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Case Report

Treatment of sleep central apnea with non-invasive mechanical ventilation with 2 levels of positive pressure (bilevel) in a patient with myotonic dystrophy type 1

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ABSTRACT

We are reporting a case of a 29 year-old female with diagnosis of myotonic dystrophy type 1 (Steinert's disease) with excessive daytime sleepiness, muscle fatigue, snoring, frequent arousals, non-restorative sleep, and witnessed apneas. Pulmonary function tests revealed a mild decrease of forced vital capacity. Nocturnal polysomnography showed an increase of apnea/hypopnea index (85.9 events/h), mainly of central type (236), minimal oxygen saturation of 72%, and end-tidal carbon dioxide values that varied from 45 to 53 mmHg.

Bi-level positive airway pressure titration was initiated at an inspiratory pressure (IPAP) of 8 and an expiratory pressure (EPAP) of 4 cm H_2O. IPAP was then gradually increased to eliminate respiratory events and improve oxygen saturation. An IPAP of 12cm H_20 and an EPAP of 4cm H_2O eliminated all respiratory events, and the oxygen saturation remained above 90%.

Bi-level positive airway pressure treatment at spontaneous/timed mode showed an improvement in snoring, apneas, and Epworth sleepiness scale decreased from 20 to 10. This case illustrates the beneficial effects of Bi-level positive airway pressure support in central sleep apnea syndrome of a patient with myotonic dystrophy type 1.

1. Introduction

Type 1 myotonic dystrophy (MD1, known as Steinert's disease) is a dominant autosomic multisystemic disorder caused by repeated expansion of trinucleotides (CTG) in the non-coded region of the gene *DMPK*, localized in the chromosome 19. Clinically, MD1 is characterized by the impairment of skeletal muscles, eyes, heart, endocrine system, respiratory system and central nervous system. It is considered the most common myotonic dystrophy at the beginning of the adult age. The sleep disorder of the type 1 myotonic dystrophy shows multifactorial etiology, maybe resulted from the muscle impairment, leading to alveolar hypoventilation, sleep obstructive respiratory disorders and effects upon the sleep regulatory circuits in the

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central nervous system. The clinical manifestations might be initiated during birth until adult age, depending on the quantity of trinucleotides repetitions in that particular individual [1]. Sleep central apnea syndrome is a respiratory disorder characterized by the interruption of the oronasal air flow and the absence of respiratory effort, of an intermittent or cyclic character, associated with symptoms (diurnal excessive sleepiness, frequent nocturnal awakenings, fatigue). The diagnosis of sleep central sleep apnea syndrome requires daytime symptoms and index of apnea/hypopnea index higher than 5 events per hour, being the central events higher than 50% of the respiratory events [2]. We describe a patient with the diagnosis of type 1 myotonic dystrophy and sleep central apnea syndrome, treated by non-invasive mechanical (NIV) ventilation with bilevels positive pressure.

2. Case report

A female patient, 29 years of age, with diagnosis of type 1 myotonic dystrophy (Southern-blotting hybridization technique with PM10MG probe, identifying a 11.0 Kb DNA fragment, which corresponds to approximately 334 CTG repetitions), being forwarded for evaluation with complaints of excessive daytime sleepiness (Epworth Scale = 20), muscle fatigue, fragmented and non-restorative sleep, snoring and witnessed apneas. At physical examination, we have observed a body mass of 24.6 kg/m^2, myopathic face, discrete bilateral palpebral ptosis and myotonic phenomena in tongue and hands ("hand grip" sign). No signs or symptoms of cardiomyopathy or cardiac insufficiency were observed. No medication was used. No other associated comorbities. Pulmonary function tests revealed mild restrictive ventilatory disorder with forced vital capacity (FVC) of 74% of the predicted value and the ratio of forced expiratory flow at the first second/FVC of 99%. Diagnostic polysomnography performed at the sleep laboratory, using the American Academy of Sleep Medicine guidelines[2], demonstrated marked increase of the apnea/hypopnea index (85.9 events/h). Of the 496 respiratory events, we observed 3 obstructive apneas, 236 central apneas, and 256 hypopneas. Baseline percutaneous oxygen saturation (SpO_2) was of 98%, with mean during sleep of 91%, and a minimum of 72%. The desaturation index was 95.1 events/hour during REM sleep and of 123.1 events/hour during non-REM sleep. The patient remained 22.8% of the total sleep time with SpO_2 below 90%. End-tidal carbon dioxide values varied from 45 to 53 mmHg. There were 145 arousals, the arousal index was 25.1/h. We have not observed Cheyne–Stokes respiration (Fig. 1). We have opted to treat with non-invasive mechanical ventilation (NIV) using bilevel positive pressure. We have also conducted a titration polysomnography in the laboratory, which normalized the apnea/hypopnea index (AHI of 3.4 events/h). The total number of respiratory events of was 16, being just 1 obstructive apnea, 16 hypopneas and none central/mixed apnea. Arousal index reduced to 15.3/h. Bilevel titration protocol during polysomnographyconsisted in initiating the EPAP setting at 4 cm of H_2O and IPAP of 8 cm of H_2O. The IPAP was gradually increased to eliminate respiratory events and oxygen desaturation. As protocol, respiratory rate was kept at 12 per minute. During the titration procedure, there was not a single presence of central apneas and the AHI remained normal. With positive airway inspiratory pressure (IPAP) of 12 cm of water and positive airway expiratory pressure (EPAP) of 4 cm of water, the oxy-hemoglobin saturation remained above 90% (Fig. 2) troughout the night. There was no objective improvement of sleep efficiency, however, the patient referred improvement on snoring, apneas and excessive daytime sleepiness (Epworth = 10).

3. Discussion

We reported a case of a patient with diagnosis of MD1 and sleep central sleep apnea syndrome, treated with Bilevel, showing improvement of the polysomnography parameters and some of the sleep-related symptoms. The presence of central apneas in patients with MD1 has been reported in patients with MD1 [3]. The etiology might be the result of a central nervous system impairment, with alterations on the central ventilatory control and afferent circuits from the intrapulmonary chemo and mechanoreceptors. The physiopathology might also include central apnea derived from an inadequate response to hypoxia and hypercapnia (*loop gain* anomaly) associated with hypercapnic respiratory insufficiency. Patients with periodic respiration and/or central apnea have ventilatory control instabilities. The *loop gain* is a physiologic measurement of this mentioned instability. There are several components of the "loop gain": the central controller (*controller gain*), the efficiency of carbonic gas excretion (*plant gain*) and the delays of blood circulation (mixing gain). As we observed the predominance of central apneas in this patient, we believe that we were faced with an anomaly of the central ventilatory command (*controller gain*).

The treatment of central sleep apnea syndrome might be obtained with positive airway continuous pressure (CPAP), nocturnal supplemental oxygen, or servo-adaptive ventilator. The use of Bilevel was associated, in patients with Cheyne–Stokes respiration, to a worsening of the central apneas and the periodic breathing [4]. Bilevel, at spontaneous/timed mode (S/T), might be considered for the correction of AHI during the central apnea syndrome associated with congestive heart failure, only if there was a therapeutic failure with the use of CPAP, supplemental oxygen and servo-adaptative ventilator [5].

Restrictive ventilatory disorders and alveolar hypoventilation syndromes in neuromuscular diseases are usually treated with Bilevel, providing support pressure and working volume. CPAP is not an adequate choice for this situation due to the continuous positive airway pressure, without generating tidal volume. The use of supplemental oxygen is not recommended due to the risk of worsening hypercapnia and gas exchanges. Considering the clinical picture, the natural history of the disease with possible evolution to restrictive ventilatory disorder and alveolar hypoventilation syndrome and the overlapping of the symptoms, we opted by treatment of Bilevel ventilatory support with spontaneous/timed mode (S/T). Neuromuscular diseases may demonstrate progressive muscle weakness with restrictive ventilatory disorder, alveolar hypoventilation syndrome, sleep obstructive apnea syndrome and other respiratory disorder related to sleep. The use of NIV with Bilevel is well established for this situation, with improvement of the respiratory symptoms, reduction of the respiratory workload, improvement of gas exchanges, improvement of

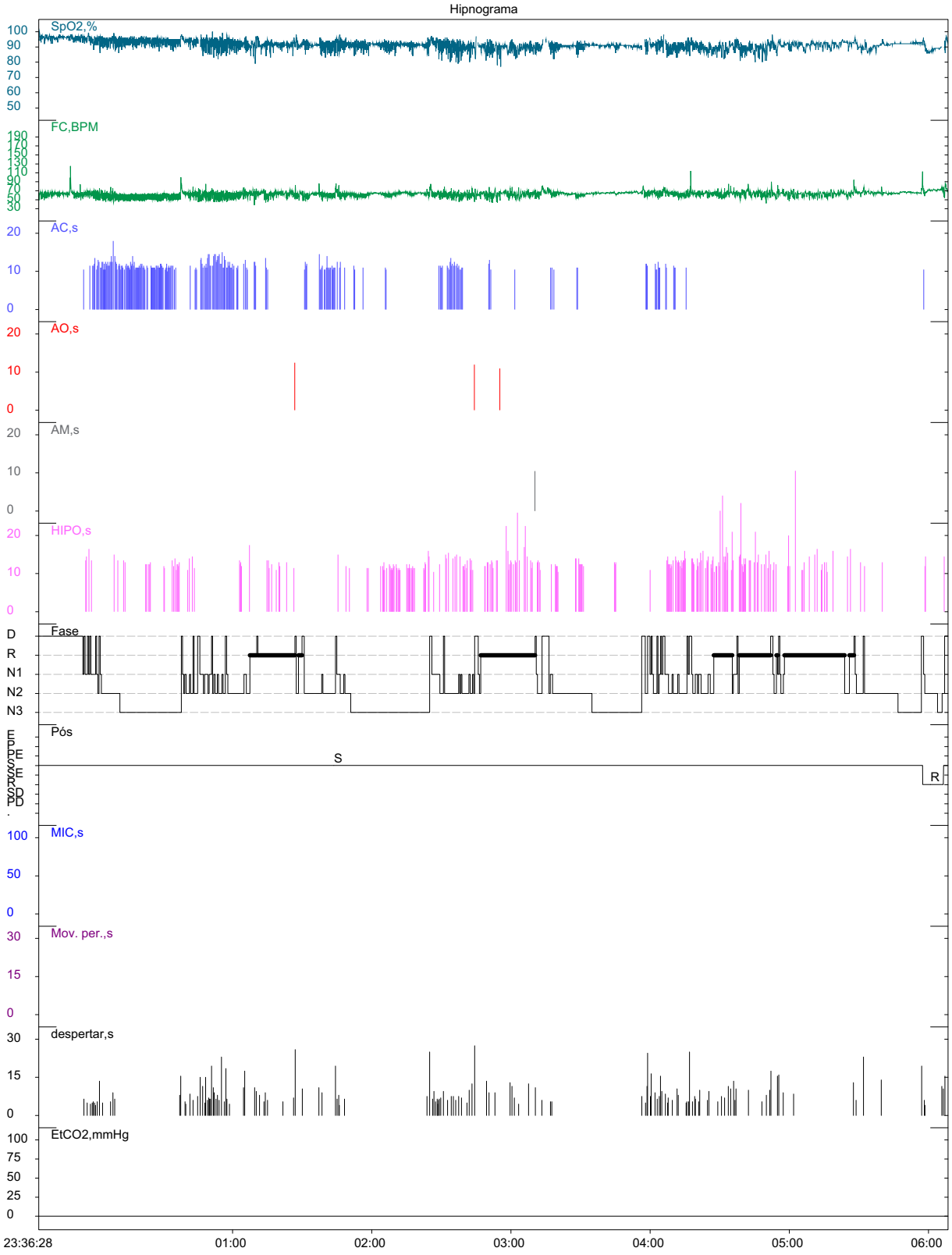

Fig. 1 – Diagnostic polysomnography report, demonstrating numerous respiratory events of central type (AC) and oxygen desaturation (SpO_2%).

patient's comfort, decreased risk of intubation, improvement of the duration and the quality of sleep, improvement of the functional *status*, and increased lifespan [6].

On the case here described, although the diagnostic polysomnography did not demonstrate important hypercapnia, the positive improvement showed by the patient suggests

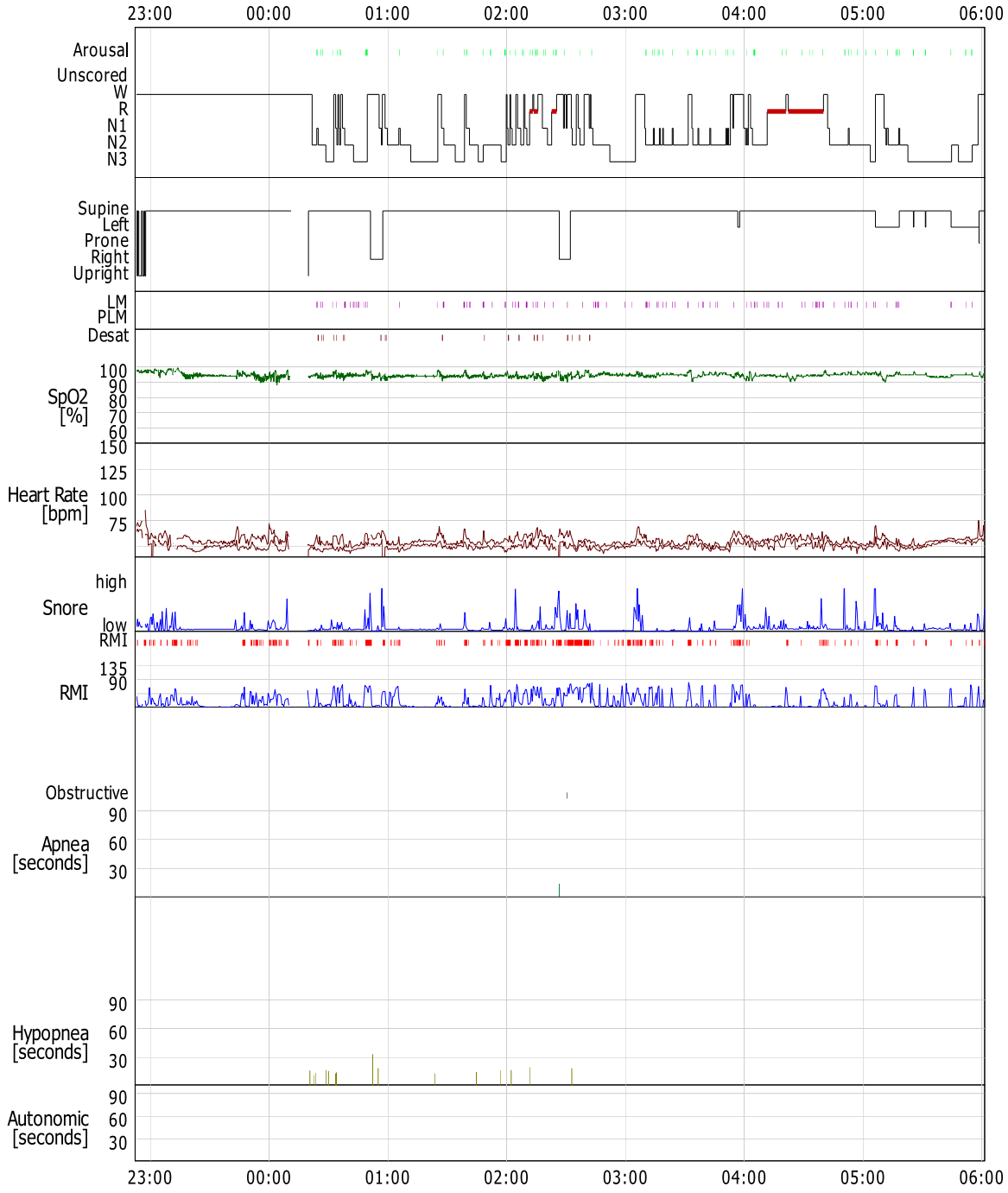

Fig. 2 – Bilevel titration polysomnography. Absence of central respiratory events and normalization of apnea/hypopnea and oxygen saturation indexes.

that she have central apnea associated with mild hypercapnia. A situation where the treatment with Bilevel is beneficial, in contrast with patients with congestive heart failure and Cheyne–Stokes respiration. To our knowledge, there is no specific information about the management of ventilatory support in central apnea in patients with MD1.

This case illustrates the beneficial effects of Bilevel for the correction of respiratory events of central origin, oxygen desaturation, and the sleep-related symptoms in a patient with myotonic dystrophy type 1.

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