Clinical case

Infantile Spasms and Down Syndrome

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Abstract

Infantile spasms were originally described by West in 1841. West syndrome is the term employed when such spasms are concomitant with delayed psychomotor development and EEG hypsarrhythmia.

The present article discusses three cases of patients with Down syndrome who had infantile spams with psychomotor retardation but a nonhypsarrhythmic EEG pattern. Despite early diagnosis and early combination drug therapy, the condition persists, with seizures, psychomotor delay and abnormal EEG patterns. The sequence of events appears likely to develop into Lennox-Gastaut syndrome (LGS).

Several published case series report good progress in patients with Down syndrome and West syndrome.

We conclude that despite adequate treatment, patients with Down syndrome and infantile spasms with psychomotor delay and abnormal but non-hypsarrhythmic EEG may have poor disease progression, with persistence of seizures and severely impaired psychomotor development.

Keywords: Infantile spasms. Nonhypsarrhythmic pattern. Down syndrome.

Introduction

Infantile spams were originally described by William James West in 1841 (1). A pattern of hypsarrhythmia was first described by Gibbs and Gibbs (2) in 1952; it is characterized by "irregular spikes and slow high-amplitude waves which vary in both duration and location from one moment to the next." In the 1960s, a triad of infantile spams, psychomotor delay and hypsarrhythmia came to be termed West syndrome (3).

Some patients, however, have epileptic encephalopathy with infantile spasms and psychomotor delay but no hypsarrhythmia; their response to treatment is less favorable.

The incidence rate for this syndrome is around 1 per 4,000 to 6,000 live births. Boys are more likely to develop it. (2)

Infantile spasms begin in the first year of life for most patients. Etiologically, the condition may be classified as either idiopathic, cryptogenic or symptomatic. Prenatal causes prevail, such as, for instance, cortical and subcortical malformations of the brain, chromosomal anomalies including Down syndrome (DS), congenital infections, and so on.

Currently, a number of treatment options are available, including valproate (VPA), vigabatrine (VGB), adrenocorticotropic hormone (ACTH), steroids, etc. Prognosis depends on multiple factors, particularly early recognition, accurate classification, and selection of drug treatment regimen.

Patients

We report three cases of patients with Down syndrome, infantile spasms, psychomotor delay and a nonhypsarrhythmic epileptic EEG record.

Table 1 summarizes the clinical features, EEG patterns, neuroimaging results, treatments, and progress.

To sum it all up, we have three patients with DS whose epileptic encephalopathy, secondary to infantile spasms, had poor treatment outcomes despite attempts with multiple combinations of anticonvulsant drugs. The condition currently persists in all three patients, with seizures, marked psychomotor delay and EEG abnormalities.

Discussion

The mechanisms that raise susceptibility to infantile spasms in patients with DS have yet to be thoroughly uncovered. Several authors suggest a potential epileptogenic role for the interaction of various DS-specific structural abnormalities of the brain, such as lower rates of inhibitory interneurons, reduced neuron density, abnormal neuronal lamination, or the persistence of dendrites with fetal-like morphology (4-9).

In patients with Down syndrome, the prognosis for West syndrome is good, according to some authors (10-13), with positive responses to drugs such as VPA, VGB and ACTH. These authors also point out that the earlier the diagnosis and onset of treatment, the better the prognosis for seizure control and psychomotor development.

Our three cases do not match the above description: despite an early diagnosis which led to early treatment with anticonvulsants, and despite their multidrug regimens, the patients are still having seizures and their psychomotor development is patently deteriorated. The difference is that hypsarrhythmia, which is characteristic of West syndrome, is absent here; these patients have multifocal cortical seizures.

It has been shown that when there is a pattern of hypsarrhythmia, the abnormal electrical discharges begin with groups of neurons in the basal ganglia and then propagate to the rest of the brain (14). In our patients, the abnormal discharges originate diffusely throughout the cortex, involving different neuron groups which probably have varying structures and functions.

The clinical course of these cases leads us to expect progression to Lennox-Gastaut syndrome, a generalized form of epilepsy which may manifest in the form of absence seizures, tonic seizures and/or atonic seizures together with mental retardation and a characteristic EEG pattern: a diffuse slow symmetrical spike-and-wave. Lennox-Gastaut is refractory to drug

Table 1.
Clinical features, EEG, neuroimaging, drug regimen, and evolution.
Patients with Down syndrome and infantile spasms

Patient	Gender/ Current age	Age of onset	Clinical manifestation	EEG	MRI	Drug regimen	Progress
1	M/3 yrs	5 months	Symmetrical flexor spasms and significant psychomotor delay	Slow, unstructured background.Multifocal spike-and-wave discharges predominating in the posterior left quadrant	Normal	TPM, VPA, VGB, CBZ, ZNS, Pyridoxine, ACTH, Prednisone	Persistence of flexor spasms and psychomotor delay
2	F/3 yrs	8 months	Symmetrical flexor spasms and significant psychomotor delay	Slow, unstructured background. Multifocal spike-and-wave discharges predominating in the posterior left quadrant	Normal	LEZ, CBZ, VPA, ZNS, ACTIH, TPM	Persistence of flexor spasms, little eye contact, lack of independent walking, stands with support
3	M/8 months	4 months	Symmetrical flexor spasms and significant psychomotor delay	Unstructured background. Bilateral parietooccipital multifocal spike-and-wave discharges	Normal	VGB, VPA, ACTH, CBZ	Persistence of flexor spasms, does not sit up, little eye contact

TPM = topiramate; VPA = sodium valproate; CBZ = carbamazepine; ZNS = zonisamide; LEV = levetiracetam; ACTH = adenocorticotropic hormone

treatment and hard to manage, and generally develops after infantile spasms with a morbid progression (15).

This short series leads us to conclude that, even with adequate treatment, patients with DS who have infantile spasms, psychomotor delay and nonhypsarrhythmic EEG abnormalities may have an unfavorable progression, with persistence of seizures and severely impaired psychomotor development.

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