

Clinical, aetiological and evolutive aspects of West syndrome in Yaoundé (Cameroon)*

Séraphin Nguéfac^{1,2#}, Boniface Moifo^{2,3}, Andréas Chiabi^{1,2}, Antoine Ledoux Defo², Evelyn Mah^{1,2}, Florence Fru¹, Paul Cédric Mbonda¹, Pierre Fernand Tchokoteu^{1,2}, Elie Mbonda^{1,2}

¹Departement of Pediatric Neurology, Yaounde Gynaeco-Obstetric and Pediatric Hospital, Yaoundé, Cameroon

²Faculty of Medicine and Biomedical Sciences, The University of Yaounde I, Yaoundé, Cameroon

³Departement of Radiology, Yaounde Gynaeco-Obstetric and Pediatric Hospital, Yaoundé, Cameroon

Email: #seraphin_nguefac@yahoo.fr

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ABSTRACT

Background: West syndrome (WS) is an epileptic syndrome of the infant occurring between the 3rd and 12th months of life and characterized by the triad: infantile spasms in flexion, extension or mixed; global developmental delay; and hypsarrhythmia on the electroencephalogram (EEG). Its incidence varies between 2.9 and 4.5 per 10,000 live births. West syndrome is caused by a brain dysfunction whose origins can be prenatal, neonatal and postnatal. Sometimes the aetiology is genetic or unknown. **Purpose:** To determine the main clinical, aetiological and major evolutive aspects of West syndrome in child neurology unit in a university-affiliated hospital in Yaoundé. **Materials and Methods:** It was a retrospective descriptive study conducted from September 2011 to January 2012 in the child neurology unit of the Yaoundé gynaeco-obstetric and paediatric hospital. The medical records of 68 children followed for West syndrome (WS) in the service during the period from February 2008 to January 2012 (48 months) were used. All infants of 1- to 16-month-old with the diagnosis of WS were included. The diagnosis of WS was based on clinical evidence of spasm in flexion and/or in extension with global development delay, and EEG evidence of hypsarrhythmia or focal/multifocal epileptic abnormalities when hypsarrhythmia is absent. For each included infant, relevant medical history and complete physical examination were performed. The following data were collected and reported on a standardized questionnaire: prenatal, perinatal and postnatal past histories, age at onset of spasms, age at

diagnosis, semiology of spasms, psychomotor development, the EEG and CT aspects and the evolutive modes of WS under treatment. Psychomotor development was assessed using the Denver developmental screening test (DDST) which assesses the mental age compared to chronological age. **Results:** The age of onset of spasms varied between 1 and 16 months with a mean of 4.69 (± 1.98) months. Males were highly represented with a sex ratio of 1.72. Flexion spasms were the most common clinical presentation (79.41%). 82.83% of the patients had a global developmental delay on the onset of spasms. Structural causes or symptomatic West syndrome was the most frequent presentation (77.94%). Perinatal aetiologies were highly represented (73.58%) with the main cause being neonatal asphyxia (55.88%). A hypsarrhythmic tracing was found on the electroencephalogram (EEG) in 73.53% of cases. The most frequent CT abnormality was cortico-subcortical atrophy (38.24%). At the end of our study, global developmental delay persisted in 89.72%. **Conclusion:** The main aetiologies of West syndrome in our context are the sequelae of neonatal asphyxia and viral embryofetopathies. There is a high incidence of associated global developmental delay. More prevention methods on risk factors for foetal distress and proper monitoring of deliveries to minimize severe neonatal asphyxia are indispensable.

Keywords: West Syndrome; Epilepsy; Aetiology; Evolution; Cameroon

1. INTRODUCTION

West syndrome (WS) is an epileptic syndrome of the infant occurring between the 3rd and 12th months of life and characterized by the triad: infantile spasms in flexion,

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#Corresponding author.

extension or mixed; global developmental delay; and hypsarrhythmia on the electroencephalogram (EEG) [1]. Its incidence varies between 2.9 and 4.5 per 10,000 live births [2-5]. The prevalence is approximately 1/4000 - 1/6000 [6], and in 70% of cases, patients are male [2,3, 7-9].

West syndrome is caused by a brain dysfunction whose origins can be prenatal, neonatal and postnatal. Sometimes the aetiology is genetic or unknown. It is an epileptic encephalopathy in which the deterioration of brain functions (cognitive, sensory and motor) is due to seizure. Stopping these seizures sometimes leads to a normal psychomotor development [10]. Certain brain lesions which are responsible for West syndrome can be prevented.

To date in Cameroon, few studies have been carried out on the subject. The objective of this study was to determine the main aetiologies and describe the major evolutive aspects of West syndrome in our milieu.

2. METHODOLOGY

It was a retrospective descriptive study conducted from September 2011 to January 2012 in the child neurology unit of the Yaounde Gynaeco-Obstetric and paediatric hospital.

The medical records of 68 children followed for West syndrome (WS) in the service during the period from February 2008 to January 2012 (48 months) were used. All infants of 2- to 16-month-old with the diagnosis of WS were included. The diagnosis of WS was based on clinical evidence of spasm in flexion and/or in extension with global development delay, and EEG evidence of hypsarrhythmia or focal/multifocal epileptic abnormalities when hypsarrhythmia are absent.

For each included infant, relevant medical history and complete physical examination were performed. The following data were collected and reported on a standardized questionnaire: prenatal, perinatal and postnatal past histories, age at onset of spasms, age at diagnosis, semiology of spasms, psychomotor development, the EEG and CT aspects and the evolutive modes of WS under treatment.

All patients underwent an EEG recording and a head CT-scan. The EEG was performed by an acquisition unit of 32 channels of Micromed-France. The setup used was in accordance with the international 10/20 with 10 electrodes. CT protocol comprised of unenhanced and contrast enhanced CT scans using a single detector CT scanner. Image acquisition was spiral from skull base to vertex, using 3 - 5 mm-thick slices. The images were reviewed by one radiologist.

Psychomotor development (developmental milestone) was assessed using the Denver II test which assesses the mental age compared to chronological age.

Data collected using the questionnaires were analysed using the software Statistic Package for Social Sciences (SPSS) 17.0. The chi-square test of Pearson was used to study the relationship between two qualitative variables. Differences were considered statistically significant for p values < 0.05.

Informed consent was obtained from parents and an ethical clearance was obtained from the National Ethics Committee.

3. RESULTS

Sixty eight infants aged between 2 and 16 months (mean: 7.10 ± 2.24 months) were included in this study. The sex ratio was 1.72% with 63.24% males. Age to sex distribution of patients is shown in **Table 1**.

The mean age of onset of West syndrome was 4.69 (± 1.98) months (**Figure 1**).

Table 2 shows that symmetric flexion spasms were the most common clinical manifestation in our patients.

In 77.94% (53/68) of cases, West syndrome had a structural or symptomatic cause (**Table 3**).

Neonatal asphyxia was the main etiological factor (55.88%) as shown in **Table 4**.

Table 1. Distribution of patients according to age and sex.

Age*	Sex		Total	%
	Female	Male		
2 - 3	1	0	1	1.47
4 - 5	2	13	15	22.06
6 - 7	12	14	26	38.24
8 - 9	6	11	17	25.00
10 - 11	4	2	6	8.82
12 - 13	0	1	1	1.47
14 - 16	0	2	2	2.94
Total (%)	25 (36.76)	43 (63.24)	68 (100.00)	100.00

*Age at diagnosis (in months).

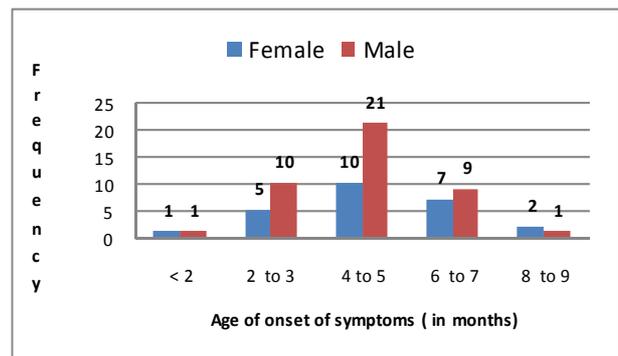


Figure 1. Distribution of patients by age at onset of symptoms and gender.

Table 2. Clinical presentation of patients.

Type of spasms	Criteria		Total	%
	Asymmetric	Symmetric		
Flexion	11	43	54	79.41
Extension	0	9	9	13.24
Mixed	1	4	5	7.35
Total (%)	12 (17.65)	56 (82.35)	68 (100.00)	100.00

Table 3. Distribution of patients according to the cause of West syndrome.

Causes	Frequency	%
Structural	53	77.94
Genetic	10	14.71
Unknown	5	7.35
Total	68	100.00

Table 4. Main aetiologies found in symptomatic patients (N = 53).

Aetiology	Frequency	%
Neonatal asphyxia	38	55.88
Infectious embryofetopathies (CMV)	6	8.82
Cerebral malformations	4	5.88
Prematurity	3	4.41
Tuberous sclerosis of Bourneville	2	2.94
Neonatal bacterial meningitis	2	2.94

Head CT-scans unveiled several types of cerebral lesions with the main one being hypoxo-ischemic lesions (**Table 5** and **Figure 2**).

Cortico-subcortical atrophy was the most common CT lesion (38.24%).

Fifty of the 68 patients (73.53%) had a hypersarhythmic EEG tracing on the EEG (**Figure 3**).

During follow up 97.06% (66/68) of our patients where spasms free, global developmental delay persisted in 61 patients (89.71%), while 55.88% (38/68) had microcephaly and 51.47% (35/68) had a progression to other seizures types (**Table 6**).

There is an association between the aetiology and prognosis (*chi-square* = 10.991 *Pearson*, *P* = 0.004). Developmental delay was greater in west syndromes with structural aetiologies (**Table 7**).

4. DISCUSSION

The age of onset of symptoms in this series ranged from 1 to 16 months with a mean of 4.69 ± 1.98 months.

Table 5. Main brain CT damage found in symptomatic patients (N = 53).

CT scan results	Frequency	%
Difused cortico-subcortical atrophy	26	38.24
Porencephaly	21	30.88
Difused cortical atrophy	11	16.18
Sub-ependymal and parenchymal calcifications	6	8.82
Cerebral malformation	4	5.88
Periventricular leucomalacia	2	2.94
Sub-ependymal and cortical nodules	2	2.94
Ischemic lacunae	1	1.47

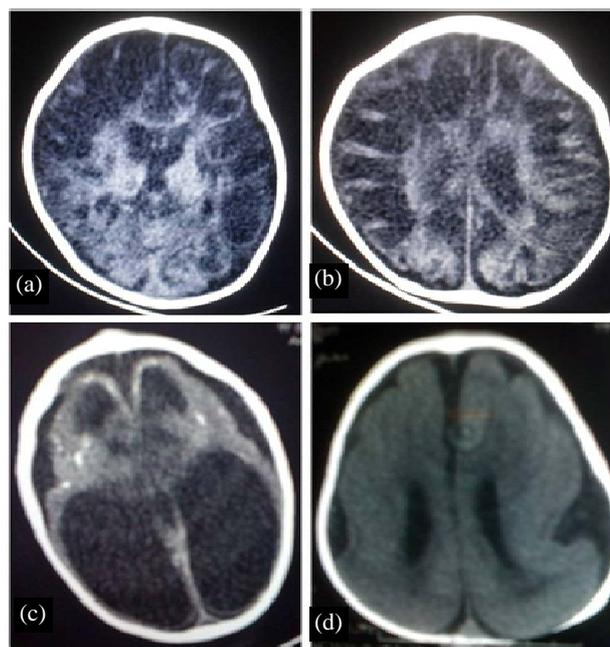


Figure 2. CT lesions of west syndrome. Hypoxo-ischemic lesion associating diffused subcortico-cortical hypodensities and proencephalic cavities (a), (b), in an infant of 5 months with a past history of severe neonatal asphyxia. Infant of 6 months with proved CMV embryofetopathy (c): parenchymal destruction, calcification and enlargement of lateral ventricles. Lissencephaly/pachygyry (d) on the CT scan of a 5 months infant with west syndrome.

Sixty-three out of 68 patients (92.64%) were 3 to 6 months old. This is quite similar to the findings of most authors who reported a peak incidence between 3 and 7 months in 50% of cases [7-9,11]. Mbonda *et al.* [8] found in their study that seizures began in the neonatal period. Spasms in the neonatal period are not necessarily related to West syndrome because they can be observed in early infantile encephalopathy or early myoclonic encephalopathy. These two nosological entities have spasms in their clinical expression.

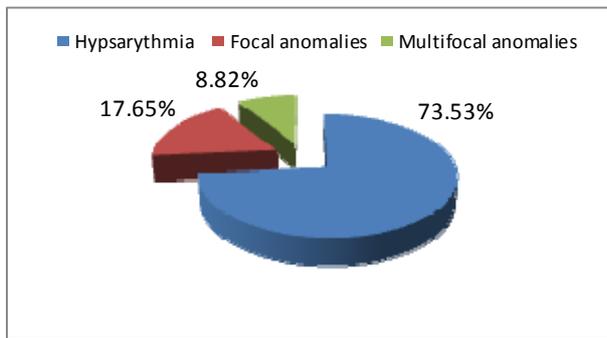


Figure 3. EEG aspects at diagnosis.

Table 6. Clinical course of our patients at the end of the study.

Clinical evolution	Frequency	%
Spasms free	66	97.06
Global developmental delay	61	89.71
Evolution to other types of seizures	35	51.47
Normal psychomotor development	7	10.29
Persisting spasms	2	2.94

Table 7. Association between aetiology and prognosis.

Aetiology	Development milestone at the end of our study		Total	%
	Normal	Delay		
Genetic	4	6	10	14.71
Structural	1	52	53	77.94
Unknown	2	3	5	7.35
Total (%)	7 (10.29)	61 (89.7)	68 (100.00)	100.00

Male predominance with a sex ratio of 1.72 corroborated data from many other studies [2,3,7-9]. Spasms in flexion represented 79.41% (54/68) of the clinical forms. Several authors describe the flexion spasms as the most frequent clinical presentation of West syndrome [4]. Symmetrical high frequency of spasms in our series reflects the widespread nature of this form of epilepsy in WS.

The EEG tracing of 73.73% infants (50/68) had a hypsarythmic aspect of diagnosis. Nguefack *et al.* and Jeavons *et al.* [9,12] found hypsarythmic patterns in 71 and 67% in their respective series, while Hwang [4] and Mohamed *et al.* [7] observed hypsarythmia in 55.6% and 60% of cases. However, absence of hypsarythmia on EEG does not exclude diagnosis of West syndrome [12].

An etiological factor probably playing a role in the onset of the disease was found in 77.94% patients (53/68). From other authors [4,6-8,11] an etiological factor is determined in 64% to 90% of cases. The main

etiological factor in our series was the effects of hypoxo-ischemic neonatal brain lesions (55.88%). In one study, Hwang [4] founded that neonatal asphyxia was the main etiological factor (50.8%) followed by cerebral malformations (21.4%) and neuro-cutaneous syndromes (8.6%). For Mohamed *et al.* [7], the first etiological factor is brain injury secondary to prematurity, followed by cortical malformations, Bourneville tuberous sclerosis and hypoxic-ischemic injury. Brain malformations encountered in 8.82% of our cases (malformations and cortical tubers). Magnetic resonance imaging [13,14] which is the goal standard imaging examination for epilepsy was not performed in our patients due to its cost and availability. Its implementation could probably increase the frequency of cerebral lesions in our patients. In spite of its low sensitivity, CT-scan remains our means of cranio-encephalic imaging. Trans-cranial ultrasounds could be an imaging alternative but was limited by the size or the closure of fontanelles, or by incomplete brain exploration. Antenatal ultrasound could have detected some abnormalities related to cerebral malformations or embryofetopathies. The sequelae of congenital cytomegalovirus (CMV) infection were the second group of aetiology in our study. Indeed because of its high cost, CMV serology is not systematically requested in the assessment of antenatal serology in our milieu.

At the end of this study, we observed complete regression of spasms in 66 patients (97.06%), persistent of spasms in 2.94%, a change to another type of seizures in 51.47%. The prevalence of global developmental delay in this group at the end of this study was 89.71%. According to other authors, complete regression of spasms is observed in 50% to 90% of cases [15-17], evolution to other types of seizures in 50% to 70% of cases [15,17], and persistency of cognitive delay in 70% to 90% of cases [4,9,15,16]. In Hwang's study [4], evolution to a global developmental delay was found in 75.4% of cases and a shift to other types of seizures in 11.2%. Riikonen *et al.* [18] found a persistent spasm in 2.7% of patients. Mbonda *et al.* [8] in Cameroon concluded to complete regression of spasms in 70.30% of patients and their persistency in 13.51% at the end of follow-up. The high incidence of developmental delay in our study could be explained by the fact that most symptomatic (or structural) West syndrome are strongly associated with a poor prognosis [5,16]. Factors associated with a poor prognosis in our study were: the structural character (or symptomatic) of the west syndrome, global developmental delay, early onset of spasms and delay in starting treatment. These factors are also described in literature [5, 16,19].

5. CONCLUSION

The two main aetiologies of West syndrome in our con-

text are the sequelae of neonatal asphyxia and viral embryofetopathies. There is a high incidence of associated global developmental delay. Antenatal assessments including search for CMV seroconversion and identification of cerebral anomalies on antenatal ultrasounds should be emphases. More prevention methods on risk factors for foetal distress and proper monitoring of deliveries to minimize severe neonatal asphyxia are indispensable.

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