CASE CONFERENCE

Narcolepsy: Clinical Presentation, Differential Diagnosis and Management

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Abstract: *Narcolepsy is a neuropsychiatric condition which usually begins in adolescence and early adulthood, and is characterized by the classic tetrad of sleep attacks, cataplexy, hypnagogic hallucinations and sleep paralysis. Despite typical clinical features it is often undiagnosed or misdiagnosed. We present a case of a thirty-one year old housewife who presented with 3 year history of excessive day time sleepiness, cataplexy, poor night time sleep, hypnagogic hallucinations. Her symptoms led marked dysfunction socio-occupational dysfunction. She was diagnosed as a case of Narcolepsy and managed with methylphenidate.*

Key Words : Narcolepsy, Management

INTRODUCTION

Narcolepsy is a neuropsychiatric condition described as a disorder of sleep-state boundary control. It is a relatively uncommon disorder with a prevalence of 1 in 2000.[1] Narcolepsy usually has its onset in adolescence and early adulthood, although it may begin even in early childhood and late adulthood. It is characterized by the classic tetrad of sleep attacks, cataplexy, hypnagogic hallucinations and sleep paralysis.[2] Most patients also suffer from marked disturbances in nocturnal sleep. Despite typical clinical features, a central problem in the management of patients with narcolepsy is the long duration for which such patients go undiagnosed or misdiagnosed.[3] The disorder also takes a significant toll on the psychological, social and occupational functioning of the patient. The patients may suffer from embarrassment, poor self-esteem, anxiety and depression due to their condition. The pharmacological management of narcolepsy typically consists of stimulant medications.

We present a case of a thirty-one year old housewife who was diagnosed as a case of Narcolepsy and discuss the diagnostic and management issues.

THE CASE

KD a 31year old illiterate housewife belonging to an urban joint family of lower socio-economic status, who was premorbidly well adjusted and had no abnormality in birth and early developmental history presented with the chief complaint of excessive daytime sleepiness since 3 years. Further exploration of her history revealed that since last 3 years patients was having frequent day time naps, disturbed night time sleep, and weakness of hands and dropping of things from hands.

The episodes of day time naps would begin at any time during the day, irrespective of the activity she was performing. Characteristically, the episode would begin without any warning and the onset was characterized by intense sleepiness, nodding of the head and inability to stand erect. Thus the patient had to interrupt whatever task she would be doing and lie down. She would make efforts to control her sleepiness by focusing on the task at hand or talking to someone but would not be able to resist it beyond five to ten minutes and would go to sleep. She would remain asleep for 15-20 minutes at a stretch, during which she would not be disturbed

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by minor noises in the house or surroundings and after waking up would feel fresh. After waking up, she would resume her unfinished work and never had any difficulty in recalling what she been doing before going to sleep. During the 3 years, the frequency of the sleep episodes increased gradually from a frequency of 3 to about 5-6 episodes per day and led to problems in completing the day today activities like cooking, washing clothes and conversations with other people.

Along with the above symptom, the patient also complained of poor night time sleep. She would go to sleep at a particular fixed time (usually 11 PM), and would be seen sleeping within 10 - 15 minutes of going to bed. As per the patient, within few minutes of going to bed, she would have vivid and intense dream like phenomenon in which she could see and hear the things. The content of such phenomenon mainly consisted of events that had occurred during the daytime, for example, she would see her family members and she engaged in various activities. Such phenomenon was however not associated with seeing or hearing frightening things or waking up from the sleep. In addition she would also frequently wake up at night. These awakenings would occur 2-3 hours after falling asleep without any specific reason like nightmares and occurred 3-4 times every night. During these awakenings she would either drink water or use the toilet and then try to sleep again and usually would fall asleep in next 15-30 minutes. However, despite the above problems, she would wake up by herself at her usual time (6 AM) without any difficulty, but wouldn't be satisfied with her night time sleep and would not feel fresh.

After a year of the onset of the above symptoms, the patient developed a new symptom in the form of an experience of sudden weakness in the body whenever she laughed. The weakness would last for a fraction of a second to few seconds and would often lead to dropping of things from her hand. As per the patient, *"whenever she would have a bout of laughter, she would feel that her body was going weak and that she would fall down. She could feel that her knees were buckling and that she could not hold her back erect. She also felt that she was losing grip on any object that she was holding at that time and that it would fall down and break".* Over the years due to the above phenomenon, patient often avoided laughing. However, such phenomenon did not occur during other emotional arousal states like crying or during sexual arousal. The above symptoms had been gradually progressing over the 2 years before her presentation to the psychiatry out-patient's department.

In addition to the above, patient had decreased libido. The patient's medical history was insignificant except for a recent increase in weight without any change in her appetite. She had gained approximately 25% of her body weight over the past two years.

Over the years all the above symptoms led to significant interference in her day to day functioning, interpersonal relationship problems with husband and mother in law, poor socialization with others, avoidance of social gathering and poor up keep of household things. There was no history suggestive of obstructive sleep apnea, restless leg syndrome, sleep walking, sleep talking, bruxism, night mares, snoring, persistent sadness of mood, anhedonia, decreased energy, depressive cognitions, cold intolerance, constipation, skin changes, menstrual disturbances, acne, hirsuitism and alcohol, nicotine, caffeine or sedative-hypnotics use. There was no family history of any psychiatric disorder.

Her physical examination was normal except for being mildly obese. Her mental state examination revealed marked distress and preoccupation with the symptoms.

With the above history and examination findings a diagnosis of narcolepsy was considered. On investigation, results of hemoglobin, total and differential count, fasting blood sugar, erythrocyte sedimentation rate, liver and renal function tests and thyroid function tests were in the normal range. Polysomnography was advised, but patient and family refused the same because of financial constraints. On the basis of clinical manifestations, patient was started on Tab. methylphenidate in a dose of 5 mg per day which was gradually increased to 10 mg per day. In addition to methylphenidate patient was asked to maintain a sleep dairy, follow sleep hygiene and have regular daytime naps. Patient and husband were psychoeducated about the nature of the illness and it was emphasized that patient was not indulging in daytime naps deliberately, but was forced to do so due to the nature of the illness. The interpersonal problems between the patient and the husband were also addressed. Patient showed remarkable improvement in all her symptoms in a month with the above management. Later patient was asked to take drug holidays during the weekends, during which husband would assist her in doing household work.

After the initial workup, patient has been under follow up treatment for last 5 years and had 7 relapses. Each relapse would follow discontinuation of medication by 4-5 weeks. After which methylphenidate would be reinstituted and patient would improve in all the symptoms.

DISCUSSION

Narcolepsy is a neuropsychiatric condition, which was first described by Gelineau in 1880.[4] It is characterized by classical tetrad of excessive daytime sleepiness, cataplexy, hypnagogic hallucinations and sleep paralysis. However, only 11% to 14% of patients report all 4 symptoms.

The excessive daytime sleepiness is usually the first, most common and most troublesome symptom to appear and it is described as overwhelming drowsiness and an uncontrollable need to sleep during the day[5-7]. These episodes occur not only in monotonous situations but also in situations where the patient is engaged in activity. The sleep episodes last for few minutes to up to a half-hour and on awakening patient reports feeling refreshed. However due to repeated episodes of sleepiness, patients usually report decreased alertness, poor attention and concentration throughout the day. Cataplexy, i.e., sudden loss of muscle tone is seen in up to 60% of all cases of narcolepsy,[8] manifests as complete weakness of most muscles, in the form of head drooping or slurring of speech to a fall due to total body paralysis lasting for a few seconds to a few minutes. Cataplexy is uncontrollable and is often triggered by intense emotions, usually positive ones such as such as laughter or excitement, but sometimes fear, surprise or anger. Sleep paralysis manifests as a temporary inability (usually lasting for only seconds to minutes) to move or speak while falling asleep or upon waking. This sleep paralysis mimics the type of temporary paralysis that normally occurs during rapid eye movement (REM) sleep. Hypnagogic hallucinations occur at the onset of the sleep and are experienced as real, and they may be particularly vivid and frightening. They may take the form of visual, tactile, auditory or multi-sensory phenomena lasting for up to a few minutes.

Our index case had symptoms of excessive day time sleepiness, cataplexy, hypnagogic hallucinations and disturbed night time sleep.

Differential diagnosis of Narcolepsy

Narcolepsy is often misdiagnosed. The differential diagnosis depends on the predominant symptom and clinical diagnosis of narcolepsy is based on presence of symptoms from the classic tetrad in various combinations. The differential diagnosis of excessive day time sleep includes sleep

apnea, sleep deprivation, restless leg syndrome, substance use or dependence, depression, Kleine-Levin syndrome, idiopathic hypersomnia, side effects of medications, poor sleep hygiene and severe infections etc. A good history from both patient and bed partner, can help in distinguishing most of these disorders. Sleep apnea is usually seen in obese males with history of loud snoring and evidence of pauses in breathing. Idiopathic hypersomnia is distinguished from narcolepsy by the presence of unrefreshing naps, more persistent daytime sleepiness, longer and less disrupted nocturnal sleep, and absence of sleep-onset REM period. Patients with restless leg syndrome will give history of compulsion to move legs; different unpleasant sensations in the legs precipitated by rest and relieved by activity, worsening of symptoms during early evening or later at night, and will be found to have accompanying iron deficiency anemia and metabolic disturbances. In addition to excessive daytime sleepiness, patients with Kleine-Levin syndrome will report overeating, hallucinations and hypersexuality. Proper evaluation can provide evidence for presence of depression, substance use or dependence, sleep deprivation and poor sleep hygiene.[9]

The differential diagnosis of cataplexy also includes partial complex seizures, syncope, and events related to psychological factors similar to pseudoseizures[10]. The preserved consciousness that is invariably associated with cataplexy aids in discriminating these episodes from those with different pathophysiologic mechanisms.

Our index case didn't have history suggestive of snoring, compulsive movements of legs, hypersexuality, increased appetite, substance abuse. Her excessive daytime sleepiness episodes were also refreshing. All this excluded the absence of other possible diagnosis.

How to diagnose Narcolepsy

An exhaustive medical history and clinical examination are essential for proper diagnosis. However, it is important to remember that none of the 4 symptoms described above are exclusive to narcolepsy.

Specialized tests, which can be performed in a sleep disorders clinic, to establish the diagnosis of narcolepsy are: polysomnogram (PSG) and the multiple sleep latency test (MSLT). The PSG is an overnight test that takes continuous multiple measurements while a patient is asleep to document abnormalities in the sleep cycle. It can help to demonstrate as to whether REM sleep occurs at abnormal times in the sleep cycle and mainly helps to exclude other causes of nocturnal sleep disruption like obstructive sleep apnoea, periodic limb movement disorder and rapid eye movement sleep behaviour disorder. The MSLT is performed during the daytime to measure a person's tendency to fall asleep and to determine whether isolated elements of REM sleep intrude at inappropriate times during the waking hours. As part of the test, an individual is asked to take four or five short naps usually scheduled two hours apart. Of late, orexin levels in cerebrospinal fluid and HLA testing are also done. Low CSF orexin levels are found in narcolepsy and rarely in other neurological conditions. A correlation exists between narcolepsy and histocompatability human leukocyte antigen (HLA) subtype DQB1*0602. In patients of narcolepsy without cataplexy, a combination of HLA subtyping and CSF orexin levels is highly specific[2].

The diagnosis of narcolepsy is based on the revised criteria given by the international classification of sleep disorders (ICSD).[2] ICDS gives 8 criteria for diagnosis of narcolepsy and the minimal requirement for diagnosis includes presence of recurrent daytime naps or lapses into sleep, occurring almost daily for at least 3 months (Criteria B) along with sudden bilateral loss of postural muscle tone occurs in association with intense emotion (Criteria C). Alternatively narcolepsy can also be diagnosed if the patient

has excessive sleepiness or sudden muscle weakness (Criteria A); Associated features, which includes sleep paralysis, hypnagogic hallucinations, automatic behaviors and disrupted major sleep episode (Criteria D), polysomnography showing (one or more of the findings) sleep latency less than 10 minutes, REM sleep latency less than 20 minutes, MSLT showing a mean sleep latency of less than 5 minutes and 2 or more sleep-onset REM periods (Criteria E) and absence of any medical or mental disorder accounting for the above symptoms (Criteria G). Other criterias for narcolepsy as per ICDS are HLA typing showing DQB1*0602 or DR2 positivity (Criteria F) and presence of other sleep disorders (e.g., periodic limb movement disorder or central sleep apnea syndrome) but are not the primary cause of the symptoms (Criteria H). However these criterias are not essential for diagnosis[2].

Our index case had excessive daytime naps (criteria B) along with catalepsy (criteria C) and hypnagogic hallucinations and fulfilled the diagnosis of narcolepsy as per ICDS.[2]

Psychosocial aspects of narcolepsy

Patients with narcolepsy face challenges at school, work and at home. Public awareness regarding this disorder is poor resulting in these patients being labeled as "lazy" or unwilling to work. Narcolepsy also leads to disruption of family life and interpersonal relationships[5, 11,12] and reduced enjoyment of certain recreational activities.[13] Students with narcolepsy report that their illness was the cause of poor grades, problems with peers and teachers and caused embarrassment.[14] Children with narcolepsy and other disorders of excessive daytime sleepiness were found to have more peer problems, conduct problems and depression.[15]

In our case also narcolepsy led to psychosocial problems in the form of interpersonal problems with husband and mother in law, difficulty in doing household work and poor socialization.

MANAGEMENT

Because of its diverse symptomatology, the treatment of narcolepsy is complex and involves use of both pharmacological and nonpharmacological measures. The non-pharmacological treatment includes maintenance of optimal sleep hygiene, including a consistent sleep-wake schedule to facilitate adequate sleep.[16] Other measures include scheduled naps during the day and avoidance of high risk work. Besides these special academic needs, family conflict, other psychosocial problems needs to be addressed.

The pharmacological treatment options include use of central nervous system stimulants (like methylphenidate, dextroamphetamine, methamphetamine, and amphetamine) and modafinil. Of the stimulants, methylphenidate is the most frequently used stimulant which improves sleep tendency in a dose-related fashion and also reduces cataplexy.

The mechanism of action of modafinil is not understood, but it has been evaluated in a multicenter, double-blind, placebo-controlled trial and have been reported to improve sleepiness.[17] Unlike traditional medications, modafinil does not appear to affect total sleep time or suppress REM sleep. The most common adverse effect is headache. Its safety in children has not been established.

For patients with cataplexy severe enough to warrant targeted treatment, the antidepressant medications have been the mainstay of treatment for years.[18] The noradrenergic compounds, such as imipramine and venlafaxine, are viewed as the most effective treatments for cataplexy. One published report of a small study indicated that the selective noradrenergic reuptake inhibitor reboxetine is efficacious.[19] Selective serotonin reuptake inhibitors have also been prescribed for cataplexy.[2]

Index case was treated with both pharmacological and nonpharmacological treatment and exemplify that patients with narcolepsy should be followed up regularly and major focus of management should be ensuring medication compliance and addressing the psychosocial issues.

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