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Narcolepsy with Cataplexy Mimicry: The Strange Case of Two Sisters

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CASE REPORTS

We report on two sisters, 17 and 12 years of age, with clinical features suggesting narcolepsy with cataplexy (NC): daytime sleepiness, spontaneous and emotionally triggered sudden falls to the ground, and overweight/obesity. MSLT showed borderline sleep latency, with 1 and 0 sleep onset REM periods. HLA typing disclosed the DQB1*0602 allele. Video-polygraphy of the spells ruled out NC diagnosis by demonstrating their easy elicitation by suggestion, with wake EEG, electromyographic persistence of muscle tone, and stable presence of tendon reflexes (i.e., pseudo-cataplexy), together with normal cerebrospinal hypocretin-1 levels. Our cases emphasize the need of a clear depiction of cataplexy pattern at the different ages, the usefulness of examining ictal neurophysiology, and collecting all available disease markers in ambiguous cases.

Keywords: Childhood, hypocretin-1, narcolepsy with cataplexy, pseudo cataplexy, video polysomnography

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Narcolepsy with cataplexy (NC) is a rare hypersomnia of central origin characterized by daytime sleepiness, cataplexy (sudden losses of muscle tone triggered by emotions, pathognomonic symptom), and other REM sleep disturbances. Reduced levels of cerebrospinal hypocretin-1 (hcrt-1 < 110 pg/mL) or ≥ 2 sleep onset REM periods (SOREMP) at MSLT should, "whenever possible" confirm NC diagnosis according to the International Classification of Sleep Disorders (ICSD-2).[1] We report two ambiguous cases who were sent to our center with suspected NC, claiming the need to document accurately cataplexy features within NC assessment.

REPORT OF CASES

Patient 1

Patient 1 is a 17-year-old female presenting with frequent episodes (up to 5-6 per day) of sudden shortness of breath since age 13 years, followed by occasional apparent loss of consciousness. Since 14 years of age, she has had sudden falls to the ground, occurring both while standing or sitting and elicited by emotions, with immobility for up to few minutes. After an initial cluster, episodes frequency settled to 1-2 per month. She also increased weight and, at 16 years, daytime sleepiness appeared. At our observation she had a BMI of 31.24 kg/m^2 and an Epworth Sleepiness Scale (ESS) score of 12. Cardiological evaluation and testing and brain MRI were normal. During 48-h polysomnography (PSG) she had SOREMPs in both daytime and nighttime sleep in the absence of sleep disordered breathing (apnea-hypopnea index [AHI] of 0/h). MSLT showed borderline sleep latency (9 min) with 1/5 SOREMP. Human Leucocyte Antigen typing revealed the HLA-DQB1*0602 allele. A typical spell, evoked by a suggestion maneuver, was recorded during video-PSG, showing ictal persistence of EMG muscle tone, deep tendon reflexes, and normal wake EEG (**Video 1**). Hcrt-1 level was in the normal range (364.4 pg/mL). A diagnosis of NC was excluded. Since we communicated the non-cataplectic nature of the spells, their frequency has decreased to 2-3 episodes per year.

Video polygraphy of pseudo-cataplexy

Video 1 shows an instance where Patient 1 was standing while a placebo suggestion was performed. She abruptly fell on the ground—EMG showed initially increased then persistent muscle tone, and EEG, partially masked by artifacts, showed wake activity. While Patient 1 was recumbent and apparently unconscious, brisk reflexes could be easily evoked, confirming the non-cataplectic nature of the spell. The episode ended after another suggestion maneuver and while the doctor was reassuring Patient 1 that the episode would soon vanish. Polygraphic montage included EEG (C3-A2; O1-A2; Cz-A2), EOG (ROC-A1; LOC-A1), EMG (chin, right masseter, nuchal, right sternocleidomastoid, right and left deltoid, right and left carpus extensor, right and left anterior tibial muscles), ECG, and thoraco-abdominal belt from the top to the bottom.

Patient 2

Patient 2, the 12-year-old sister of Patient 1, had sudden episodes of vertigo followed by apparent brief loss of consciousness and falls to the ground with unresponsiveness to external stimuli for a few seconds to some minutes since 11 years of age. These episodes, after an initial cluster of 10 per day over a week, decreased to 1-2 per day. According to parent's report, the episodes were similar to those of Patient 1. Psychiatric evaluation disclosed attention deficit hyperactivity disorder (ADHD), and normal head-up tilt table test excluded vasovagal syncope. At our evaluation, she complained mild restless legs symptoms and daytime sleepiness (ESS score of 15); sleep talking since childhood was reported. Her BMI was 29.7 kg/m^2. MSLT showed borderline sleep latency (9 min 12 sec). No SOREMP occurred during daytime or nighttime sleep on 48-h PSG (AHI = 0/h). She was HLA-DQB1*0602 positive and had normal brain MRI. Video-PSG of a spell occurring while watching funny videos showed persistence of wake EEG activity, EMG muscle tone, and deep tendon reflexes (**Video 2**). Hcrt-1 was in the normal range (253.7 pg/mL). Atomoxetine was given for ADHD, and she reported improved daytime sleepiness and significant spells reduction (1-2 per month).

Video polygraphy of pseudo-cataplexy

Video 2 shows an instance where Patient 2 was standing and watching funny videos and abruptly fell on the ground—EMG initially showed a reinforcement then a persistence of muscle tone and EEG, masked by artifacts, wake activity. While Patient 2 was recumbent and unresponsive to external stimuli, osteo-tendinous reflexes could be easily evoked, also when muscle tone was apparently of low amplitude on EMG channels. Polygraphic montage included EEG (C3-A2; O1-A2; Cz-A2), EOG (ROC-A1; LOC-A1), EMG (chin, right masseter, nuchal, right sternocleidomastoid, right and left deltoid, right and left carpus extensor, right and left anterior tibial muscles), ECG, and thoraco-abdominal belt from the top to the bottom.

DISCUSSION

Our cases show that the diagnosis of cataplexy based on clinical history alone may be misleading and suggest the need to further frame cataplexy and its mimics by documenting the episodes in the diagnostic work-up of suspected NC. According to ICSD-2, MSLT should be performed in the absence of a definite history of cataplexy, and HLA typing is neither sensitive nor specific for NC diagnosis confirmation.[1] Indeed, as cataplexy is easy to document and peculiar, especially in children close to disease onset,[2] we suggest the need to search for it considering ictal video-PSG useful in uncertain cases,[3] and also for phenotype-genotype research purposes. NC objective biomarkers, namely SOREMPs and low/undetectable hcrt-1, have to be investigated in all challenging patients, and normal hcrt-1 may occur only in peculiar cases.[4] Differential diagnosis of cataplexy should include a careful work-up to rule out cardiovascular conditions such as vasovagal syncope,[5] drop attacks,[6] and epilepsy.[7] Misdiagnosing as NC other neurologic or psychiatric disorders, or cases of malingering, may have serious consequences for patients and their families, as well as high costs for the society. Overlaps between NC and psychiatric traits[3] or disorders[8] may also exist and require multidisciplinary approach and further investigations.[9]

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