters were included in the statistical evaluation: the age of onset of spasms and partial seizures, gender, family history of seizures, presence of parental consanguinity, presence of developmental delay or neurological deficit prior to the onset of spasms, etiology, characteristics of cognitive and motor involvement during the active phase of WS and later follow-ups, response of epilepsy to treatment, and clinic status of epilepsy during follow-ups.

Continuous variables are expressed as means ± SD, and categorical variables are presented as frequencies and percentages. The chi-square test was used to compare the differences in categorical variables among the groups. SPSS 17.0 statistical software (SPSS, Chicago, IL, USA) was used for the statistical analysis. In all analyses, $P < 0.05$ was taken to indicate statistical significance.

This study was approved by Ethics Committee of Cerrahpaşa Medical Faculty, University of Istanbul, Turkey.

3. Results

A total of 109 patients with WS were included in this study. The study population consisted of 65 male (59.6%) and 44 (40.4%) female with a mean follow-up duration of 8 years (3–16 years) (Table 1).

The number of patients as distributed to the groups with different neuro-developmental and social conditions was as follows: Group A, $n = 9$ (8.3%), Group B, $n = 63$ (57.8%), and Group C, $n = 30$ (27.5%). Seven deceased subjects were not included in these groups. Six patients (5.5%) free of epilepsy and AEDs were classified as the Group in remission. Epileptic seizures were under control by AEDs in 50 patients (45.9%, Group under control) and persisted despite AEDs in 46 (42.2%, Group active) (Table 2).

Table 1
Demographic and clinical features of the patients.

	$n = 109$[a]/%
Follow-up duration, years	8 (3–16)
Gender	65M/44F
Mean age at the last visit, years	9.5 ± 4 (3–19)
Age at onset of IS, months	6 ± 6 (1–36)
Type of IS	
Symmetrical	104/95.4
Asymmetrical	5/4.6
Patients with pre-spasm partial seizures	35/31.2
Patients with pre-spasm neuro-developmental involvement	79/72.5
Etiological groups	
Symptomatic	99/90.8
Hypoxic injury	44
CNS infections	9
Chromosomal anomaly	8
Cortical dysplasia	6
Cerebrovasculer diseases	4
Tuberosclerosis	3
Metabolic diseases	3
Others	22
Cryptogenic	9/8.3
Idiopathic	1/0.9
Patients with parental consanguinity	30/27.5
Patients having relatives with epilepsy and/or febrile seizures	17/15.6
Patients with inborn metabolic diseases	3/2.7
Cranial MRI results	
Normal	29/26.6
Diffuse cortical and/or subcortical involvement	57/52.3
Unilateral cortical and/or subcortical involvement	16/14.7
Others	2/1.8

IS: infantile spasm. CNS: central nervous system.
[a] Seven deceased patients were included.

Valproic acid (p53) (30–50 mg/kg/day), vigabatrin (p26) (50–100 mg/kg/day), and ACTH (p21) (0.5–1 mg/day) are the first-line drugs for WS (Table 3).

The number of females ($n = 7$) versus males ($n = 2$) in Group A was compared with the number of females ($n = 34$) versus males ($n = 59$) in groups B and C combined, and a statistically significant difference was found in favor of females. Females showed better long-term performance in neuro-developmental and social outcomes ($P = 0.04$).

Patients were divided into three groups according to the age at onset of IS: 0–3, 4–9, and ≥10 months. There were no correlations among prognostic variables, such as neuro-developmental and social performances and severity of epilepsy, among the types of IS, the age at onset of IS, and the presence or absence of neuro-developmental deficits before the onset of IS. Interestingly, the presence of partial seizures showed an inverse relationship with the age at onset of IS, as partial seizures were present before IS in 81.3%, 24.5%, and 21.2% of patients with spasm onset at ≥10, 4–9, and 0–3 months, respectively ($P < 0.001$) (Table 4).

Seventy of 74 (94.6%) patients with pre-IS neuro-developmental involvement and 23 of 28 (82.1%) patients with normal pre-IS development were present in Group C, and this was significant ($P = 0.03$).

The presence of pre-spasm focal seizures and the type of spasm did not show a significant relationship with clinical outcome with regard to the neuro-developmental and social performances of the patients. Of 93 patients in Groups B and C, 85 (91.3%) showed sWS.

Eighty-five of 92 patients (91.3%) with sWS were in Groups B and C, and only 7 (7.6%) were in Group A. One of nine patients in the cWS group and a single patient in the iWS groups were in Group A. Symptomatic etiology was significantly related to poor prognosis ($P = 0.01$).

The presence of active epilepsy was significantly related to the neuro-developmental and social performances of the patients. All