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ORIGINAL ARTICLE

Cryptogenic West syndrome: Clinical profile, response to treatment and prognostic factors☆,☆☆

María Calderón Romero*, Elena Arce Portillo, Mercedes López Lobato, Beatriz Muñoz Cabello, Bárbara Blanco Martínez, Marcos Madruga Garrido, Olga Alonso Luego

Servicio de Neuropediatría, Hospitales Universitarios Virgen del Rocío, Sevilla, Spain

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KEYWORDS
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Abstract
Introduction: West syndrome (WS) is an age-dependent epileptic encephalopathy in which the prognosis varies according to the, not always identified, underlying origin.
Objectives: To define the profile of cryptogenic (a least studied isolated sub-group) WS, in Spain. To study its outcome, response to different treatments, and to establish prognostic factors.
Patients and methods: The study included a review of the medical records of 16 patients diagnosed with cryptogenic WS during the period, 2000–2015. The mean follow-up time was 6.6 years, with a minimum of 2 years.
Results: The large majority (11/16) were male. The mean age at onset was 6 months, and 6/16 had a family history of idiopathic epilepsy. The first line treatment with vigabatrin had an electrical–clinical response in 5/16 patients, with the remaining cases responding to adrenocorticotropic hormone (ACTH). Almost half (44%) of the patients progressed to other types of epilepsy, with no difference between those treated with vigabatrin or ACTH. A greater number of adverse effects were obtained with ACTH, with no retinal involvement being observed with vigabatrin. The aetiological cause was found in 2/16. Being female, late onset, and early control of the hypsarrhythmia, were factors of a good prognosis.
Conclusions: The overall prognosis of cryptogenic WS was more serious than expected. Although the incidence of Lennox–Gastaut syndrome was low, the progression to focal epilepsy was the most common, with it appearing within the first 2 years of the diagnosis. The initial response to vigabatrin was lower than expected, but the long-term result was comparable to ACTH.

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* Corresponding author.
E-mail address: calderonromero@hotmail.com (M. Calderón Romero).

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Síndrome de West criptogénico: perfil clínico, respuesta al tratamiento y factores pronósticos

Resumen
Introducción: El síndrome de West (SW) es una encefalopatía epiléptica dependiente de la edad con pronóstico variable según la etiología subyacente, no siempre identificada.
Objetivos: Definir el perfil del SW criptogénico en nuestro medio, subgrupo menos estudiado de forma aislada. Estudiar su evolución, respuesta a los distintos tratamientos y establecer factores pronósticos.
Pacientes y métodos: Revisión de historias clínicas de 16 pacientes diagnosticados de SW criptogénico durante el período 2000-2015. El tiempo de seguimiento medio fue 6,6 años y mínimo de 2 años.
Resultados: 11 de 16 fueron varones, la edad media de inicio fue de 6 meses y 6/16 presentaban antecedente familiar de epilepsia idiopática. El tratamiento de primera línea con vigabatrina tuvo respuesta electroclínica en 5/16 pacientes, respondiendo los casos restantes a hormona adrenocorticotropa (ACTH). El 44% de los pacientes evolucionaron a otras epilepsias, sin diferencia entre los tratados con vigabatrina o ACTH. Se obtuvo un mayor número de efectos adversos con la ACTH, no se evidenció afectación retiniana con la vigabatrina. Durante el seguimiento se llegó a la causa etiológica en 2/16. El sexo femenino, el comienzo tardío y el control precoz de la hipsarritmia resultaron factores de buen pronóstico.
Conclusiones: El pronóstico global del SW criptogénico resultó más grave de los esperado. Aunque la incidencia de síndrome de Lennox-Gastaut fue baja, la epilepsia focal resultó la evolución más frecuente apareciendo en los 2 primeros años del diagnóstico. La respuesta inicial a vigabatrina fue menor a la esperada, pero el resultado a largo plazo resultó superponible a la ACTH.

Introduction

West syndrome (WS) is an age-dependent epileptic encephalopathy characterised by the triad of (1) infantile spasms, usually clustered; (2) evidence of hypsarrhythmia in the electroencephalogram (EEG), with tracings showing a chaotic, multifocal and bilateral pattern of high-amplitude waves; and (3) regression of psychomotor development, although the latter may be absent.[1,2]

Its estimated incidence ranges from 2 to 4 in 10 000 individuals depending on the series, and therefore it is the most frequent form of epilepsy in the first year of life outside of neonatal and febrile seizures.[1,3]

Due to the numerous underlying causes and the variability in neurologic development in these patients, it is often categorised into different diagnostic groups. The most common classification continues to be the one proposed by the International League Against Epilepsy (ILAE), which categorises infantile spasms as symptomatic or cryptogenic.[4]

The symptomatic category corresponds to patients with an obvious underlying cause and/or a history of developmental delay or epileptic seizures prior to the onset of spasms, and accounts for approximately 80% of all patients with WS. Patients in whom an underlying condition is suspected but has not been identified after the aetiological investigation are categorised as having cryptogenic WS and account for the remaining 20% of cases. In the cryptogenic group, patients have normal psychomotor development at onset that goes on to deteriorate progressively in most cases. However, in a minority of cases, approximately 5% of patients with infantile spasms, the outcomes are favourable, with full resolution of the spasms and normal psychomotor development, which has led some authors to consider it a separate aetiological group labelled *idiopathic*,[5] although this category has yet to be adopted by the ILAE. This aetiological category is based on disease outcomes, so it can only be applied through the followup of patients.

Since developmental delays present at diagnosis could be explained by both the underlying disease and the epileptic encephalopathy itself (spasms that were not detected previously or presence of hypsarrhythmia prior to onset), some authors propose abandoning the distinction between symptomatic and cryptogenic WS in favour of a classification based on the development preceding onset. In the United Kingdom Infantile Spasms Study (UKISS), 61% of patients had proven aetiology, 33% had no identified aetiology, and 6% had not been fully investigated.[4] A recent study of the ILAE proposes replacing these terms with 3 new aetiologic groups: genetic, structural-metabolic and unknown.[6]

When it comes to the aetiological diagnosis of WS, neuroimaging is the method that offers the highest yield. The underlying cause is identified in 70% of the patients after an adequate history-taking and physical examination and magnetic resonance imaging of the head.[7] Several studies have evaluated the yield of other diagnostic tests, such as genetic and metabolic investigations.[6,8,9] They conclude that in