

THE IMPORTANCE OF HLA DQB1*0602 TYPING IN SLOVENE PATIENTS WITH NARCOLEPSY

LEJA DOLENC-GROŠEL and DAVID B. VODUŠEK

Institute of Clinical Neurophysiology, Division of Neurology, University Medical Centre, Ljubljana, Slovenia

Abstract: The HLA class II region genes DQB1*0602 and DQA1*0102 are currently the best genetic predictors for narcolepsy in humans [1]. The aim of this study was to identify the HLA DQ alleles (DQB1*0602 and DQA1*0102) in Slovene sporadic narcoleptic patients. 11 patients who fulfilled ICSD criteria for narcolepsy entered the study. DRB1*1501 DQB1*0602 was present in all the patients while DQA1*0102 was absent in 2 patients. We propose that DQB1*0602 typing is important in diagnosing narcolepsy in Slovene patients.

Key Words: Narcolepsy, HLA DQ Alleles (DQB1*0602) Typing.

INTRODUCTION

Narcolepsy is a sleep disorder which is characterised by excessive sleepiness that is typically associated with cataplexy and other REM (rapid eye movement) sleep phenomena such as sleep paralysis and hypnagogic hallucinations. The International diagnostic criteria for narcolepsy [2] are based on clinical observation with or without polysomnographic recording, because no specific laboratory markers have so far been identified. The HLA class II region genes DQB1*0602 and DQA1*0102, however, occur in almost all patients, while being present in only 25% of the control Caucasian population [3]. According to the reported prevalence stated by Mignot *et al.* [3], there should be 400 patients with narcolepsy in Slovenia (2 million inhabitants). There are, however, only 40 clinically confirmed cases on our record.

METHODS

Eleven consecutive sporadic patients who fulfilled ICSD criteria for narcolepsy from the out-patient clinic of the Institute of Clinical Neurophysiology, Division of Neurology, University Medical Centre Ljubljana, were entered into the study. In addition to a neurological examination, whole night sleep recording, and a mean sleep latency test (MSLT) were performed. Their Human Leukocyte Antigen (HLA) DQ alleles DQB1*0602 and DQA1*0102 were determined by the PCR oligotyping technique.

RESULTS AND DISCUSSION

On clinical observation, complaints of excessive sleepiness and sudden loss of muscle tone in association with intense emotion (cataplexy) were found to be present in all the patients. However, other REM sleep features were missing in some patients (hypnagogic hallucinations in 5 of 11 and sleep paralysis in 6 of 11 patients). The mean sleep latency test (MSLT) was abnormal (less than 5 minutes, and two or more sleep-onset REM periods) in all the patients. DQA1*0102 was absent in 2 patients (Tab. 1), while DQB1*0602 was present in all patients. 6 out of 11 patients were DQB1*0602 homozygotes.

Tab. 1. Clinical observation, polysomnographic recordings and HLA typing in narcoleptic patients (present = +, absent = -). DQB1*0602 homozygotes (++)

patient	excessive sleepiness	cataplexy	hypnagogic hallucinations	sleep paralysis	MSLT < 5 min	2 or more REM on MSLT	DQB1*0602	DQA1*0102
No 1	+	+	-	-	+	+	++	+
No 2	+	+	+	+	+	+	+	+
No 3	+	+	+	-	+	+	++	-
No 4	+	+	+	+	+	+	++	+
No 5	+	+	-	+	+	+	+	+
No 6	+	+	+	+	+	+	+	+
No 7	+	+	+	+	+	+	++	-
No 8	+	+	+	-	+	+	++	+
No 9	+	+	-	-	+	+	++	+
No 10	+	+	-	-	+	+	+	+
No 11	+	+	-	-	+	+	+	+

Despite the small number of patients in our study, we propose that DQB1*0602 typing is important in diagnosing narcolepsy in Slovene patients. These results need to be confirmed in a larger study.

REFERENCES

1. Lin, L., Hungs, M. and Mignot, E. Narcolepsy and the HLA region. **J. Neuroimmunol.** 117 (2001) 9-20.
2. Guilleminault, C. Narcolepsy. In: **The International Classification of Sleep Disorders: Diagnostic and Coding Manual**. Diagnostic steering committee, (Thorpy MJ. Ed.) American sleep disorders association, Allen Press, Rochester 1990, 38-42.
3. Mignot, E., Young, T., Lin, L. and Finn, L. Nocturnal sleep and daytime sleepiness in normal subjects with HLA-DQB1*0602. **Sleep** 22 (1999) 347-352.