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Atonic elements combined or uncombined with epileptic spasms in infantile spasms

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HIGHLIGHTS

- Atonia combined or uncombined with spasms was an ignored phenomenon in infantile spasms.
- Atonic elements combined or uncombined with spasms were artificially divided into three subtypes.
- Atonic elements in infantile spasms might be a variant of epileptic spasms or a new seizure type.

ABSTRACT

Objective: To study the atonic elements combined or uncombined with epileptic spasms in infantile spasms.
Methods: The demographic data, clinical characteristics, electroencephalogram (EEG), and polyelectromyography (PEMG) features were analyzed in 12 infantile spasm patients with atonic elements.
Results: A total of 29 EEGs were recorded. Hypsarrhythmia or hypsarrhythmia variants were identified during interictal EEG. Insular or clustered epileptic spasms occurred in all. Three subtypes of atonic elements combined or uncombined with epileptic spasms (spasm-atonic, pure atonic, and atonic-spasm seizures) were observed electroclinically, which could present insularly or in cluster or altered with epileptic spasms in the same cluster. The ictal EEG showed generalized high-amplitude slow waves presenting alone or combined with other patterns. The corresponding PEMG showed an obvious electrical silence alone or preceding or following a crescendo-decrescendo pattern generated from myoelectric burst.
Conclusions: Atonic elements combined or uncombined with epileptic spasms was a newly noticed phenomenon in infantile spasms, which was artificially divided into three subtypes here. It might be a variant of epileptic spasms or a unique seizure type.
Significance: Atonic elements combined or uncombined with epileptic spasms was a previously ignored phenomenon in infantile spasms, which should be seriously considered in clinical practice.

1. Introduction

Infantile spasms is an age-related epileptic encephalopathy caused by multiple and diverse factors and was first described by West (1841). It may be onset directly or an evolution from Ohtahara syndrome. The age of spasm onset is usually between 3 and 12 months, with a peak at 5 months in 90% of cases, whereas an onset below the age of 3 months or between 1 and 3 years is rare (Panayiotopoulos, 2005). Infantile spasms is characterized by a unique type of seizure called epileptic spasms and gross EEG abnormalities of hypsarrhythmia (Panayiotopoulos, 2005). Epileptic spasms is a hallmark of infantile spasms, which might also be coupled with other seizure types, such as focal and tonic seizures (Hrachovy et al., 1994a,b).

The first detailed description of atonic seizures was given by Hunt (1922), who called the condition "static epilepsy". Then, the terms akinetic seizures (Lennox, 1945) and astatic seizures

Abbreviations: ACTH, adrenocorticotropic hormone; AEDs, antiepileptic drugs; ILAE, International League Against Epilepsy; MRI, magnetic resonance imaging; PEMG, polyelectromyography; VEEG, video-electroencephalogram.

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(Lennox, 1951) were used for a while till the term atonic seizure was established by the Commission on Terminology and Classification of the International League Against Epilepsy (ILAE) (Bancaud et al., 1981). Atonic seizures have been reported to occur in various syndromes, such as at least 50% of cases of Lennox–Gastaut syndrome and probably in 2–3% of an epileptic population (Niedermeyer, 1990). In our clinical practice, we noticed that atonic elements combined or uncombined with epileptic spasms could occur in some infantile spasm patients. However, to date, no report has been published on this phenomenon. In the present study, we report a cohort of infantile spasm patients with atonic elements observed electroclinically.

2. Patients and methods

Twelve subjects were retrospectively recruited from approximately 410 infantile spasm patients who underwent video-electroencephalogram (VEEG) between January 2013 and June 2016 in our hospital and satisfied the following criteria: (1) onset with epileptic spasms or progression from Ohtahara syndrome, (2) demonstration of hypsarrhythmia or hypsarrhythmia variants on the interictal EEG. The hypsarrhythmia variants included hypsarrhythmia with increased interhemispheric synchronization, asymmetrical or unilateral hypsarrhythmia, hypsarrhythmia with episodes of generalized or regional voltage attenuation (which in its maximal expression is referred to as the "suppression-burst variant" of hypsarrhythmia), and hypsarrhythmia primarily comprising generalized slow-wave activity with little spike or sharp-wave activity (Hrachovy and Frost, 2013). (3) Atonic elements were recorded during VEEG monitoring.

VEEG monitoring was performed in all patients using a Nihon Kohden digital video-EEG-1100K instrument. EEG electrodes were positioned over the scalp according to the international 10–20 system. All patients also underwent polyelectromyography (PEMG) investigation, recording the activity from deltoid and quadriceps femoris. EEG and PEMG activities were recorded with bandpasses of 0.3–70 and 5.3–120 Hz. All the EEG recordings were performed both while awake and during sleep and were evaluated by a qualified neurophysiologist.

In addition, the following demographic data were also analyzed: sex, age at onset, birth history, response to the treatment, and outcome. Biochemical studies and blood and urine metabolic screening were performed in all patients. Brain magnetic resonance imaging (MRI) was also performed. Three patients (patients 3, 6, and 11) had received genetic analysis, including epilepsy-related gene detection and chromosome examination. All patients were psychometrically evaluated clinically.

3. Results

3.1. General characteristics (Table 1)

A total of 12 patients were included, of which 11 were male. Three (patients 5, 7, and 8) of them were evolved from Ohtahara syndrome, with a seizure onset at 15 days, 12 h, and 12 days after birth, respectively. For the other nine patients, five experienced attacks between 3 and 12 months, whereas the others had spasms below the age of or at 3 months or more than 1 year. The mean age of spasm onset was 7.3 months. Most patients had unremarkable pregnancy and birth history, excluding patient 4 who had hypoxic ischemic encephalopathy after birth. Patients 4, 9, and 11 had neonatal hypoglycemia, which induced brain damage in one of them (patient 9). Patients 4 and 12 had histories of epilepsy during neonatal and early infantile periods, presenting focal seizures controlled by antiepileptic drugs (AEDs) such as phenobarbital. Blood and urine metabolic screening showed methylmalonic aciduria combined with homocystinemia in patient 1 and was normal in all the other patients. Brain MRI was normal in seven patients, whereas the others showed various abnormalities, including delayed myelination in three patients (patients 1, 3, and 6), corpus callosum hypoplasia in two patients (patients 1 and 3), encephalomalacia and encephalatrophy in patient 9, and parietal cortex

Table 1
General characteristics of the 12 patients in our study.

No.	Sex	Birth history	Seizure onset	Seizure types	Metabolic screening	MRI	Development at last follow-up	AEDs	ACTH/ketogenic diet
1	M	Normal	7 months	Spasms, spasm-atonic	MMACHC	DM, CCH	Severe delay	B_6, LEV, NZP	Ineffective/no
2	M	Normal	9 months	Spasms, spasm-atonic	(−)	Normal	Severe delay	TPM	No/no
3	M	Normal	4 months	Spasms, spasm-atonic	(−)	DM, CCH	Severe delay	TPM, VPA, CZP, VGB	Reduced/ ineffective
4	M	Hypoglycemia HIE	4 months	Spasms, spasm-atonic	(−)	Normal	Severe delay	B_6, TPM, VPA	Reduced/control
5	M	Normal	15 days	Spasms, atonic, atonic-spasms	(−)	Normal	/	B_6, TPM	No/no
6	M	Normal	13 months	Spasms, atonic	(−)	DM	Severe delay	B_6, VPA, TPM, CZP, OXC, ZNS	Ineffective/ ineffective
7	M	Normal	12 h	Spasms, spasms-atonic, atonic, myoclonic, focal seizures, spasm-tonic	(−)	Normal	/	B_6, LEV, PB, TPM	Reduced/no
8	M	Normal	12 days	Spasm, spasms-atonic, atonic, focal seizures, spasm-tonic	(−)	Normal	Dead	B_6, TPM, VPA	Ineffective/no
9	M	Hypoglycemia brain damage	8 months	Spasms, atonic	(-)	Encephalomalacia, encephalatrophy	Severe delay	B_6, TPM, VGB, LTG	Ineffective/no
10	M	Normal	15 months	Spasms, atonic	(−)	WMA of parietal cortex	Severe delay	VPA, LEV, TPM, LTG, VGB	Control then relapse/no
11	F	Hypoglycemia	3 months	Spasms, spasms-atonic, spasm-tonic	(−)	Normal	Severe delay	B_6, LEV, VPA, TPM, CZP	Reduced/no
12	M	Normal	3 months	Spasms, spasms-atonic	(−)	Normal	Severe delay	VPA, TPM, LTG, VGB	No/no

HIE: hypoxic ischemic encephalopathy; MMACHC: methylmalonic aciduria combined with homocystinemia; DM: delayed myelination; CCH: corpus callosum hypoplasia; WMA: white matter abnormalities; AEDs: antiepileptic drugs; B_6: vitamin B_6; TPM: topiramate, VPA: valproic acid, CZP: clonazepam, VGB: vigabatrin, OXC: oxcarbazepine, LEV: levetiracetam, PB: phenobarbital, LTG: lamotrigine.