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Narcolepsy with cataplexy in patients aged over 60 years: a case-control study

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ABSTRACT

Objective: Narcolepsy with cataplexy (NC) is a chronic disabling disease; however, there are insufficient data on older NC subjects.**Methods:** A cross-sectional evaluation on health and social status, including intensity and progression of NC symptoms, was performed on 42 NC patients (age 71.9 years \pm 7.5) and 46 age-and-sex-matched controls (age 72.2 years \pm 7.0).**Results:** A greater proportion of patients than controls suffered from hypertension and type 2 diabetes. More controls had a history of treated depression; however, according to the Geriatric Depression Scale, more NC patients scored in the range of depression. There were no significant differences in Addenbrook Cognitive Examination scores. Average physical fitness assessed by the Short Physical Performance Battery was lower in the NC group. The frequency of meeting with family, friends, and participation in hobbies or sports did not differ between the two groups.**Conclusions:** Symptoms of NC were present throughout life. Comorbidities and lower physical fitness, which are known to be present in young and middle-aged NC subjects, were also present in older patients. Although NC subjects were less professionally active during their lifetime, they did not differ from controls in important social parameters in older age.

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1. Introduction

Narcolepsy with cataplexy (NC) is a chronic neurological disease with a prevalence of approximately 0.045% in North America and Europe [1]. The pathologic basis of the disease is a deficiency of neurons in the lateral hypothalamus that produce hypocretin [2]. The HLA DQB1*06:02 allele is present in nearly 100% of cases [3]. Narcolepsy with cataplexy is very likely a T-cell-mediated autoimmune disease similar to other HLA-associated diseases such as type 1 diabetes and celiac disease, with its onset triggered by an external stimulus such as streptococcal infection or vaccination against H1N1 influenza [4].

The leading symptoms of NC are excessive daytime sleepiness (EDS) and cataplexy, and roughly half of patients experience

hypnagogic hallucinations (HH) and sleep paralysis (SP). Additionally, most patients have fragmented nighttime sleep. Dysregulation of rapid eye movement (REM) sleep is typical, with REM sleep occurring within the first 15 minutes of sleep onset, termed sleep onset REM periods (SOREMP), during the day and night [5]. The age at onset varies from childhood to approximately 60 years of age, with manifestation most often at 15–20 years of age, and a second peak between 35 and 40 years [6]. In many patients, the latency from first manifestations to diagnosis is rather long [7]. The intensity of key NC symptoms – EDS and cataplexy – usually remains stable throughout life [5] but may also decrease slightly with age [8,9].

Narcolepsy with cataplexy is a lifelong disease; however, most cohort studies in narcolepsy describe de novo patients or patients followed in specialized centers, and thus the average age of patients in these studies is usually in early adulthood or middle age. Information regarding the clinical picture of the NC and its changes in older subjects, comorbidities arising with age, functional capabilities, cognitive function, and psychosocial consequences of NC in older populations is limited.

The aim of the present study was to perform a cross-sectional evaluation on health status, including intensity of NC symptoms,

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quality of life, and social status in NC patients aged >60 years, in comparison with age- and sex-matched controls.

2. Methods

2.1. Participants and study design

The study was conducted at a tertiary hospital, in a sleep disorders center providing long-term care of hypersomnia patients, between 2012 and 2015. Patients aged >60 years of age and previously diagnosed with NC were invited to participate in the study. All patients fulfilled the diagnostic criteria of the *International Classification of Sleep Disorders*, second edition (ICSD2) [10]. The records of subjects diagnosed before 2005, the year of ICSD2 publication, were carefully checked, and conformity with ICSD2 was verified. None of the patients were tested for CSF hypocretin, as this examination was unavailable. Only patients were included with undisputable cataplexy that was present in their history and/or at the time of the study.

A total of 73 narcoleptic patients were identified from the departmental database that met the age criterion and had a diagnosis of NC. Of these, 29 regularly attended the clinic, at least once per year, while five attended irregularly; all were included in the study. Of the remaining patients, 18 were successfully contacted who had not attended the department for years (eight were included in the study, 10 refused to participate due to difficulties in reaching the hospital because of generally poor health or mobility, and/or residence far from the department, and/or low motivation), and six were found to be deceased. Thus, a total of 42 patients with NC participated in the study [18 male (42.9%), 24 female (57.1%), mean age 71.9 ± 7.5 years].

Sleep comorbidities, particularly obstructive sleep apnea (OSA), restless legs syndrome (RLS), and REM sleep behavior disorder (RBD) were also diagnosed according to the ICSD2 [10].

Forty-six age-matched and sex-matched controls [19 men (41.3%) and 27 women (58.7%), mean age 72.2 ± 7.0] were subjected to the same protocol. Control subjects were recruited from a leisure activity center for the elderly, the University of the Third Age (Charles University, First Faculty of Medicine), or were neighbors of the three co-authors. A wide range of control subjects was aimed for.

Both groups were selected from the same region (Prague and Central Bohemian region). For both groups, the subjects needed to be able and motivated to attend the department and participate in a long interview and examination; thus, the subjects who were very unwell were not included.

Instruments

All participants were examined in person. The examination lasted approximately two hours and consisted of the following:

- A structured interview regarding current disease status and its development throughout life, including sleep duration and intensity of the symptoms. The interview included the following items:
 - Age of EDS and cataplexy onset
 - Age at diagnosis
 - Intensity of EDS by decade from disease onset on a scale of 0–3 (none, mild, medium, and severe)
 - Severity and frequency of cataplexy from onset; severity on a scale of 0–4 (none, virtually imperceptible, slight drop of chin or hands, noticeable fall to knees, fall) and the rate on a scale of 0–5 (none, <1 per year, 1–11 per year, 1–3 per month, 1–6 per week, ≥ 1 daily)

- Severity of HH by decade on a scale of 0–5 (none, <1 per year, 1–11 per year, 1–3 per month, 1–6 per week, ≥ 1 daily)
- Severity of SP frequency by decade on a scale of 0–5 (none, <1 per year, 1–11 per year, 1–3 per month, 1–6 per week, ≥ 1 daily)
- Presence of automatic behavior
- Estimate of 24-hour sleep duration by decade from 20 years of age, irrespective of age at onset
- Interview concerning NC symptoms was carried out with the exception of retrospective estimation of 24-hour sleep duration only in NC patients and not in controls.
- A structured interview regarding overall health in the past and at present, with focus on the most common diseases, their course and treatment, including weight [implicitly body mass index (BMI)] and smoking status. In some cases, the type of comorbid disease was only approximately known, thus illnesses were designated into groups: cardiovascular, endocrinological and metabolic, gastrointestinal, urological, respiratory, rheumatological, oncological, orthopedic and status after injuries, neurological, psychiatric, and sleep. Due to previously observed higher incidences of metabolic and cardiovascular diseases, comparison of select diseases in these categories was performed separately. In the women, gynecological history was additionally investigated.
- A structured interview on quality and social aspects of life, including information on: marriage, completed education, number of children, employment, and leisure activities including sports and social activities.
- Completion of Czech versions of questionnaires and scales:
 - Epworth Sleepiness Scale (ESS): norm in the general population ≤ 10 [11]
 - Geriatric Depression Scale (GDS): in the general population 0–5 points corresponds to normal affect without depression, 6–10 points mild depression, and >10 points overt depression requiring detailed examination [12]
 - State-Trait Anxiety Inventory (STAI X-2): in the general population 20–29 corresponds to no or mild anxiety, 30–44 medium anxiety, 45–55 intense anxiety, and 56–60 extremely intense anxiety [13]
 - Visual analog scale (VAS) from Euro Quality of Life (EQ-5D): subject assesses current health status from 0 to 100, where 0 is the worst and 100 the best imaginable health status [14]
 - Addenbrook Cognitive Examination (ACE): assessment of cognition in areas: attention and orientation, memory, verbal output, language, and visual-spatial abilities [15].
- Short Physical Performance Battery (SPPB) consists of a balance test (standing with feet together, standing in a semi-tandem position and a tandem position), a gait speed test, and a test on rising from a chair. Values 10–12 represent good physical fitness, 7–9 reduced physical fitness (pre-frailty) and indicates clinical evaluation and further care, and <6 represent frail seniors at high risk of dependence [16].

Information on the development of narcolepsy, general health, and polysomnographic (PSG) data were supplemented from patient documentation. The Ethical committee of the General University Hospital in Prague approved the study, and all subjects provided signed and informed consent.

Statistical analyses

Data from the two groups were statistically compared using Statistica 12 software (StatSoft, Inc. 2013). Categorical data were tested by the Chi-squared test, ordinal data by the Mann-Whitney test, and normally distributed continuous variables were compared using Student's *t*-test or ANCOVA.

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