Epileptic spasms in congenital disorders of glycosylation

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VIDEO ONLINE

ABSTRACT – *Aim.* Congenital disorders of glycosylation (CDG) are a group of rare metabolic diseases, characterized by impaired glycosylation. Multi-systemic involvement is common and neurological impairment is notably severe and disabling, concerning the central and peripheral nervous system. Epilepsy is frequent, but detailed electroclinical description is rare.
Methods. We describe, retrospectively, the electroclinical features in five children with CDG and epileptic spasms.
Results. Epileptic spasms were observed in patients with ALG1-, ALG6, ALG11-CDG and CDG-Ix, and occurred at an early age, before 6 months in all cases, except one who had spasms that started at 18 months. In this patient, spasms had an unusual aspect; they did not occur in clusters and were immediately preceded by a myoclonus. All but one child also presented rare myoclonias. On EEG, background activity was poorly organized with abundant posterior spike and fast rhythm activity, but without hypsarrhythmia. At the last evaluation (age range: 6-12 years), two patients still presented epileptic spasms and subcortical myoclonias, one showed rare generalized tonic-clonic seizures, and two were seizure-free.
Conclusion. CDG disorders can be associated with epileptic spasms showing particular features, such as absence of hypsarrhythmia, posterior EEG anomalies, and an unusual combination of epileptic spasms with myoclonus. These features, associated with pre-existing developmental delay and subcortical myoclonias, may shift toward CDG screening. [*Published with video sequence and supplemental EEG plates on www.epilepticdisorders.com*]

Key words: congenital disorders of glycosylation, epilepsy, epileptic spasms, myoclonus

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Since their first description in 1980 (Jaeken *et al.*, 1980), congenital disorders of glycosylation (CDG) are still a rare but rapidly expanding family of inherited diseases, nowadays including over 70 identified autosomal recessive genetic disorders (Freeze *et al.*, 2012; Barone *et al.*, 2014).

Biochemically, these disorders are characterized by impaired glycosylation of proteins and lipids, caused by mutations in genes required for the synthesis of the glycan moiety or for the attachment of these glycans to proteins and lipids. According to their specific pattern on transferrin isoelectric focusing (TIEF), CDGs are divided into two groups. CDG type I comprise defects in the biosynthesis of dolichol-linked oligosaccharides in the cytosol or the endoplasmic reticulum, as well as defects involving the transfer of oligosaccharides onto nascent glycoproteins. CDG type II encompass all defects of further trimming and elongation of N-linked oligosaccharides in the endoplasmic reticulum and the Golgi apparatus (Schwarz *et al.*, 2004; Jaeken, 2010, 2012). Following a recent revision of the nomenclature (Jaeken *et al.*, 2009), CDG subtyping is now based on the affected gene.

The exact prevalence of this group of disorders is unknown. There are approximately 1,000 cases published in the literature (Vodopiutz and Bodamer, 2008; Dupré *et al.*, 2010). Of the CDG forms identified worldwide, 80% correspond to phosphomannomutase (PMM) 2 deficiency (PMM2-CDG or CDG-Ia) (Jaeken, 2010; Freeze *et al.*, 2012). Phosphomannose-isomerase (MPI) deficiency (MPI-CDG) and glucosyltransferase I (ALG6) deficiency (ALG6-CDG), referred to as CDG-Ib and CDG-Ic, respectively, have been reported in more than 60 individuals worldwide (Jaeken, 2010).

However, in France, PMM2-CDG represents 62% of diagnosed CDG families, followed by MPI-CDG (6%), ALG1-CDG (mannosyltransferase 1 [MT-1] deficiency) or CDG Ik (6%), and ALG6-CDG (4%). About 15% of CDG families have a yet unidentified glycosylation defect, and thus remain to be subtyped, under the designation of CDG Ix (Dupré *et al.*, 2010).

Because of the fundamental biological role of glycoproteins, impaired glycosylation mechanisms lead to multisystemic involvement and thus to a broad spectrum of clinical features (de Lonlay *et al.*, 2001; Vodopiutz and Bodamer, 2008; Morava *et al.*, 2008; Funke *et al.*, 2013). Neurological impairment is often severe and disabling and includes structural abnormalities, such as rapidly progressive cerebellar atrophy and cortical atrophy, myopathies including congenital muscular dystrophies and limb-girdle dystrophies, seizures, stroke and "stroke-like" episodes, developmental delay, and demyelinating neuropathy (de Lonlay *et al.*, 2001; Drouin-Garraud *et al.*, 2001;

Grubenmann *et al.*, 2004; Kranz *et al.*, 2004; Jaeken, 2010; Freeze *et al.*, 2012; Rahman *et al.*, 2013).

Since CDG is a rare disorder, the exact incidence of epilepsy in these patients is yet to be determined, ranging from 0 (patients with only visceral disease) to 100% (patients with severe forms of neurological impairment). This also appears to correlate to the underlying genetic defect (de Lonlay *et al.*, 2001; Morava *et al.*, 2008; Dupré *et al.*, 2010). Epilepsy is uncommon in the most frequent form of CDG, PMM2-CDG, but frequently present in other types of CDG (Fiumara *et al.*, 2016). Seizures can begin from the neonatal period to later childhood and are described either as easily manageable or pharmacoresistant (de Lonlay *et al.*, 2001; Clayton and Grunewald, 2009; Dupré *et al.*, 2010; Jaeken, 2010; Freeze *et al.*, 2012; Funke *et al.*, 2013; Fiumara *et al.*, 2016; OMIM database).

CDG disorders are considered as one of the underlying aetiologies for early-onset epilepsy and inborn errors of metabolism (Wolf *et al.*, 2005; Bahi-Buisson *et al.*, 2006; Fois, 2010; Noh *et al.*, 2012; Rahman *et al.*, 2013; Fiumara *et al.*, 2016). However, detailed characterization of seizure semiology and neurophysiological patterns is rare. We report the presence of epileptic spasms without hypsarrhythmia in five children with CDG syndrome.

Methods

Among the patients with CDG syndrome followed in the Pediatric Neurology and the Metabolism Department in Necker Enfants Malades Hospital, Paris, France, polygraphic video-EEG recordings performed between 2000 and 2013 in the Neurophysiology Department of the same hospital revealed, in five children, the presence of epileptic spasms. We retrospectively studied their clinical data, epileptic manifestations, and EEG findings.

In all patients, TIEF showed a type I pattern of serum transferrin, and molecular studies revealed three different mutations in four of the five children (*table 1*).

All patients had undergone one to 11 polygraphic video-EEG recordings in the Necker Enfants Malades Hospital.

Video-EEG recordings included polygraphic parameters, such as electrocardiogram (ECG), respiration measurements, and surface electromyography (EMG). The number of electrodes (silver chloride cup electrodes) was chosen depending on age and head size (ranging from 9 to 21) and placed according to the 10/20 international system using the medial frontal polar (FPz) as reference electrode. EMG was recorded by two cup electrodes placed 2 cm apart on one or both deltoid muscles. Recordings lasted at least one hour up

to 24 hours. Signals were amplified (x1,000), band-pass filtered at 0.01-97 Hz, and digitized at 256 Hz using the Deltamed Coherence EEG system (Deltamed/Natus Paris, France).

Results

Patient 1

Patient 1 was an 11-year-old female and the third child to healthy, unrelated parents. Two aunts (on the father's side) with psychomotor delay of unknown aetiology died during infancy; both were born at term with uneventful pregnancy. From birth onwards, feeding difficulties, poor eye contact, pendulum eye movements, and severe global hypotonia were observed. Segmental myoclonias started at the age of 2 months; at 4 months of age, she presented clusters of flexor spasms, described as asymmetric, upon awakening and during drowsiness that could be decreased in frequency by anticonvulsant therapy (vigabatrin, hydrocortisone, and topiramate).

Studies of metabolic blockage and enzyme activity revealed a deficiency in MT-1 and a molecular study confirmed the diagnosis of ALG1-CDG.

The video-EEG recording performed at the age of 9 months (under treatment with vigabatrin, hydrocortisone, and topiramate) showed a preserved, although slow for age, background activity, with occipital anomalies predominating on the right side without any hypsarrhythmia (*supplementary figures 1A, 2A*). During sleep, the recorded distal hand and feet myoclonias had no EEG correlate. During awakening, a long-lasting cluster of spasms was recorded with typical EEG features, but with very subtle clinical manifestations (*see video sequence [at 5 seconds] and supplementary figure 3*).

Patient 2

Patient 2 was a 10-year-old male and a first child to unrelated parents. Pregnancy was complicated by maternal hypertension and foetal growth retardation. Absent eye contact, psychomotor retardation, and severe axial hypotonia, as well as pyramidal signs were noted in the first three months of life. At the age of 4 months, he started with clusters of symmetric flexion spasms upon awakening. A few months later, in addition to spasms, daily generalized tonic seizures and very frequent distal myoclonias, particularly during sleep, occurred. Spasms responded to vigabatrin treatment, but segmental myoclonic jerks concerning the head and shoulders persisted and severe encephalopathy with spastic tetraplegia was established.

Studies of metabolic blockage and enzyme activity revealed a deficiency in MT-1 and a molecular study of the *ALG1* gene confirmed the diagnosis of ALG1-CDG. Eleven polygraphic video-EEGs were recorded between the age of 13 months and 7 years. Awake and sleep EEG showed abundant occipital anomalies (*supplementary figures 1B, 2B*). At the age of 18 months, a long-lasting (15-minute) cluster of epileptic spasms on arousal was recorded (*see video sequence [at 4 minutes] and supplementary figure 4*). Myoclonic jerks had no EEG correlate. The posterior anomalies persisted after cessation of spasms.

Patient 3

Patient 3 was a 12-year-old male, and a third child to healthy, unrelated parents. One older brother (born in 1996) presented the same disorder. The patient had moderate hydramnios during the third trimester of pregnancy; he was born at term. Since early life, feeding difficulties were noted, as well as an absence of eye contact, severe global hypotonia, and pyramidal signs. At the age of 6 months, he started having daily clusters of spasms upon awakening and frequent segmental myoclonic jerks. Despite several antiepileptic treatments (vigabatrin, hydrocortisone, valproic acid, topiramate, clonazepam, and clobazam), spasms and myoclonic jerks persisted, as well as severe axial hypotonia, pyramidal signs, severe psychomotor retardation, and agitated behaviour.

A molecular study revealed two allelic mutations in the *ALG6* gene, confirming the diagnosis of ALG6-CDG.

Four polygraphic video-EEGs were recorded between 11 and 21 months of age, disclosing an occipital polyrhythmic background activity with bilateral independent posterior spikes and sharp waves (*supplementary figures 1C, 2C*). Frequent segmental non-epileptic myoclonias were noted.

At the age of 11nbsp;months, a cluster of typical symmetric epileptic spasms was recorded after awakening, lasting for 30 minutes, as well as one isolated tonic spasm (*see video sequence [at 6 minutes, 14 seconds] and supplementary figures 5 and 6*). Posterior anomalies persisted and at the age of 21 months, these were also recorded as subclinical rhythmic sequences (*supplementary figure 7*).

Patient 4

Patient 4 was a 14-year-old male, and an only child of consanguineous parents. The patient had an unremarkable pregnancy, and was born at full term. Developmental delay was described, with late head control and free walking at the age of 2 years.

Table 1. Electroclinical features of 5 CDG patients presenting epileptic spasms, followed in Necker-Enfants Malades Hospital, Paris, between 2000 and 2013.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Actual age	10 years	11 years	12 years	14 years	6 years
Age at last evaluation	10 years	11 years	4 years	14 years	6 years
Gender	Female	Male	Male	Male	Female
CDG subtype	ALG1-CDG (CDG Ik)	ALG1-CDG (CDG Ik)	ALG6-CDG (CDG Ic)	CDG Ix	ALG11-CDG (CDG 1p)
Age at diagnosis of CDG	1 year (2006)	2 years (2006)	1 year (2004)	4 years	1 year
Complication during pregnancy	None	Maternal hypertension, foetal growth retardation	Moderate hydramnios	None	None
Early feeding difficulties	Yes	No	Yes	No	No
Muscular hypotonia	Yes	Yes	Yes	Yes	Yes
Early pyramidal signs	Yes	Yes	Yes	Yes	Yes
Microcephaly	Yes (-4SD)	Yes	Yes (-3.5SD)	No	Yes (-3SD)
Age at the beginning of spasms	4 months	4 months	6 months	18 months	5 months
Myoclonias	Segmental non-epileptic myoclonias	Segmental non-epileptic myoclonus; very rare discrete cortical myoclonias only in sleep at the age of 2 years	Segmental non-epileptic myoclonus	Cortical myoclonias	None
Other seizure types	Febrile GTCS	Tonic seizures	None	Rare tonic and tonic-clonic seizures during sleep; isolated, multifocal, cortical myoclonias	Focal clonic seizures

Table 1. Electroclinical features of 5 CDG patients presenting epileptic spasms, followed in Necker-Enfants Malades Hospital, Paris, between 2000 and 2013. (*Continued*).

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
EEG	Posterior theta rhythm, interposed with high-voltage and slow delta waves predominating on the right side, rare posterior spikes. Absence of physiological sleep graphoelements.	Posterior theta delta rhythm; abundant bilateral high-voltage spikes and spike wave activity in posterior regions. Absence of physiological sleep figures.	Polyrhythmic background with posterior theta and delta rhythm; rare bilateral independent posterior spikes and sharp waves.	Disorganized slow theta background activity, physiological sleep figures present.	Posterior high-voltage theta delta rhythm; abundant bilateral high voltage spikes and spike wave activity in posterior regions. Absence of physiological sleep figures.
Seizure evolution	Persistence of epileptic spasms and distal myoclonias.	Cessation of epileptic spasms (since 2/2014), persistence of rare segmental myoclonias	Persistence of epileptic spasms and distal myoclonias	Rare GTCS, no jerks	Cessation of epileptic spasms (since 6/2013)
Cranial MRI	(At the age of 6 months): normal myelination, discrete supratentorial atrophy, moderately thin corpus callosum, no posterior fossa abnormalities	Hypomyelination (or important abnormal myelination) at infra and supratentorial areas. Moderate cerebellar atrophy. Thin corpus callosum.	(At the age of 7 months): discrete myelination delay; no posterior fossa abnormalities	Normal myelination, normal configuration of the posterior fossa, moderate ventricular dilatation.	Pericerebral collection or enlarged subarachnoids spaces. Normal myelination and normal posterior fossa.
Evolution	Severe psychomotor retardation, spastic tetraplegia	Severe psychomotor retardation, no head control	Severe psychomotor retardation	Free walking, language delay, good interaction, behaviour problems (heteroaggressivity)	Severe psychomotor retardation, spastic tetraplegia.

GTCS: generalized tonic-clonic seizure; SD: Standard deviation.

At the age of 18 months, massive jerks started, as well as rare generalized tonic or tonic-clonic seizures during sleep. Antiepileptic therapy (phenobarbital, levetiracetam, clonazepam, clobazam, and lamotrigine) controlled seizures only partially. At the age of 11 years, severe language retardation, agitated behaviour, pyramidal syndrome, and strabismus were present.

Studies for enzymatic activity associated with CDG were normal and the molecular study of CDG genes failed to identify any mutation, establishing the diagnosis of CDG Ix.

Five video-EEGs were performed between 4 and 8 years of age.

Interictal EEG showed slow, disorganized background activity, but physiological sleep graphoelements without interictal paroxysmal anomalies (*supplementary figure 8*).

At the age of 4 years, seizures were recorded during wakefulness or drowsiness; isolated segmental cortical myoclonias and massive jerks evoking into epileptic spasms, although with unusual components (*see video sequence [10 minutes, 18 seconds] and supporting figure 9*). At the age of 11 years, seizures were poorly controlled and development severely delayed, associated with an aggressive and impulsive behaviour, however, with the ability to walk alone and to speak a few words.

Patient 5

Patient 5 was a 4-year-old female, and a first child of healthy, unrelated parents. The patient was born at term, after an uneventful pregnancy. Since early life, absent eye contact and global hypotonia were described. At the age of 5 months, epileptic spasms occurring in long-lasting clusters were observed, as well as long-lasting focal clonic seizures, which were pharmacoresistant (to vigabatrine, hydrocortisone, ACTH, carbamazepine, topiramate, clobazepam, clonazepam, stiripentol, and zonisamide). After the introduction of a ketogenic diet at the age of 23 months, spasms diminished rapidly with regards to frequency and duration of clusters, and occurred as isolated jerks which then completely disappeared. Antiepileptic treatment could slowly be reduced and stopped.

A molecular study confirmed the diagnosis of ALG11-CDG.

Five video-EEGs were performed between 9 months and 2 years of age.

Interictal EEG showed slow, disorganized background activity with very abundant bilateral independent occipital anomalies (*supplementary figures 1D, 2D*). At the age of 2 years, spasms were recorded, either isolated or in short clusters of 3-5, and sometimes, as seen in Patient 4, with an unusual aspect

associated with two distinct phases (*see video sequence [11 minutes, 38 seconds] and supplementary figures 10 and 11*).

Discussion

We report five children presenting epileptic spasms without hypsarrhythmia associated with various CDG syndromes. Despite the fact that epilepsy is one of the main neurological features described in CDG patients, detailed characterization of ictal semiology and neurophysiological patterns is rare (de Lonlay *et al.*, 2001; Morava *et al.*, 2008; Clayton and Grunewald, 2009; Dupré *et al.*, 2010; Jaeken, 2010; Freeze *et al.*, 2012; Funke *et al.*, 2013; Fiumara *et al*, 2016), and epileptic spasms without hypsarrhythmia associated with myoclonus have not yet been reported.

Epileptic spasms showed a typical EEG pattern in all patients, associated with particular features including only subtle motor manifestations, more sustained contractions, chewing movements, a combination of myoclonus and spasm, or a marked asynchrony and asymmetry. In contrast, typical hypsarrhythmia was never present during wakefulness or sleep.

Patients 1 and 2 (corresponding to two of the five patients described by Dupré *et al.,* 2010), both suffering from ALG1-CDK, started epileptic spasms at 4 months of age; the seizures in Patient 1 were pharmacoresistant. EEG showed very abundant occipital anomalies. Severe, refractory epilepsy has been previously described in ALG1-CDG (Clayton and Grunewald, 2009; Dupré *et al.,* 2010; Jaeken, 2010; Freeze *et al.,* 2012). All of the 11 ALG1-CDG patients published so far had "severe", "multifocal", "refractory" seizures or presented with an "early epileptic encephalopathy" (Grubenmann *et al.,* 2004; Kranz *et al.,* 2004; Dupré *et al.,* 2010; Fiumara *et al*, 2016). EEG was reported as "abnormal" in four children, "multifocal" in one child, and "with electroclinical features of Ohtahara syndrome" in another (Grubenmann *et al.,* 2004; Kranz *et al.,* 2004; Dupré *et al.,* 2010; Fiumara *et al*, 2016). The presence of epileptic spasms in this population, however, has never been described.

Concerning ALG6-CDG, the patient described here started refractory, generalized tonic seizures and clusters of epileptic spasms at 6 months of age. Similar to ALG1-CDG, there was no hypsarrhythmia and also very abundant interictal posterior anomalies. The majority of the 54 ALG6-CDG patients published so far (Haeuptle and Hennet, 2009; Ishikawa *et al.,* 2009; Dercksen *et al.,* 2012; Fiumara *et al*, 2016; Jaeken *et al.,* 2015) also had early-onset epilepsy. However, few publications describe seizures types and EEG tracings. Grunewald *et al.* (2000) reported eight patients with: febrile seizures (3/8), atonic seizures (2/8), myoclonic

seizures (2/8), generalized tonic-clonic seizures (1/8), as well as normal interictal EEG findings (6/8). Some case reports (Sun *et al.,* 2005; Ishikawa *et al.,* 2009; Al-Owain *et al.,* 2010; Dercksen *et al.,* 2012; Fiumara *et al,* 2016) also describe "severe epilepsy", febrile seizures, generalized seizures, complex partial seizures, atonic and myoclonic seizures, as well as generalized tonic-clonic seizures. EEG is, in some children, reported as "abnormal" (Dercksen *et al.,* 2012), but not further detailed. Overall, in the literature, many different seizure types in ALG6-CDG patients are reported, but epileptic spasms have not been described so far.

Our patient with ALG11-CDG presented typical epileptic spasms that were either in very long-lasting clusters or isolated, as well as very abundant posterior anomalies, but also focal clonic seizures and rare isolated massive jerks with a combination of myoclonus and spasm. Only four patients with ALG11-CDG subtype have been published so far (Rind *et al.,* 2010; Thiel *et al.,* 2012). Seizures were present in all children, but not further detailed, and EEG was described with generalized epileptic activity. Patients presented with early feeding difficulties, muscular hypotonia, and early-onset seizures.

Electroclinical presentation in our patient with CDG Ix was different compared to the other patients. EEG background activity was very slow and amplified, showing multifocal anomalies but preserved features of sleep. Seizures began later, at the age of 18 months, and consisted of tonic and tonic-clonic seizures, as well as sudden massive jerks, presenting as a combination of myoclonus and spasm. So far, 25 patients with CDG Ix have been described (Morava *et al.,* 2008, Millón *et al.,* 2011), presenting very heterogeneous clinical features. Epilepsy is reported in seven of them, but seizure types and EEG features are not detailed.

Epileptic spasms in the context of CDG have only been described in a case report of two siblings with dolichol kinase (DOLK) deficiency (DOLK-CDG or CDG-Im). Both started spasms at the age of 4 months (Helander *et al.,* 2013), with typical hypsarrhythmia on EEG. Both children presented other seizure types, such as generalized tonic-clonic and focal seizures, with complete seizure control which was easily obtained. Psychomotor retardation was less severe compared to our patients with free sitting at the age of 2 years and walking and bike riding at the age of 10 years.

Epileptic spasms in the absence of hypsarrhythmia have, to our knowledge, never been reported in CDG, and were, in our patients, associated with ALG1-, ALG6-, ALG11-CDG and CDG Ix subgroups. Interestingly, none of the 31 patients suffering from PMM2-CDG followed at our hospital presented epileptic spasms. Seizures in these patients occurred in one third (11/31), at an older age (medium: 4 years), and in 75% cases associated with fever, either (6/11) as brief generalized tonic-clonic events or prolonged focal seizures which often revealed a stroke-like episode (personal data; in preparation).

Absence of hypsarrhythmia in the presence of epileptic spasms was described in cortical lesions as focal cortical dysplasia or tubers in tuberous sclerosis complex (Dulac *et al.,* 2002; Caraballo *et al.,* 2003, 2011). In four of our five patients with CDG syndrome, common features included abundant occipital spikes, polyspikes, and fast rhythmic bursts with lateralization. Together with asymmetry and asynchrony of spasms, as well as focal seizures in one child, posterior structural anomalies were suspected before the diagnosis of glycosylation disorder. This was further underlined by the presence of associated symptomatology during the clusters with behavioural changes, chewing movements, facial fear expression, and hypersalivation. However, brain MRI did not disclose any focalized cerebral lesion in any of the patients.

In conclusion, our data show that epileptic spasms, notably when associated with myoclonus, are a possible feature of epilepsy in non-PMM2-CDG and exhibit particular EEG patterns which should be taken into consideration when investigating a child with epileptic spasms. For children diagnosed with CDG, we recommend polygraphic video-EEG recording for precise identification and characterization of seizures, allowing for more specific antiepileptic treatment. In addition, for children presenting with severe psychomotor retardation, microcephaly, epileptic spasms, together with interictal posterior anomalies without underlying focal MRI lesion, screening for CDG disorders should be considered.

Legend for video sequence

Patient 1. A 9-month-old girl with a long-lasting cluster of spasms (lasting for 7 minutes) upon awakening. Clinical manifestations of spasms are subtle, consisting of very discrete elevation of the shoulders and extension of arms, accompanied by discrete activity arrest and/or eye revulsion. In between the spasms, the child shows chewing movements and in the second part of the cluster, crying. Some discrete distal myoclonias of both arms are apparent. EMG1: right deltoid; EMG2: left deltoïd.

Patient 2. An 18-month-old boy with a long-lasting cluster of spasms upon awakening, with cortical myoclonias in sleep. At the start, there are discrete eye revulsion movements, progressively accompanied by motor manifestations consisting of asymmetric (predominately of the right arm) and asynchronous brief jerks concerning the head, shoulders, trunk, and arms. During the whole cluster, the child appears frightened and demonstrates chewing movements between the jerks. EMG2: right deltoid; ECG: left deltoid.

Patient 3. An 11-month-old boy with a long-lasting cluster of spasms upon awakening. Discrete motor manifestations consisting of flexion of both legs, associated with extension of the arms and movements of the head, are apparent. Between spasms, the patient demonstrates chewing movements and salivation. EMG1: right deltoid; EMG2: left deltoïd.

Patient 4. A 4-year-old boy with four isolated massive jerks with sudden extension of the arms and legs, accompanied by eye revulsion and head deviation towards the right side, followed by chewing movements, during sleep or wakefulness. Cortical myoclonus in sleep is also apparent. EMG2: right deltoid; ECG: left deltoid

Patient 5. A 2-year-old girl with discrete brief tonic contractions with extension of the four limbs, sometimes predominating over the right arm and left leg, associated with eye revulsion, either isolated or in series. Isolated jerks with subtle extension of both arms and massive flexion of both legs, accompanied by eye revulsion, are also apparent. EMG2: right deltoid; ECG: left deltoid.

Key words for video research on www.epilepticdisorders.com

Phenomenology: myoclonus, spasms
Localisation: occipital
Epilepsy syndrome: epileptic spasms
Aetiology: congenital disorders of glycosylation

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TEST YOURSELF

(1) Are epileptic spasms a possible feature in glycosylation disorders? If yes, for which subtype(s) have they been described?

(2) What other epileptic manifestations can be associated with spasms in non-Ia congenital disorders of glycosylation patients?

(3) What are the particular electroclinical patterns associated with spasms in non-Ia congenital disorders of glycosylation?

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, under the section "The EpiCentre".