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Sleep Disorders and Autoimmunity: Insomnia as the Presenting Sign of Morvan Syndrome Associated with CASPR2 Antibodies

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Demonstrating the relation between narcolepsy and HLADR2 haplotype in 1984 was the first clue that provide insight into the association of sleep disorders (SDs) with immunity (1). In the following years, it has been shown that SDs accompany many autoimmune neurological diseases. Today, SDs are reported in more than half of the patients with autoimmune encephalitis (AE) and can persist beyond the acute phase of the disease. Major SDs such as insomnia, parasomnia, hypersomnia, and sleep-disordered breathing can all be observed within the course of AE (2). SDs affect the quality of life markedly, although they are not paid enough attention. The mechanisms that cause sleep disturbance in AE cases have not been fully elucidated yet.

Highlights

- **Autoimmune etiology should be considered in cases with unexplained sleep disorders.**
- **Insomnia may be the presenting sign of Morvan syndrome associated with CASPR2 antibodies.**
- **Sleep disorders with autoimmune etiology respond favorably to immunotherapy.**

SDs are observed in nearly 90% of patients with anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis, the prototype of an autoimmune disease characterized by acute onset neurological and psychiatric symptoms. Moreover, it has been revealed that SDs vary in relation to the course; while there is decreased sleep amount in the acute phase, hypersomnolence is observed in the recovery phase (3).

Insomnia with fragmented sleep and excessive daytime sleepiness was the symptom that leads to discovery of anti-IgLON5 disease and was observed in 70% of the patients (4). Neuromyelitis optica spectrum diseases could cause sleep disturbances if they involve the hypothalamus and periependymal region of the third ventricle (5).

SDs are an important feature of Morvan syndrome (MS) which is characterized by peripheral nerve hyperexcitability and central nervous system findings. Auto-antibodies against contactin-associated protein 2 (CASPR2) have been found in 80% of MS patients, and more rarely, antibodies against leucine-rich glioma inactivated 1 (LGI1) antigen can be present. Insomnia is an early and prominent symptom that affects nearly 90% of the patients (6,7). Agrypnia excitata, a clinical picture characterized by motor and sympathetic hyperactivity with severe and persistent insomnia, has also been reported in MS, and functional impairment in the thalamo-limbic network is thought to underlie this severe symptom (8). SDs have also been reported in anti-LGI1-related limbic encephalitis, and REM sleep behavior disorder may also accompany clinical findings in the early period. It is remarkable that SDs respond favorably to immunotherapy in voltage-gated potassium channel (VGKC) complex autoimmunity (7). In our clinical experience, we followed up a young female otherwise healthy patient with severe insomnia as the presenting sign along with hyperhidrosis, myokymia, and seizures. Due to the suspicion of MS, anti-CASPR2 antibody assessment has been performed and was found strongly positive. Our patient's sleep disturbances were relieved after immunotherapy with pulse steroid and intravenous immunoglobulin treatment.

We would like to emphasize that SDs could be an early and prominent finding of AEs and those patients who complain of unexplained sleep disturbances should be evaluated for auto-antibody assessment. Symptomatic treatment is recommended in addition to immunotherapy for these patients (2). Detailed clinical identification, close monitoring of sleep symptoms, alongside polysomnographic studies of SDs in these patients will provide a better understanding both for the course and for the mechanism of SDs and their specific treatments.

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