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Case Report

Moebius syndrome and narcolepsy: A case dissertation

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ABSTRACT

Moebius syndrome (MS) is a congenital syndrome characterized by unilateral or bilateral aplasia of the VI and VII cranial nerves, with consequent convergent strabismus and bilateral peripheral facial paralysis. This syndrome might be associated with diurnal excessive sleepiness and muscular hypotony, mimetizing in this manner, narcolepsy. The diagnostic criteria for narcolepsy depend on the presence of REM sleep during the day. As with patients with MS we do not have ocular movements due to the VI nerve paralysis, the absence of horizontal ocular movements might make it difficult to confirm narcolepsy in these patients. The common clinical characteristics of these patients are due to a possible impairment of the same structures that are affected in the central nervous system. However, the mechanism by which it occurs remains to be fully understood. Further electrophysiological researches are necessary to better clarify the association of these two diseases. The objective of this dissertation is to describe and discuss a case of Moebius syndrome with diurnal excessive sleepiness as a differential diagnosis for narcolepsy.

1. Introduction

Moebius syndrome (MS) is a congenital syndrome characterized by uni or bilateral aplasia of the VI and VII cranial nerves, with subsequent convergent strabismus and bilateral facial paralysis. Other cranial nerves might also be affected with minor frequency as the IX and X nerves. Mental and psychotic disturbances are also observed in these patients. MS might also be the result of maternal exposure to drugs such as benzodiazepines or misoprostol during the 4th to 8th week of pregnancy. Anatomopathological studies have shown a nuclear hypoplasia of the VI and VII nerves in patients with MS, suggesting malformation of the brain stem. Image studies such as cranial computerized tomography and nuclear magnetic resonance might reveal significant alterations in these patients [1–3].

Authors point out that, at polysonogram, these patients do not present REM sleep and there is the registry of low amplitude electromyogram of the mandible during all the sleep stages. The audible potential of the brain stem (APBS) frequently show an elongation of the evoked potential waves in this population with MS, indicating a dysfunction at the

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level of the brain stem. MS might still be associated with diurnal excessive sleepiness (DES) and cataplexy, which make it a differential diagnostic for narcolepsy [1].

Narcolepsy is a rare disease that may occur during any age. The onset of symptoms appears between 15 and 25 years of age. It is characterized by incontrollable attacks of sleep (with frequent naps with REM sleep) during the day, being classically described by an association between diurnal excessive sleepiness, sleep fragmentation, cataplexy, sleep paralysis and hypnagogic or hypnopompic hallucinations [4]. Although there is an association between the histocompatibility complex DR2/DQB1*0602 and narcolepsy, its etiology remains unknown. There are papers describing the symptoms of narcolepsy in patients with pathologies such as temporal processes, brain vascular episodes or demyelinazation of the brain stem and diencephalon [5–7].

The objective of this case dissertation is to describe a case of Moebius Syndrome and diurnal excessive sleepiness as a differential diagnosis for narcolepsy.

2. Case dissertation

T.P.S., female, 21 years old, single, high school graduate, unemployed, natural of São Paulo. She came to the outpatient facility with complaints of loss of motor tonicity of major muscle groups since the age of 5 years, worsening in the last 3 years. The frequency of the crisis varied from 2 to 6 times a day and was precipitated by moments of intense emotion.

She also showed fragmented sleep, diurnal sleepiness (Sleepiness Scale of Epworth 13), sleep paralysis, hypnagogic hallucinations, somniloquy, somnambulism, nightmares, difficulty of concentration and memory reduction, besides irritability, snoring from 3 to 4 times a week, awakening with suffocating sensation and body aches. She also referred sleepiness during more hours than the usual.

Her sleep routine was marked by 3–4 awakening during the night, waking up tired, invariably. She used to go to bed at 23 h and 30 min and wake up at 06 h and 00 min, taking approximately 10 min to initiate sleep. Denied use of alcohol or any other drugs. During the anamnesis, there were identified episodes of anxiety and depression due to prejudice concerning her physical appearance. As comorbidities, she also presented asthma and rhinitis. Family maternal history of snoring and her grandmother showed sleep apneas. She was being treated with inhaled budesonide, nasal budesonide and loratadine.

Physically, her weight was of 56.8 Kg, height of 1.54 m, corporeal mass index (CMI) of 24.2 kg/m^2, abdominal circumference of 72 cm and cervical circumference of 31 cm. Demonstrated Mallanpati II degree and tonsils grade I. Nasal evaluation showed hypertrophy and pallor of the inferior nasal cavities, septal deviation of II degree in the right area II. No other alterations were observed and at neurological examination the patient demonstrated peripheral facial paralysis with bilateral convergent strabismus. Brain magnetic resonance revealed nonspecific findings. It were not characterized the facial colliculi either the bilateral seventh cranial nerve. The neurological exam demonstrated bilateral convergent strabismus and bilateral peripheral paralysis.

The polysonogram was followed by the test of multiple sleep latencies (TMSL), together with the search for the alleles HLA-DQB1*0602 and HLA-DR by PCR Duplex. The Epworth Scale was equal to 17 (Tables 1 and 2). The research for the allele HLA-DQB1*0602 was positive and the allele HLA-DR was negative.

Although not all the traditional criteria for narcolepsy were fully present, we began the treatment with methylphenidate 5 mg in the morning and 5 mg in the afternoon, for a month. The treatment chosen was based on the presence of DES without any other identifiable causes and by the difficulty in identifying the REM sleep on the electrophysiological diagram in patients with MS. The patient was seen a last time on February 10th, 2014 and was stable, with important clinical improvements with the use of methylphenidate 20 mg per day and of amytriptilin 50 mg before bedtime.

3. Discussion

Sleep disorders have been described and valued upon MS, although the number of studies is still very small. An evaluation of 19 participants demonstrated that all enrolled patients with MS did refer some type of parasomnia, 50% of them refer poor quality of sleep and 25% of these patients with MS suffered from diurnal excessive sleepiness. Cataplexy was referred to by only 3 of these patients and only one of them did show the allele HLA DQB1*0602. However, in this study they did not perform polysonogram or the sleep multiple latency test [2].

It is well known that the present diagnostic criteria for the diagnostic f narcolepsy depend on the clinical findings and electrophysiological studies. The diagnostic criteria for narco-

Table 1 – Polysonogram parameters.

Latency to begin sleep (min)	19.7
Latency to begin REM sleep (min)	407
Sleep efficiency (%)	77.5
Time awake after beginning of sleep (min)	89.2
Awakening index (events/h)	19.5
N1 (%)	27.4
N2 (%)	53.3
N3 (%)	16.2
REM (%)	3.1
IAH (events/h)	0
IDR (events/h)	0.3
SaO2 minimum (%)	97
Desaturation index (events/h)	0

Apnea and hypopnea indexes (AHI); Respiratory disorder index (RDI); Arterial oxygen saturation arterial (SaO2).

Table 2 – Parameters of the sleep multiple latency test.

Average[a] of sleep latencies (min)	7.7
Episodes of REM sleep during the test	0

[a] Average referred to 5 nap opportunities.

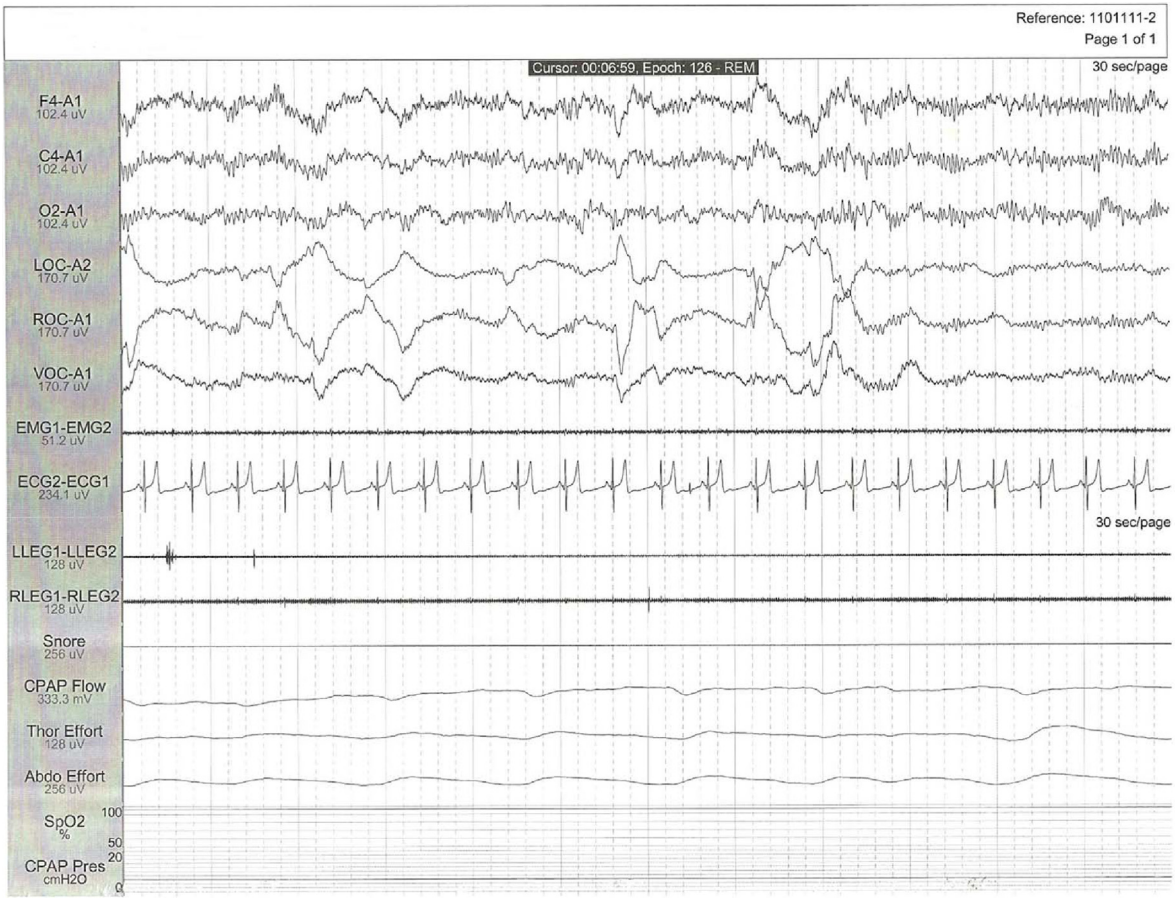

Fig. 1 – Epoch of REM sleep with multiple eye movement (ROC-A1 and LOC-A1).
Note: **In patients with MS, there is no rapid eye movement, as seen at this time of the REM of a patient with normal ocular motility.**

lepsy are the sleep multiple latency test demonstrating average latencies of less than 8 min and, at least, two episodes of REM sleep during the five nap opportunities in adults [4].

It is also known that the REM sleep is characterized, among other elements, by the rapid eye movement and muscle hypotony (Fig. 1). The absence of horizontal eye movements due to the paralysis of the VI nerves and the frequent muscle hypotony of the mandible in these patients makes it very difficult to identify REM on their exams [3]. As a consequence, we can underestimate the presence of REM on the polysonogram and sleep multiple latency tests, with the resulting impossibility of reaching diagnostic criteria for narcolepsy.

In MS, we might find necrosis in several areas of the brain stem, stem and high vertebral stem hypoplasia, besides nuclear agenesis of cranial nerves. Although the most accepted theory of narcolepsy is the one of autoimmunity with destruction of the hypocretin-producing cells in the hypothalamus, the physiology of narcolepsy is still unclear [4]. Expansive processes of the medium line such as craniopharyngiomas, vascular and demyelinating lesions of the brain stem and hypothalamus have been related to signs and symptoms of narcolepsy in some patients [5,6,8]. These findings strengthen the importance of the brain stem upon the physiopathology of these two entities. MS is characterized by heterogeneous lesions in the brain stem and high medulla spinalis [9]. This fact could explain the different sleep complaints found among this population.

The cataplexy attacks and other clinical characteristics of narcolepsy of these patients are most likely a consequence of the impairment of commonly affected structures on these two illnesses. In theory, the structural alterations on the brain stem region present in some of the patients with MS, would lead to narcolepsy with cataplexy [1]. For the abovementioned reasons, it becomes very difficult to distinguish the symptoms of sleepiness and cataplexy in the patients due to the congenital lesions observed in MS or to an associated narcolepsy. Further studies must be conducted to better characterize the affected areas in patients with MS and correlate them with the symptoms of diurnal excessive sleepiness and cataplexy.

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