

HOSTED BY



ELSEVIER

Available online at [www.sciencedirect.com](http://www.sciencedirect.com)

ScienceDirect

[www.elsevier.com/locate/ssci](http://www.elsevier.com/locate/ssci)

CrossMark

## Case Report

# Narcolepsy with cataplexy after A/H1N1 vaccination – A case reported from Cuba

Yaimi Rosales Mesa, Miguel Gonçalves Meira e Cruz\*

Portuguese Association of Chronobiology and Sleep Medicine

## ARTICLE INFO

## Article history:

Received 31 October 2013

Accepted 28 December 2013

Available online 22 August 2014

## Keywords:

Narcolepsy

hypersomnolence

cataplexy

H1N1 vaccination

## ABSTRACT

Narcolepsy with cataplexy is a rare sleep disorder with a neurological basis which has been recently linked to H1N1 vaccination either in children or adults. Cases from Europe, United States and Brasil were registered. Authors describe a case report of a 15 years old boy who developed narcolepsy with cataplexy after H1N1 vaccination in Havana. As far as it is concerned this is the first case reported from Cuba.

© 2014 Brazilian Association of Sleep. Production and Hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/3.0/>).

## 1. Introduction

Narcolepsy with cataplexy is the most common type of central hypersomnia and is usually defined as a syndrome characterized by excessive daytime sleepiness (EDS), cataplexy, hypnagogic or hypnopompic hallucinations, sleep paralysis and disturbed nocturnal sleep [1].

Inability to remain fully alert is frequently the major problem for narcoleptic patients, which persistently affects their lives on a daily basis. Paradoxically adequate nighttime sleep continuity is not easy to achieve for those individuals [2]. Also not necessarily present, narcolepsy often occurs with a transient loss of muscle tone triggered by emotional stimuli (cataplectic attack). Therefore, diagnosis is based on clinical criteria confirmed by polysomnographic study followed by a multiple sleep latency test (MSLT) [3]. Although it can affect any age, the peak age of onset is the second decade of life with a reported incidence of 3.84/100,000 person years [4]. Narcolepsy onset is rare after age of 55 or prior to age 10 [5] but the interval between onset and diagnosis can be longer than 10 years [6], making it sometimes difficult to

establish the exact time of onset. Diagnostic delay is however less common when cataplexy is present and in younger patients [7]. Hypocretin, a neuropeptide originating from the hypothalamus, has been involved in the pathogenesis of narcolepsy with lower or undetectable levels of cerebrospinal fluid hypocretin-1 in most narcoleptic patients with cataplexy. Furthermore, there is a strong association with human leukocyte antigen (HLA) DQB1\*0602, which is involved in the control of the hypocretin receptor. More recently, associations with environmental factors such as streptococcal infection [8], seasonal influenza [9] and A/H1N1 2009 influenza [10] were reported and studied.

Authors describe a patient with narcolepsy with cataplexy after A/H1N1 vaccination in Hospital Almeijeiras in Havana as this is the first known case reported from Cuba.

## 2. Case report

A 15-year-old boy complaining of unexplained fatigue was first attended by the pediatrics office on November 2010. Such

\*Corresponding author.

E-mail address: [mmc@gentesaudavel.pt](mailto:mmc@gentesaudavel.pt) (M.G. Meira e Cruz).

discomfort started in June, two months after being vaccinated against the 2009 pandemic influenza A/H1N1 virus with Pandemrix™. Physical and neurological examinations were both negative and, at this time, pediatrician hypothesized secondary hypothyroidism which was not confirmed. By August, he gained additional 15 kg due to increased appetite including food ingestion during the night time and early in the morning. Two months later (October) he presented with sleep attacks during classes and poor sleep complains and after another two months (by December) he started showing a loss of muscular tone first affecting the perioral and periocular region, complaining of difficulties when trying to talk.

These sensations often occurred with dizziness and were interpreted as pretenses by his teachers and thus were subject to reprimand. These attitudes had forced him to change school. There were subsequent changes in his mood with a somewhat depression-like symptoms. There was no evidence of sleep paralysis, hallucinations or any other sleep disturbance. Skull magnetic resonance imaging and thyroid laboratory tests were all normal.

Polysomnographic study was performed in February 2011 disclosing a total sleep time of 7 h 35 min with sleep efficiency of 93.7% and a sleep latency of two minutes and the first period starting in REM sleep with an absence of any other prevalent pathologic findings as sleep-related breathing disorders or periodic limb movements. The MSLT immediately after the PSG test documented 4 sleep onset rapid eye movement periods (SOREMPs) with latencies up to 5 min (1.31 min in average). Identification of HLA-DQ6 was made by the PCR-SSP technique in February 2012. CSF hypocretin level could not be determined because this test was not available at that time in our hospital.

Based on the clinical findings and objective measures it was diagnosed as narcolepsy with cataplexy. The patient started treatment with methylphenidate (10 mg 3 times/day) for hypersomnolence. Despite subjective improvement on daytime sleepiness, a new MSLT in April 2011 showed no significant differences compared with the previous one. The patient was instructed to follow some sleep hygiene important roles as regular schedules and scheduled short naps in order to improve excessive sleepiness and was advised to avoid situations, which may lead to emotional stimulation and thus cataplectic attacks. No pharmacologic treatment was initiated for cataplexy since related symptoms were not severe and this was not a major concern for the patient. In February 2012 the patient showed some worry about side effects of methylphenidate like alopecia, sudoresis, increased frequency of headaches and cutaneous irritation, which led to the decision to abandon therapy. The patient is now 18 years old and is studying in university completing the first year. As the major part of his classes is in the afternoon, he can sleep at home during the morning. However, when he has classes during the morning he often falls asleep. Teachers are however aware of his condition. Currently he is followed in the sleep consultation department of our hospital.

### 3. Discussion

In 2010, first cases about a possible relationship between H1N1 flu vaccination and narcolepsy with cataplexy were

reported in the north of Europe [11]. Almost at the same time additional cases were independently reported in France, Canada and the United States [8] and by January 2011, there were 162 reported cases of narcolepsy after vaccination with Arepanrix™ [12]. Biological mechanisms behind this link are not clear, but an immunitory response to the vaccine adjuvant used in this patient is most likely since side effects suggestive of strong immune stimulation were reported after A/H1N1 vaccination, particularly with Pandemrix™ [13]. In those cases reported in the literature the onset of symptoms ranged from two days to five months after vaccination and many of them received vaccines with ASO3 as an adjuvant, which is the same adjuvant used in Pandmrix™. This supports the immunitary role and the link between vaccination and development of narcolepsy symptoms. The present case evolved after A/H1N1 vaccination with Pandemrix™. Diagnosis of narcolepsy was carried out according to the current guidelines and the short time that elapsed between vaccination and emergence of the clinical symptoms makes plausible the hypothesis of a link between both events. One important limitation of this work must be mentioned and it is regarding the fact that a single case was presented and thus the establishment of a probable association between H1N1 vaccination and narcolepsy can be indeed criticized with the argument that it can configure a subjective inference. On the other hand, it remains crucial to understand the widespread distribution of this relationship around the globe as well as its particular characteristics and mechanisms for what these reports can be of major relevance.

As founded by other authors, post-vaccine narcolepsy is more frequent than it was previously thought. Furthermore it requires an early diagnosis in order to prevent hypocretiner-gic neuronal damage, which will aggravate this peculiar and highly debilitating sleep-related neurologic condition.

### REFERENCES

- [1] Dauvilliers Y, Arnulf I, Mignot E. Narcolepsy with cataplexy. *Lancet* 2007;369:499-511.
- [2] Roth T, Dauvilliers Y, Mignot E, Montplaisir J, Paul J, Swick T, et al. Disrupted nighttime sleep in narcolepsy. *J Clin Sleep Med* 2013;9(9):955-65.
- [3] American Academy of Sleep Medicine. International classification of sleep disorders. Diagnostic and coding manual, second ed.. American Academy of Sleep Medicine; 2005.
- [4] Siber MH, Krahn LE, Olson EJ, Pankratz VS. The epidemiology of narcolepsy in Olmsted County, Minnesota: a population-based study *Sleep* 2002;25:197-202.
- [5] Guilleminault C, Cao M. Narcolepsy: diagnosis and treatment. In: Kryger MH, Roth T, Dement WC, Principles and practice of sleep medicine. Philadelphia: WB Saunders; 2010. p. 957-68.
- [6] Morrish E, King MA, Smith IE, Shneerson JM. Factors associated with a dela yin the diagnosis of narcolepsy. *Sleep Med* 2004;5:37-41.
- [7] Furuta H, Thorpy MJ, Temple HM. Comparison in symptoms between aged and younger patients with narcolepsy. *Psychiatry Clin Neurosci* 2001;55:241-2.
- [8] Aran A, Lin L, Nevsimalova S, Plazzi G, Hong SC, Weiner K, et al. Elevated anti-streptococcal antibodies in patients with recent narcolepsy onset. *Sleep* 2009;32:979-83.

- [9] Picchioni D, Hope CR, Harsh JR. A case control study on the environmental risk factors for narcolepsy. *Neuroepidemiology* 2007;29:185-92.
- [10] Miller E, Andrews N, Stellitano L, Stowe J, Winstone AM, Shneerson J, et al. Risk of narcolepsy in children and young people receiving AS03 adjuvanted pandemic A/H1N1 2009 influenza vaccine: retrospective analysis. *Br Med J* 2013; 346:f794.
- [11] National Institute for Health and Welfare recommends discontinuation of Pandemrix vaccinations. National Institute for Health and Welfare. ([http://www.thl.fi/en\\_US/web/en/pressrelease?id=22930](http://www.thl.fi/en_US/web/en/pressrelease?id=22930)); 2010.
- [12] Zaracostas J. WHO backs further probes into possible link between H1N1 vaccine and narcolepsy in children. *Br Med J* 2011;342:d909, <http://dx.doi.org/10.1136/bmj.d909>.
- [13] Waddington CS, Walker WT, Oeser C, Reiner A, John T Wilkins, et al. Safety and immunogenicity of AS03B adjuvanted split virion versus non-adjuvanted whole virion H1N1 influenza vaccine in UK children aged 6 months-12 years: open label, randomised, parallel group, multicentre study. *Br Med J* 2010;340:c2649, <http://dxdoi.org/10.1136/bmj.c2649>.