Case report

Narcolepsy syndrome

M N P Perera[1], J Wanigasinghe[2]

Sri Lanka Journal of Neurology, 2014, **3**, 26-27

Introduction

Narcolepsy is a syndrome, characterized by a pentad; excessive day time sleepiness (EDS), cataplexy, hypnagogic hallucinations, sleep paralysis and nocturnal sleep disturbance[1]. It is a chronic brain disorder that involves poor control of sleep-wake cycles. Those affected enter Rapid Eye Movement (REM) sleep within a short period compared to normal sleeper with intrusion of features of REM sleep into wakeful state. The pathophysiological basis of the disease is the loss of hypocretin secreting neurons in the hypothalamus which is postulated to be related to a multifactorial inheritance. A strong genetic association with HLA-DQB1*0602 and polymorphism in the T cell receptor alpha locus is described. Recent evidence also suggests an autoimmune basis due to isolation of antibodies against the anti- Tribbles homolog[3].

Narcolepsy is a rare disorder with an estimated prevalence of 0.07% and presenting in childhood is even rarer[2]. We present an 8-year-old boy who presented with classic features of narcolepsy syndrome followed by good response to therapy.

Case report

An 8-year-old, previously healthy boy of non-consanguineous parents presented initially with abnormal orofacial movements which manifested as brief episodes of lower lip biting. This was followed by a march of events appearing one after the other; lateral tongue movement, episodic change in size of palpebral fissure and episodic protrusion of tongue. After about three months he developed features of excessive day time sleepiness such as sleeping during school, in the middle of conversation and even during favorite television programs. He was also noted to have abnormal limb movements in sleep with frequent a wakening but did not experience snoring or hypnagogic hallucinations. Seven months since onset of first symptoms, he developed episodes of falling down whenever he laughed loud. Retrospective analysis revealed an increase in his body weight by nine kilograms over a nine month period. His school performance also gradually deteriorated with worsening aggressive behavior.

He appeared lethargic during examination with BMI between +2 SD and +3 SD. Systemic examination including neurological examination was normal.

MRI brain with pituitary sliced view did not show any significant focal lesions. EEG was normal and polysomnogram did not show features of obstructive sleep apnoea.

He was treated with methylphenidate and imipramine in addition to non-pharmacological measures such as improved sleep hygiene, organized sleep schedules, caffeine containing food and beverages and regular exercise before sleep. These resulted in improvement of the EDS and the cataplexy.

Discussion

Narcolepsy syndrome is a sleep disorder with subtle and gradual onset. The progression varies but may take several years to develop all clinical symptoms[4]. This results in difficulties in arriving at a definite diagnosis early in the illness. The symptoms of narcolepsy syndrome includes EDS; the commonest experienced by all patients. It is the first symptom to be clinically apparent as well[4]. It consists of involuntary sleep episodes of variable lengths ranging from hours to minutes[4]. Cataplexy is the only symptom specific to narcolepsy which occurs at the beginning of narcolepsy or several years later[4,5]. It is defined as transient episodes of loss of muscle tone of brief duration (<2 minutes), with preserved consciousness. It is often triggered by emotion[5]. Hypnogogic hallucination (HH) occurs at the sleep onset and includes visual, tactile, kinetic and auditory phenomena[4]. Sleep paralysis (SP) is a transient inability to move or speak while falling sleep or awake and last a few seconds or minutes. There is preserved consciousness during these hallucinations[4]. Disturbed nocturnal sleep includes difficulties in staying asleep due to insomnia, vivid dreaming, sleep talking, acting out while dreaming, or periodic leg movements[4]. Other symptoms that are less frequently experienced in narcolepsy include weight gain, deterioration of school performances, poor concentration[4], orofacial movements, periodic limb movement during sleep[6] and emotional lability.

[1]*Lady Ridgeway Hospital,* [2]*University of Colombo, Sri Lanka.*

Among the above symptoms, cataplexy is the most specific symptom and is rarely present outside of narcolepsy. When cataplexy is not present, diagnosis must be made after excluding other possible causes of daytime sleepiness and fatigue, along with a positive multiple sleep latency test (MSLT). A PSG also helps to find whether REM sleep occurs at abnormal times in the sleep cycle and can rule out the possibility that an individual's symptoms result from another condition. When no other serious medical condition is present, low cerebrospinal fluid (CSF) hypocretin-1 can establish hypocretin deficiency as the cause of narcolepsy. Human leukocyte antigen (HLA) typing of narcolepsy patients shows certain alleles located on chromosome 6 are strongly associated with narcolepsy-cataplexy and it supports the hypothesis of possible of autoimmune aetiology.

Treatment of narcolepsy requires both non-pharmacologic and pharmacologic measures. Non-pharmacologic measures are avoiding sleep deprivation, scheduled naps, caffeine containing foods such as chocolate, cola drinks, coffee and tea, undisturbed sleep environment, regular exercise in the evening and fixed sleeping schedules.

The pharmacological treatment strategies include use of several classes of drugs. Amphetamines like compounds are mainly useful to improve EDS. These include drugs like methylphenidate, methamphetamine and amphetamine. Although EDS is improved subjectively, sleep variables are never completely normalized with these compounds[8]. Out of these methylphenidate is well tolerated and effective in many and because of its relatively short duration of action (3-4 h) it can be used on an "as needed" basis.

The other class of medications used in narcolepsy is compounds such as modafanil or armodafinil. They are milder stimulants with relatively lesser side effects and limited tolerance and dependence, thus favoring them as the first line used for EDS. However, it has limited efficacy on cataplexy and other sleep variables[1]. Armodafinil has relatively longer wake-promoting effects.

Gamma hydroxybutyrate, a sodium oxybate belong to another group of drugs used in narcolepsy. It is efficacious for EDS, cataplexy, hypnagogic hallucination, sleep paralysis and disturbed nocturnal sleep. A large-scale, double-blinded, placebo-controlled clinical trial in the United States has shown its efficacy on narcolepsy-cataplexy placing it as the first line treatment for the above[10,11]. Its effect on EDS is relatively quick, but anti-catapletic effect may take one to twelve weeks to appear. Antipsychotics are the other group of drugs that are used in narcolepsy. Tricyclic antidepressants (TCA), selective serotonin reuptake inhibitors (SSRIs), selective serotonin-norepinephrine reuptake inhibitors (SNRI) are reported to be effective for cataplexy[1]. TCA such as imipramine is the most commonly used anti-cataplectic agent and it also effective in sleep paralysis and hypnagogic hallucinations[1]. Though SSRIs show comparatively lesser side effects, its potency is not impressive since evidence shows predominance of the norepinephrine system for the control of cataplexy[1] rather than the serotonin system. Venlafaxine; a selective norepinephrine reuptake inhibitor (SNRI) is reported to be effective for cataplexy. Hypocretin replacement, gene therapy, cell transplantation and immunomodulation are emerging therapies in narcolepsy.

This case history highlights the importance of careful clinical evaluation. Narcolepsy syndrome can be easily misdiagnosed as either epilepsy or movement disorder during initial part of illness because of the abnormal orofacial movements and cataplexy. Though we did not have facilities to do MSLT and serological tests – clinical evaluation, normal MRI and treatment response point towards the diagnosis.

References

1. Nobuhide H, Seiji N. Recent advances in the treatment of narcolepsy. *Current Treatment Options in Neurology* 2011; **13**: 437-57.
2. Hood BM, Habard MG. Paediatric narcolepsy discussion: complexities of diagnosis. *J Paediatrics Child Health* 2002; **38**(6): 618-21.
3. Niranjana N M, Sejal V. Jain, Hina C, Barbara E. Hallinan, Narong S. Is Streptococcal Infection a Trigger? *J Clin Sleep Med* 2013; **9**(3): 269-70.
4. Narcolepsy Fact Sheet: National Institute of Neurological Disorders and Stroke. Sep 2014. www.ninds.nih.gov
5. Darina O, Coltte B, Catherine C, Bryan L, Brian S, Joan G. Investigation of an increase in the incidence of narcolepsy in children and adolescents in 2009 and 2010. Final report of national narcolepsy study sleeping committee. www.dohc.ie
6. Supriya K, Jambhekar, Gulnur, Elizabeth J. Periodic limb movement during sleep in children with narcolepsy. *Journal of Clinical Sleep Medicine* 2011; **7**(6): 597-601.
7. Macleod S, Ferrie C, Zuber SM. Symptoms of narcolepsy in children misinterpreted as epilepsy. *Epileptic Disord* 2005; **7**: 13-17.
8. Milter MM, Hajdukovic R. Relative efficacy of drugs for treatment of sleepiness in narcolepsy. *Sleep* 1991; **14**(3): 218-20.
9. Aran A, Einen M, Lin L, Plazzi G, Nishino S, Mignot E. Clinical and therapeutic aspects of childhood narcolepsy-cataplexy: a retrospective study of 51 children. *Sleep* 2010; **33**(11): 1457-64.
10. U.S. Xyrem Multicenter Study Group. Sodium oxybate demonstrates long-term efficacy for the treatment of cataplexy in patients with narcolepsy. *Sleep Med* 2004; **5**(2): 119-23.
11. A randermized, double blind, placebo-controlled multicenter trial comparing the effects of three doses of orally administered sodium oxybate with placebo for the treatment of narcolepsy. *Sleep* 2002; **25**(1): 42-9.