



# Type 1 narcolepsy without cataplexy and treatment progress: a case report

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**Abstract:** Narcolepsy is a sleep disorder with the main manifestations of excessive daytime sleepiness, cataplexy, sleep paralysis, sleep hallucinations, and nighttime sleep disturbance. It is still not fully recognized by clinicians, and many patients are often misdiagnosed with epilepsy, syncope, or mental disorders. In the present study, we report the first case of narcolepsy diagnosed at the district, with a complete medical history, objective examinations, and cerebrospinal fluid and hematological tests, but no cataplexy. Multiple sleep latency test (MSLT) showed that the average sleep latency was 3.1 min, and abnormal REM sleep episodes were detected in 4 naps. The average REM latency was 1.3 min. We review the knowledge and researches on this disease in Mainland China in the past 10 years. Data from China in 2014 showed a significant increase in the incidence of narcolepsy in 2011 after the H1N1 epidemic in China in 2009. Despite the low incidence rate, diagnosis of narcolepsy is still confusing and needs clinicians' attention. Whether the incidence of narcolepsy may increase after covid19 remains to be observed. So far, there is no clear evidence to support immunotherapy. In conclusion, further studies are needed to verify more treatments and improve the patient's life quality.

**Keywords:** Narcolepsy; sleep disorder; polysomnographic (PSG), case report

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## Introduction

Narcolepsy is a sleep disorder with the main manifestations of excessive daytime sleepiness, cataplexy, sleep paralysis, sleep hallucinations, and nighttime sleep disturbance. It is the most common disease that causes daytime sleepiness other than obstructive sleep apnea (OSA). Approximately 0.026–0.05% of the US population is affected by this disease, making it a rare condition (1,2); however, we cannot rule out the possibility that many potential patients have not been diagnosed. Narcolepsy is considered to be a genetic autoimmune disease of the brain that usually onsets in childhood or adolescence (3). Diagnosis requires polysomnographic (PSG) recordings and a multiple

sleep latency test (MSLT). The average sleep latency of narcolepsy is less than 8 min, with more than 2 early-onset cycles of rapid eye movement (REM) sleep. Narcolepsy can be combined with increased appetite, obesity, and snoring, making it easily misdiagnosed as OSA-hypopnea syndrome. Recent studies have suggested that REM-related OSA is also closely related to narcolepsy (4).

According to the International Classification of Sleep Disorders III, narcolepsy is classified as Types 1 and 2. Type 1 narcolepsy is mainly characterized by excessive sleepiness and cataplexy caused by emotional factors (i.e., laughter and anger), and may also manifest as sleep paralysis, hallucinations before falling asleep, nighttime sleep disturbance,

cardiovascular–metabolic abnormalities (i.e., obesity, type 2 diabetes, OSA, and other cardiovascular diseases), neurological complications (i.e., mood disorders, anxiety, eating disorders, and attention deficit hyperactivity disorder), and other sleep disorders (restless leg syndrome, periodic leg movements, and REM sleep behavior disorder) (5). Type 1 narcolepsy is associated with irreversible damage of the hypocretin neurons. Hypocretin level in the cerebrospinal fluid (CSF) <110 pg/mL can confirm the diagnosis of type 1 narcolepsy, while 20% of these patients have no cataplexy. HLA DQB1\*0602 allele positivity is also often detected in type 1 patients, suggesting that the disease has a certain genetic background. The symptoms of type 2 narcolepsy are similar to those of type 1, but without cataplexy, and the level of hypocretin in the CSF is normal (6). Its pathogenesis is unknown, but it may be related to the partial loss of hypocretin neurons. Some type 2 patients may progress to type 1, while the rest remain stable. Daytime sleepiness may improve spontaneously in 20–25% of patients, who may become completely asymptomatic (7). The following case is presented in accordance with the CARE reporting checklist (available at <http://dx.doi.org/10.21037/apm-21-220>).

### Case presentation

Our center recently diagnosed a case of type 1 narcolepsy through PSG recordings, MSLT, monitoring of hypocretin level in the CSF, and detection of HLA DQB1\*0602. The patient was a 22-year-old male who showed recurrent daytime sleepiness without apparent causes, which occurred more frequently at rest, such as walking, reading, watching TV, and driving, and lasted for about 10 min each time. Brief rest or strong external stimuli could awaken the patient. More recently, the frequency of attacks was about 2–3 times a day. During the course of the disease, the patient experienced 4 near falls with weakened legs before going to sleep, without actual cataplexy, with the most recent one occurring in 2017. The patient had vivid dreams almost every night, and the dreams seemed real and clear. The patient woke up about 2–3 times at night and felt that the sleep quality was not satisfied. The patient had no obvious snoring. He had visual and auditory hallucinations before sleep, but no hallucinations after waking up. The patient had 3 episodes of sleep paralysis, all happened before 2018. The body weight of the patient increased by approximately 6 kg from 2018 to 2020. There was no obvious change in personality and no other changes.

The patient's mother frequently fell asleep while

watching TV. The patient denied other related family histories and other medical histories.

The MSLT results were as follows. The average sleep latency was 3.1 min, and abnormal REM sleep episodes were detected in 4 naps. The average REM latency was 1.3 min.

Additional test in the sleep center, Affiliation Hospital of Peking University showed his hypocretin level was 55 pg/mL, and gene test reveal the allele HLA DQB\*0602: 330.68 positive (*Figure 1*).

The patient is in good condition with the therapy of cognitive behavioral therapy and nap in the daytime. The sleep condition was improved when followed up early January, 2020. No special drug was taken.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this study and any accompanying images.

### Discussion

Narcolepsy was first reported by a French doctor, Gelineau, in 1880 (1,8). To this date, this disease is still not fully understood. In clinical practice, many patients are still misdiagnosed with epilepsy, syncope, or mental disorders, especially in less developed areas (9). Narcolepsy has a significant impact on public safety and personal life due to the possibility of cataplectic attacks, which warrant the attention of clinicians.

In Mainland China, systematic reports of narcolepsy include a 2011 report on 154 patients in Beijing (3), a 2014 report on 162 patients in Shanghai (10), a 2019 report on 148 patients in Xi'an (11), and a 2019 report on 165 patients in Shandong (12). Moreover, there was a 2002 report on 28 narcolepsy patients in Hong Kong, and a 2018 report on 157 patients in Taiwan (7,13). It is believed that the incidence of narcolepsy is higher in high-latitude areas than in the equatorial regions. However, according to current reports of the disease from various regions, there is no obvious correlation with latitude. Researchers from Finland and Switzerland reported that the influenza vaccine, Pandemrix, induced narcolepsy boom (9). Data from China in 2014 showed a significant increase in the incidence of narcolepsy in 2011 after the H1N1 epidemic in China in 2009 (4). Later studies found that narcolepsy was correlated with immune-mediated hypocretin deficiency. From 2019 to 2020, in addition to viral infections, it has been reported that group A



**Figure 1** Positive multiple sleep latency test results.

hemolytic streptococcal infection, abnormal T-cell immunity, and paraneoplastic syndrome can lead to narcolepsy (14). Moreover, the low reporting rate in lower latitudes, which often have a high incidence of viral infection and theoretically should have a high incidence rate of narcolepsy, may be related to a variety of factors, including awareness of the disease and local medical infrastructure (13).

With recent improvements in narcolepsy awareness, drugs targeting hypocretin have been developed, but there are still no effective and reliable drugs to treat the condition, and most drugs treat only the symptoms (9). Modafinil/armodafinil can alleviate excessive daytime sleepiness; antidepressants, such as venlafaxine, can alleviate cataplexy, but are not effective for excessive daytime sleepiness; and sodium oxybate is effective for cataplexy and daytime sleepiness (15). Through standardized diagnostic criteria and accurate evaluation, our center classified the disease type and developed an individualized treatment plan for the patient.

## Conclusions

In the city with the population of 200 million, despite the low incidence rate, diagnosis of narcolepsy is still confusing

and needs clinicians' attention. Whether the incidence of narcolepsy may increase after covid19 remains to be observed. So far, there is no clear evidence to support immunotherapy. Further studies are needed to verify more treatments and improve the patient's life quality.

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## Footnote

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**Ethical Statement:** The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this study and any accompanying images.

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## References

1. Barateau L, Dauvilliers Y. Recent advances in treatment for narcolepsy. *Ther Adv Neurol Disord* 2019;12:1756286419875622.
2. Raggi A, Plazzi G, Ferri R. Health-Related Quality of Life in Patients With Narcolepsy: A Review of the Literature. *J Nerv Ment Dis* 2019;207:84-99.
3. Han F, Lin L, Warby SC, et al. Narcolepsy onset is seasonal and increased following the 2009 H1N1 pandemic in China. *Ann Neurol* 2011;70:410-7.
4. Hoshino T, Sasanabe R, Mano M, et al. Prevalence of Rapid Eye Movement-related Obstructive Sleep Apnea in Adult Narcolepsy. *Intern Med* 2019;58:2151-7.
5. Stefani A, Högl B. Diagnostic Criteria, Differential Diagnosis, and Treatment of Minor Motor Activity and Less Well-Known Movement Disorders of Sleep. *Curr Treat Options Neurol* 2019;21:1.
6. Vitiello M, Antelmi E, Pizza F, et al. Type 1 narcolepsy in anti-Hu antibodies mediated encephalitis: a case report. *Sleep Med* 2018;52:23-5.
7. Cremaschi RC, Hirotsu C, Tufik S, et al. High fatigue frequency in narcolepsy type 1 and type 2 in a Brazilian Sleep Center. *Sleep Med* 2018;52:234.
8. Vignatelli L, Plazzi G, Peschechera F, et al. A 5-year prospective cohort study on health-related quality of life in patients with narcolepsy. *Sleep Med* 2011;12:19-23.
9. de Biase S, Gigli GL, Valente M. Important decisions in choosing the pharmacotherapy for narcoleptics. *Expert Opin Pharmacother* 2019;20:483-6.
10. Wu H, Zhuang J, Stone WS, et al. Symptoms and occurrences of narcolepsy: a retrospective study of 162 patients during a 10-year period in eastern China. *Sleep Med* 2014;15:607-13.
11. Lang Jin, Liang Shi, Ying Zhang. Antidepressants for the treatment of narcolepsy: A prospective study of 148 patients in northern China. *J Clin Neurosci* 2019; 63:27-31
12. Jin L, Shi L, Zhang Y, et al. Antidepressants for the treatment of narcolepsy: A prospective study of 148 patients in northern China. *J Clin Neurosci* 2019;63:27-31.
13. Zhang X, Kantelhardt JW, Dong XS, et al. Nocturnal Dynamics of Sleep-Wake Transitions in Patients With Narcolepsy. *Sleep* 2017;40:10.
14. Deerhake ME, Barclay WE, Shinohara ML. Are Neuropeptide-Reactive T Cells behind Narcolepsy? *Immunity* 2018;49:796-8.
15. Mansukhani MP, Covassin N, Somers VK. Neurological Sleep Disorders and Blood Pressure: Current Evidence. *Hypertension* 2019;74:726-32.

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