

# REPORT OF TWO NARCOLEPTIC PATIENTS WITH REMISSION OF HYPERSOMNOLENCE FOLLOWING USE OF PREDNISONE

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ABSTRACT - This article focuses on 2 clinical case reports of narcoleptic patients who experienced an absence of excessive sleepiness during treatment of other illnesses with 40 mg daily intake of prednisone.

KEY WORDS: narcolepsy, prednisone, treatment.

## **Relato de dois casos de pacientes com narcolepsia com melhora dos sintomas após uso de prednisona**

RESUMO - Este artigo refere-se à discussão de 2 casos de pacientes portadores de narcolepsia que apresentaram remissão de hipersonolência diurna excessiva durante tratamento de outras doenças com 40 mg de prednisona.

PALAVRAS-CHAVE: narcolepsia, prednisona, tratamento.

Narcolepsy is characterized by excessive daytime sleep and cataplexy. Sleep paralysis, hypnagogic hallucinations and sleep fragmentation can be added to this clinical picture<sup>1,2</sup>. Narcolepsy involves an unknown physiopathology but with a known association with the HLA DQB1\*0602 allele<sup>3</sup>. This would strengthen the hypothesis of a genetic origin. Other physiopathological hypotheses derive from the environment, infections and the immunological system. Abnormalities in the neurotransmission of hypocretin were recently described in narcoleptics<sup>4</sup>. Hypocretin is a neuropeptide synthesized by neurons whose cell bodies are located in the lateral hypothalamus. One of its functions is to modulate wakefulness. The association of hypocretin to dopaminergic pathways in frontal brain and noradrenergic pathways in the brain stem is well established. The smaller concentration of hypocretin in cerebral spinal fluid (CSF) has only been characterized in narcoleptics with cataplexy<sup>5</sup>. In an immunohistochemical study, a reduction in the quantity of hypocretinergic cells of the lateral hypothalamus was observed in patients with

cataplexy<sup>6</sup>. This observation was made following autopsy.

Patients with frequent outbursts of cataplexy highlight a greater prevalence of the HLA DQB1\*0602 allele along with a marked diminution of hypocretin in CSF when compared with patients with rare, atypical or absence of cataplexy.

A reduction in tumor necrosis factor (TNF) and interleukin-6 (IL-6) levels were described in narcoleptic patients and in one of our studies<sup>7</sup>, we noticed a reduction in subpopulations of T CD4 and B-lymphocytes in narcoleptic patients presenting frequent cataplectic attacks<sup>8</sup>.

Immunosuppressants have not normally been used when treating narcolepsy. One single case was found concerning a narcoleptic boy who had been treated with corticoid pulse therapy in the initial stages of the disease<sup>9</sup>.

This paper set out to describe the recovery from daytime somnolence associated to narcolepsy in two patients who took prednisone for bronchitis and ulcerative retocolitis respectively. Patients gave writ-

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ten consent to participate in studies concerning narcolepsy (UNIFESP-EPM 1139/03) and consented to the publication of their case report.

### CASES

**Case 1** – A 22-year old male, was diagnosed with narcolepsy in August 2004. He presented excessive daytime somnolence, frequent cataplexy and hypnagogic hallucinations. The initial symptoms started when he was 13. Epworth Sleep Scale was 15. HLA DQB1\*0602 was positive. Polysomnographic recordings showed no specific alterations and in the MSLT test we noted a sleep latency of 4 minutes with 2 episodes of REM sleep. Our patient received metilfenidate (20 mg/day) and imipramine (25 mg/day) for 6 months with significative diminution of the symptoms. Prednisone (40 mg/day) was initiated for treatment of inflammatory intestinal disease and after a week's treatment, the patient highlighted less somnolence and absence of cataplectic attacks. The patient ceased taking medication for narcolepsy on his own accord. After several months he was apparently free from any narcoleptic symptoms but continued to use prednisone.

**Case 2** – A 42 year-old male was diagnosed with narcolepsy in May 2003. He presented excessive daytime sleep and cataplexy. The initial symptoms started when he was 33. Epworth Sleep Scale was 18. Nocturnal polysomnographic recordings showed no specific alterations and MSLT tests showed a sleep latency of 3 minutes with 2 REM sleep episodes. HLA DQB1\*0602 was positive. He was medicated with metilfenidate (20 mg/day) and amitriptyline (24 mg/day) for 2 years with good control of symptoms. Following an asthma attack he was placed on 40 mg/day of prednisone for a fortnight. Several days after the beginning of corticoid treatment he displayed less daytime somnolence. He stopped metilfenidate intake and during 4 weeks went without any stimulants. He remained free of daytime somnolence during this period.

### DISCUSSION

Our understanding of narcolepsy has improved in recent years. The greater prevalence of the HLA DQB1\*0602 allele in patients with narcolepsy and cataplexy is well known<sup>3,4</sup>. The discovery of hypocretin and its reduction through cell loss in the lateral hypothalamus in patients with frequent cataplexy is one possible explanation for the main clinical symptoms in narcolepsy<sup>4</sup>.

Currently, the treatment of narcolepsy is based

only on symptomatological control. Given that modafinil is not an authorized medication in Brazil, we used only metilfenidate to control the daytime somnolence and administered tricyclics to minimise cataplectic attacks. Currently, there is no treatment that can halt the evolution of the disease, as the exact physiopathological mechanism is unknown<sup>6</sup>.

Analysing recent papers on narcolepsy, we noted a single report of corticoid use<sup>9</sup>. The discussion of that case report claimed that the possible immunological auto-agression occurs only during the initial stages of the disease.

For our patients, two hypotheses can be formulated to explain the changes in their narcoleptic outlook. Corticoides can reduce somnolence through an arousing and independent effect without any relation to the mechanisms underpinning narcolepsy. Some interactions of the hypothalamic-pituitary-adrenal (HPA) axis and sleep are known<sup>10</sup>. There is also a possible impact on physiopathological mechanisms of narcolepsy leading to a reduction of symptoms.

We believe that these case reports can add to the debat surrounding pathophysiological mechanisms involving narcolepsy.

### REFERENCES

1. Yoss RE, Daly DD. Criteria for the diagnosis of the narcoleptic syndrome. *Mayo Clin Proc* 1957;32:320-328.
2. ICSD-2. International classification of sleep disorders, 2.Ed. Diagnostic and coding manual. American Academy of Sleep Medicine, 2005.
3. Mignot E, Lin L. Complex HLA DR and DQ interactions confer risk of narcolepsy-cataplexy in three ethnic groups. *Am J Genet* 2001;68:686-699.
4. Nishino S, Ripley B, Overeem S, Lammers GJ, Mignot E. Hypocretin (orexin) deficiency in human narcolepsy. *Lancet* 2000;355:39-40.
5. Peyron C, Faraco J, Rogers W, et al. A mutation in a case of early onset narcolepsy and a generalized absence of hypocretin peptides in human narcoleptic brains. *Nat Med* 2000;6:991-997.
6. Black JL 3<sup>rd</sup>. Narcolepsy: a review of evidence for autoimmune diathesis. *Int Rev Psychiatry* 2005;17:461-469. Review.
7. TNF and IL-6 levels in narcoleptic patients. *Revista Einstein*, submitted.
8. A study of T CD4, CD8 and B lymphocytes in narcoleptic patients. *Arq Neuropsiquiatr*, submitted.
9. Hecht M, Lin L, Kushida CA, Taheri S, Mignot E. Report of a case of immunosuppression with prednisone in an 8-year-old boy with an acute onset of hypocretin-deficiency narcolepsy. *Sleep* 2003;Nov1; 26:809-810.
10. Buckley TM, Schatzberg AF. On the interactions of the hypothalamic-pituitary-adrenal (HPA) axis and sleep: normal HPA axis activity and circadian rhythm, exemplary sleep disorders. *J Clin Endocrinol Metab*. 2005;90:3106-3114.