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Central sleep apneas with Cheyne-Stokes breathing in a patient with narcolepsy type 1

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1. Introduction to the case

A Caucasian 14 years-old boy came to our attention because of sleep attacks and cataplexy. After a full sleep assessment, which included a normal video-polysomnography (V-PSG, Fig. 1a), a pathological maintenance sleep latency test (average latency 4 min, 4 SOREMPs), a positive haplotype for HLA DQB1 0602, and an undetectable orexin in CSF, a diagnosed of narcolepsy type 1 (NT1) was confirmed. An effective treatment with sodium oxybate (SO) 3g + 2.5g/night combined with venlafaxine 75 mg/day was established. This drug combination resulted effective on daytime sleepiness, cataplexy and sleep related hallucinations.

Seven years later, he reported a relapse of daytime sleepiness, nocturia and polydipsia. On a video-polysomnography (v-PSG) a severe central sleep breathing disorder with Cheyne-Stokes breathing (CSA-CSR) emerged (AHI 54.3/h, AHI REM 53/h, AHI NREM 57.7/h, central apneas 51.5/h, obstructive apneas 1.4/h, cycle length 46.5 s; see Fig. 1b) [1].

Neurological and cardiological evaluations, including echocardiography, were normal (ejection fraction 57 %) as well as blood creatinine, urea and electrolytes. A brain MRI with contrast was normal. The patient denied the utilization of opioids, of alcohol and of other illicit substances.

In order to exclude that CSA-CSR was induced by SO, we replaced SO with pitolisant 18 mg/day. Eight weeks later, a V-PSG showed the persistence of the CSA-CSR, without any amelioration (AHI 59.8/h, AHI REM 58/h, AHI NREM 60.2/h, central apneas 43.2/h, obstructive apneas 0.1/h cycle length 47.8 s; see Fig. 1c).

Considering the age of onset and polydipsia, we hypothesized a Rapid-onset Obesity with Hypothalamic dysfunction, Hypoventilation and Autonomic Dysregulation (ROHHAD). However, the patient had no nocturnal hypercapnia (as documented by the PSG-related capnography), no brain lesion, and no dysfunction of the hypothalamus/hypophysis axis (antidiuretic, thyreostimulant, thyrotropin-releasing, cortisol-releasing, growth hormons, prolactin and cortisol levels were normal).

A therapy with auto-Servo-Ventilation (EPAP of 4 cmH2O and a pressure support of 10 cmH2O) was titrated under PSG and resulted well tolerated and effective, with a complete regularization of breathing (see Fig. 1d). A concomitant immediate improvement of sleepiness after initiating ASV was noted in absence of any change of activating drugs (pitolisant).

. At the last follow-up, the patient was treated with venlafaxine 75 mg/day for cataplexy, methylphenidate immediate-release 10 mg/twice-a-day to improve vigilance, trazodone extended-release 50 mg/day for mild insomnia, and ASV with optimal compliance. The clinical course was favourable concerning sleep quality and sleepiness (Epworth sleepiness scale 9).

2. Image analysis

A) baseline NT1-diagnostic v-PSG with normal breathing pattern during sleep.
B) v-PSG performed during therapy with SO (5.5 mg/day, started 7 yrs before), showing a sequence of central apnoeas in the context of a Cheyne-Stokes respiration (CSR).
C) v-PSG performed after having withdrawn SO for 8 weeks, showing the persistence of CSR.
D) v-PSG performed during auto servo-ventilation (pressure support of 10 cmH20) showing a complete recovery of sleep-related breathing function.

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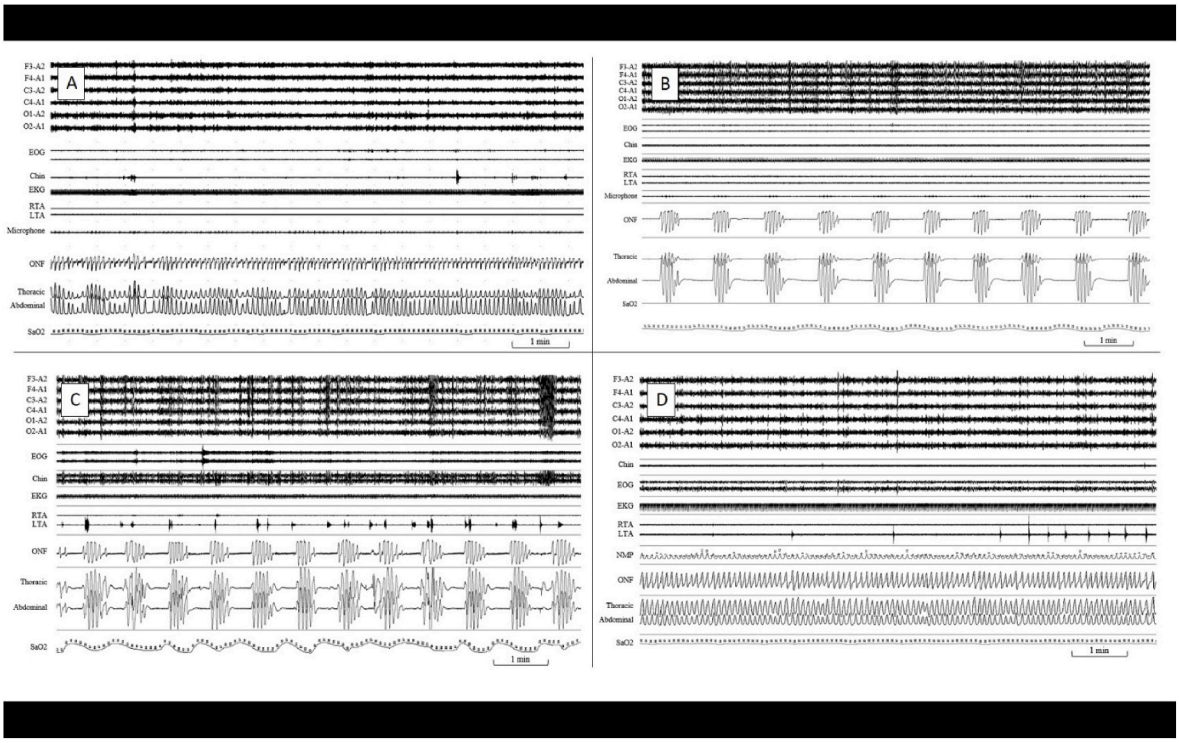

Fig. 1. Four polysomnographic samples of NREM sleep, lasting 10 min each, extracted from four different nights of recordings placed in chronological order. EOG = electrooculograms, Chin = mylohyoid muscle electromyogram, EKG = electrocardiogram, LTA = left tibialis anterior, RTA = right tibialis anterior muscle, ONF = oronasal flow, Thoracic = thoracic movements, Abdominal = abdominal movements, SaO2 = pulse oxymetry, NMP = nasal mask pressure.

3. Discussion

This is the first report of an overlap between NT1 and CSA-CSR, without remission after SO withdrawal. We evaluated this option because three cases indicate that SO can induce SRB, remitting after withdrawal [2–4]. Based on the current nosography we should interpret the picture as an overlap of NT1 with idiopathic CSA-CSR; however, it is interesting to speculate on the secondary etiology of CSA-CSR, which could be linked to the NT1-related orexin dysregulation. In fact, orexin-containing neurons project to the pre-Botzinger region of the rostral ventrolateral medulla and to the phrenic motoneurons, exerting a stimulatory effect. Also, the CO2 ventilatory response of locus coeruleus is stimulated by the orexinergic system [5]. Moreover, NT1 patients have a depressed hypoxic responsiveness [6]. Based on the evidences cited, CSR is not expected to be the consequence of a NT1-related orexin deficiency, which should theoretically lead to breathing depression and not to a periodic pattern. The effect of venlafaxine and pitolisant on breathing was considered, however, the absence of relative supporting literature and the good clinical efficacy convinced us not to change therapy.

CRediT authorship contribution statement

M. De Pieri: Study, Conceptualization, and design, Acquisition of data, Data handling and results. **M. Manconi:** Data handling and results. **S. Riccardi:** Data handling and results. **S. Miano:** Study, Conceptualization, and design, Data handling and results, All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] American academy of sleep medicine. AASM manual for the scoring of sleep and associated events. 2020.
[2] Frase L, Schupp J, Sorichter S, Randelshofer W, Riemann D, Nissen C. Sodium oxybate–induced central sleep apneas. Sleep Med 2013;14(9):922–4. https://doi.org/10.1016/j.sleep.2013.03.023.
[3] Hartley S, Quera-Salva MA, Machou M. Sodium oxybate and sleep apnea: a clinical case. J Clin Sleep Med 2011;7(6):667–8. https://doi.org/10.5664/jcsm.1480.
[4] Seeck-Hirschner M, Baier PC, von Freier A, Aldenhoff J, Göder R. Increase in sleep-related breathing disturbances after treatment with sodium oxybate in patients with narcolepsy and mild obstructive sleep apnea syndrome: two case reports. Sleep Med 2009;10(1):154–5. https://doi.org/10.1016/j.sleep.2007.11.018.
[5] Vicente MC, Dias MB, Fonseca EM, Bícego KC, Gargaglioni LH. Orexinergic system in the locus coeruleus modulates the CO2 ventilatory response. Pflügers Archiv 2016;468(5):763–74. https://doi.org/10.1007/s00424-016-1793-x.
[6] Han F, Mignot E, Wei YC, et al. Ventilatory chemoresponsiveness, narcolepsy-cataplexy and human leukocyte antigen DQB1*0602 status. Eur Respir J 2010;36 (3):577–83. https://doi.org/10.1183/09031936.00174609.