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 move-

ments. 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/m² (> 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/mL (normal > 110 pg/mL).

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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