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Narcolepsy-Cataplexy: Is Streptococcal Infection a Trigger?

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CASE REPORTS

Narcolepsy-cataplexy is an uncommon sleep disorder which may present in childhood. We report a case of an 8-year-old presenting with narcolepsy-cataplexy following a streptococcal infection. Autoimmune etiology for narcolepsy has been suggested. In our patient increased anti-streptolysin O and anti-DNAse B titers were noted. As suggested by recent cases, the streptococcal infection was likely a trigger for narcolepsy onset in this genetically predisposed child. The patient was initially diagnosed as having Sydenham chorea due to motor movements. However, these transient movements may be due to the narcolepsy onset. Narcolepsy in childhood may present with atypical symptoms; it might be difficult to obtain accurate history and can be misdiagnosed as in the reported case. A high index of clinical suspicion is needed to diagnose these patients.

Keywords: Narcolepsy, streptococcal infection

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Narcolepsy with hypocretin deficiency occurs in approximately 1 out of 3,000 individuals. The incidence in children is not known. The loss of hypocretin-secreting neurons in hypothalamus is implicated in the disease process, which is believed to be autoimmune. Recently, post-infectious etiologies have been implicated. We report a case of an 8-year-old presenting with narcolepsy-cataplexy after a streptococcal infection.

REPORT OF CASE

An 8-year-old biracial male presented to our clinic for a second opinion. Two months prior to presentation, he had a sore throat and fever of 102°F. Rapid strep test for Streptococcus pharyngitis was negative. Three weeks later, he had rapid onset of somnolence. He was sleeping more than 10 hours in night with 45 to 60-min naps every 3-4 hours. He had brief asynchronous jerks of all extremities prior to falling asleep and slurred speech after laughing. A video EEG and MRI brain were normal. Thyroid and liver function tests, and EBV, and Lyme titers were normal. Anti-streptolysin O (ASO) and anti-DNAse B (ADB) were elevated to 200 IU/mL (normal 0-100 IU/mL) and 587 U/mL (normal 0-170 U/mL), respectively. He was diagnosed with Sydenham chorea (SC) and started on penicillin.

He continued to have increased sleepiness and was referred to us. He also had a decline in school performance and moodiness. He denied hallucinations, vivid dreams, or sleep paralysis. Mother noted increased jitteriness/shaking when he laughed. His Epworth Sleepiness Scale score was 19, and BMI was 19.7 kg/m^2 (> 90th percentile). His physical examination was normal. There were no complex motor movements.

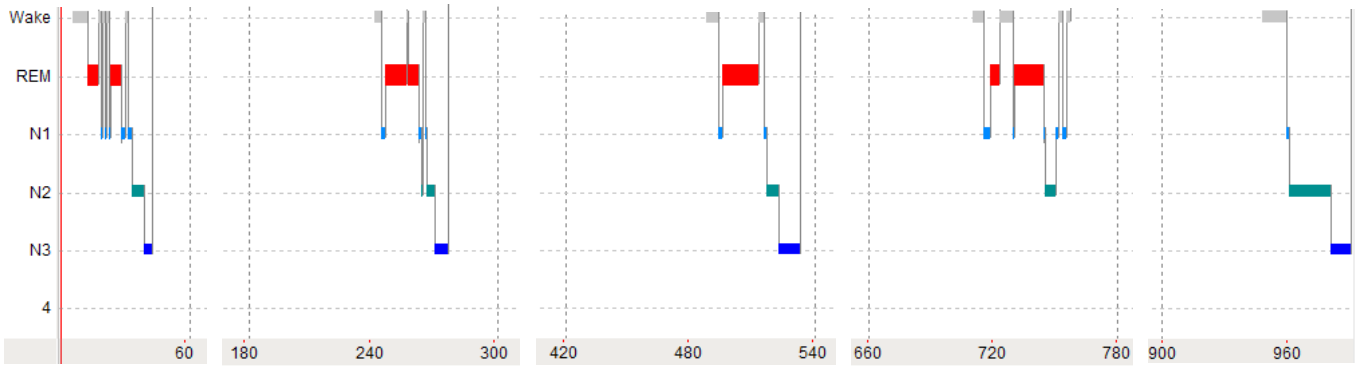
Differential diagnosis included narcolepsy or hypersomnia associated with sleep (OSA, PLMD) or neurological disorders. A lumbar puncture showed normal cerebrospinal fluid (CSF) protein, glucose, and cell count. The CSF neurotransmitter metabolites tetrahydrobiopterin and neopterin profiles were normal. CSF hypocretin was 8.6 pg/nL (normal > 110 pcg/nL). His polysomnography suggested sleep efficiency of 59% and restlessness. His multiple sleep latency test (MSLT) showed an average sleep latency of 3.9 (2.1-6.3) min, with sleep onset REM (SOREMs) present in 4 of 5 naps (**Figure 1**). The HLA DR2 (DR 15) and HLA DQB1*0602 allele were positive. He was diagnosed with narcolepsy. His episodes of slurred speech associated with laughter represented cataplexy. He was started on modafinil 100 mg twice a day. His sleepiness improved significantly with some improvement in nighttime awakenings.

DISCUSSION

Narcolepsy-cataplexy is believed to be autoimmune, given the strong genetic association with HLA DQB1*0602, and polymorphisms in the T-cell receptor alpha locus.[1] Recent studies show antibodies against the anti-Tribbles homolog 2 (TRIB2) in new onset narcolepsy-cataplexy.[1,2] Recently, there are reports of narcolepsy following H1N1 influenza infection and vaccination.[3] The risk of narcolepsy is 5.4 times higher (95% CI, 1.5-19.1) in patients with a physician-diagnosed streptococcal infection.[4] Moreover, prior to the onset of narcolepsy, a higher prevalence of streptococcal throat infections was noted in most prepubertal and peripubertal versus postpubertal children.[5] Furthermore, higher ASO and ADB titers were found in patients with recent diagnoses, as compared to age-matched controls and patients with long-standing disease.[6] Similar to other post-streptococcal sequelae, there may be cross-reactivity between the antibodies against group A Streptococcus and hypocretin secreting neurons. In a genetically predisposed individual, this may trigger the onset of narcolepsy.

Interestingly, this patient had complex motor movements which led to diagnosis of SC. However, these are associated with new-onset narcolepsy in children.[7] Moreover, SC is an occasional feature of encephalitis lethargica (EL), a neurological disorder characterized by hypersomnia and posterior hypothalamic lesions,[8] associated with elevated ASO titers.[9]

Figure 1—MSLT showing 4 out of 5 naps with SOREMs in our patient



MSLT, multiple sleep latency test; SOREMs, sleep onset REM.

Narcolepsy-cataplexy is a multifactorial disease. The diagnosis in prepubertal children may be difficult. Recent observations from the Pediatric group of Sleep Research Network have suggested increased new cases of childhood narcolepsy following infections.[10] The Network is currently working on examining this issue in a systematic manner.

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10. www.sleepresearchnetwork.org (Pediatric sleep disorders section)

SUBMISSION & CORRESPONDENCE INFORMATION

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