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Case report

Nocturnal frontal lobe epilepsy in mucopolysaccharidosis

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Abstract

Nocturnal frontal lobe epilepsy (NFLE) is an epileptic syndrome that is primarily characterized by seizures with motor signs occurring almost exclusively during sleep. We describe 2 children with mucopolysaccharidosis (MPS) who were referred for significant sleep disturbance. Long term video-EEG monitoring (LT-VEEGM) demonstrated sleep-related hypermotor seizures consistent with NFLE.

No case of sleep-related hypermotor seizures has ever been reported to date in MPS. However, differential diagnosis with parasomnias has been previously discussed.

The high frequency of frontal lobe seizures causes sleep fragmentation, which may result in sleep disturbances observed in at least a small percentage of MPS patients. We suggest monitoring individuals with MPS using periodic LT-VEEGM, particularly when sleep disorder is present.

Moreover, our cases confirm that NFLE in lysosomal storage diseases may occur, and this finding extends the etiologic spectrum of NFLE.

Keywords: Sleep disturbances; Epilepsy; Mucopolysaccharidosis

1. Introduction

Nocturnal frontal lobe epilepsy (NFLE) is an epileptic syndrome primarily characterized by seizures that occur almost exclusively during sleep. Seizures are characterized by autonomic activation and bizarre motor behaviour of increasing complexity and duration; they range from simple and brief stereotyped motor events to paroxysmal arousals and major attacks [1,2]. The ictal signs associated with these seizures suggest that frontal lobes may be involved.

NFLE is a heterogeneous disorder with onset during infancy or childhood [3]; it may present in sporadic and familial forms, induce various seizure types, and be drug resistant in approximately 30% of patients. Symptomatic aetiology is present only in 13% of NFLE patients and most NFLE cases remain cryptogenic [1]. The majority of symptomatic patients experience symptoms due to focal cortical dysplasia [2]. Only 1 case with aspartylglucosaminuria and NFLE has been reported to date [4].

We describe 2 patients with mucopolysaccharidosis (MPS) who were referred for significant sleep disturbance. Long term video-EEG monitoring (LT-VEEGM) of these patients demonstrated sleep-related hypermotor seizures consistent with NFLE.

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2. Case reports

2.1. Case 1

Patient 1 was carried to term over the course of a normal pregnancy. After 1 year of age, the patient experienced psychomotor retardation, hyperactivity, coarse facial features, joint stiffness and macrosomia. At the age of 29 months, a genetic diagnosis of MPS type II was made. Electroencephalogram (EEG) showed spike–wave (SW) complexes over frontal regions. At 5.1 years the Stanford–Binet scale showed a mental age of 4.5 (IQ of 87). MRI, performed almost yearly between the ages 3 and 10 years, showed mild diffuse brain atrophy.

At the age of 8 years, the child received enzyme replacement therapy with Idursulfase, but this did not halt the neurological progression. At the age of 7 years, the patient suddenly presented with frontal non-convulsive status epilepticus (NCSE). Disappearance of ictal EEG activity was observed after ethosuximide therapy.

At the age of 10 years, significant sleep disorder and behavioural regression appeared. According to the patient's parents, sleep was disturbed by short episodes of sudden wakening with vocalizations, and chaotic motor activity. These episodes recurred several times a night.

To better understand the origin of the patient's sleep disorder, LT-VEEGM (2 nights) was performed. Because of significant hyperactivity, leads were positioned only for scalp EEG, surface electromyography (EMG) of the right and left deltoid muscles, electrocardiogram and abdominal pneumogram. During sleep, EEG showed spikes and sharp waves that were often repetitive over the frontal regions (Fig. 1A). Sleep was disturbed by frequent attacks of hyperkinetic automatism involving the inferior limbs (mainly pedalling), autonomic changes (mainly hyperventilation and tachycardia starting soon after the beginning of clinical motor signs), vocalization, frightened expression, and tonic/dystonic posturing of the left leg and foot (Fig. 2A). Ictal semiology was highly stereotyped. The duration was 12–15 s. At the end of each episode the patient was awake and required a number of minutes to fall back to sleep. Ictal EEG was partially obscured by movement artefacts; however, clinical seizures were often preceded by diffuse attenuated EEG activity and followed by rhythmic slow wave activity at 4–6 Hz over the frontal regions. In addition to these episodes, which we called major, we observed briefer attacks (duration of 3–8 s) that were characterized only by the latter part of major attacks (abrupt wakening, vocalization, frightened expression and tonic posturing of the left leg and foot).

The occurrence of motor symptoms of varying complexity during sleep was separately assessed by distinguishing between major and minor attacks. We were able to count 269 attacks (1 every 2–5 min) throughout the night: 159 were major attacks, and 110 were minor attacks. Paroxysmal episodes often occurred with periodic repetition. The numerousness of episodes produced fragmented sleep, in which it was difficult to recognize discrete sleep stages.

Antiepileptic treatment with clobazam and carbamazepine completely controlled seizure recurrence, and the quality of sleep and behaviour were significantly improved.

2.2. Case 2

Pregnancy and delivery were without complications. At the age of 3 years, a diagnosis of MPS-IIIA was suspected in this male patient on the basis of clinical phenotype (developmental delay during the 2nd year of age and facial dysmorphisms). The diagnosis was subsequently genetically confirmed. MRI, performed at 3 and 9 years, showed mild diffuse brain atrophy.

Our observation occurred at age 11; profound cognitive impairment, impaired speech development, hearing loss, uncontrollable hyperactivity and sleep disturbance were present.

According to the parents, sleep was disturbed by short episodes characterized by sudden wakening and chaotic motor activity. These episodes recurred several times each night. Two nights of LT-VEEGM were performed. Because of significant hyperactivity, leads were placed only on the scalp for EEG and the right and left deltoid muscles for surface EMG. During sleep, EEG showed spike and SW activity mainly over the frontal regions (Fig. 1B). Moreover, sleep was disturbed by frequent stereotyped attacks characterized by motor automatism (mainly pedalling), rotation of the trunk, vocalization and frightened expression (Fig. 2B). Paroxysmal episodes occurred throughout the night, often with a periodic repetition. Major attacks were 5–15 s in duration. Ictal EEG was obscured by movement artefacts. Additionally, we observed briefer attacks (1–3 s in duration) that were characterized only by some jerks of the legs; this was similar to the initial part of the major attacks. In 1 night, we were able to count 18 major attacks and 56 minor attacks. During the second night of monitoring, 10 mg of clobazam were administered, and the number of the seizures was significantly reduced. However, because of significant sedation and unsteadiness of the patient, clobazam was stopped after a few days. The parents refused other antiepileptic treatments for the patient.

3. Discussion

We describe 2 MPS patients referred for significant sleep disorder that was characterized by sudden