NARCOLEPSY

***Lj.Radulovic, S.Vujisic, N.Ivanovic, S.Vodopic**
Clinical Centre of Montenegro, Podgorica

A.M. is a 19 years old university student without any previous illness. During the fourth year of high school, episodes of motor paralysis began to occur during awakening when she is conscious, but she needs a few minutes to start to move. The episodes are manifested a couple of times monthly. Simultaneously, but rarely, there are hypnagogic hallucinations such as sound and fear in a semi awake condition and she cannot react. Practically, last three years she has attacks of irresistible sleepiness, especially when she feels comfortable. She falls asleep during lectures or when she writes a message. She sleeps for a short time during writing and that refreshes her.

An 77 year-old man repeatedly experienced what he described as occasional "trance-like" states accompanied by drowsiness for about 9 years after he experienced ischemic stroke. These became increasingly frequent, finally reaching 3-5 times daily. In addition, he experienced sudden "drop attacks" during the previous 3 years. During that time, he did not receive a proper diagnosis or treatment despite several hospitalizations. Initially he was treated for epilepsy before receiving a proper diagnosis of narcolepsy.

Despite the fact that we spend a third of our lives in sleeping, the exact mechanism for the origin and significance of this physiological phenomenon is not yet known. To have a good, refreshing sleep is not only to keep your head on your pillow at night and wake up in the morning, but physiologically complex phenomenon with a specific cycle of a quality and duration necessary to maintain the vitality of our body.

Many ancient physicians tried to explain it, so they created a number of theories during the centuries, from Aristotle's assumption that it arises from the fumes in the stomach (sleep attacks are more common after meals) to some newer, that reduced stimuli from the environment during the night leads to "brain inactivity." Modern medicine has a theory of a role of neuronal recovery sleep, memory and immune system, as well as deletion of biologically unimportant memory.

It is assumed that one-half of the world's population has one of the numerous consequences of this very important process, and one of the most common sleep disorders is excessive daytime sleepiness or narcolepsy.

International Classification of Diseases defines narcolepsy as a sleep disorder of unknown cause, characterized by extensive (pronounced) drowsiness that is commonly associated with cataplexy (despondency) and other phenomena during one of the stages of sleep (called REM sleep), such as during sleep paralysis (hypnagogic paralysis) and unreal experiences during sleep (hypnagogic hallucinations).

During centuries narcolepsy is considered as a controversial entity, and it was treated as a symptom of various diseases, such as epilepsy, hysteria or encephalitis. Last half century, with the development of techniques and possibilities of objective measurements of sleep it is considered as a separate disease, which is not as rare as anticipated. The exact prevalence is unknown, but is thought to be approximately 0.02 to 0.05% among whites with equal representation of both sexes. Earlier studies have suggested a genetic basis of the

*email: ljardulovic2003@yahoo.com

disease with high morbidity in affected families, but it is now considered that the risk of a child of a suffering people is approximately 1%.

The major pathophysiology of human narcolepsy has been recently discovered based on the discovery of narcolepsy genes in animals; the genes involved in the pathology of the hypocretin/orexin ligand and its receptor. Mutations in hypocretin-related genes are rare in humans, but hypocretin ligand deficiency is found in a large majority of narcolepsy with cataplexy. Hypocretin ligand deficiency in human narcolepsy is probably due to the post-natal cell death of hypocretin neurons. Although a close association between human leucocyte antigen (HLA) and human narcolepsy with cataplexy suggests an involvement of autoimmune mechanisms, this has not yet been proved. Hypocretin deficiency is also found in symptomatic cases of narcolepsy and EDS with various neurological conditions, including immune-mediated neurological disorders, such as Guillain-Barre syndrome, MA2-positive paraneoplastic syndrome and neuromyelitis optica (NMO)-related disorder. Even not pathognomonic for this illness low cerebrospinal fluid hypocretin-1 levels is one of the established diagnostic test of narcolepsy.

To make the clinical diagnosis of this disease, it is necessary presence of repeated, almost daily, sleepiness or sleep attacks during the 6 months with clinical confirmed appearance of cataplexy, or sudden loss of muscle tone during a strong emotions. These attacks of irresistible sleepiness occur in unusual circumstances, such as talking, standing, walking, driving. They occur more frequently in the afternoon, after a heavy meal, a warm weather, while patient have reduced physical activity. Usually attacks last less than 30 minutes, they are easy to be disrupted with the external stimuli, and between them there is a period of 2-3 h of wakefulness. The patient feels

rested after them, but due to the irregular structure of sleep after a few hours patient falls in a sleep again and one-third in the course of them has dreams. Many patients complain of sleepiness during the day, during which they are able to perform automated, purposeless activity (writing nonsense, move objects around them, aimless walking, or even driving a car), which they cannot later recall.

The actual diagnosis of narcolepsy is based on overnight studies done in the sleep lab to rule out other causes of sleepiness. This is followed by the multiple sleep latency test (MSLT) where patients are offered four or five 20-min nap opportunities 2 hours apart, and the time it takes to fall asleep (sleep latency) is measured. As false positive and negative results frequently occur, interpretation of MSLT results should be done by an experienced physician. An average sleep onset of less than 8 minutes with 2 or more sleep-onset REM (dreaming) periods (SOREMPs) is considered diagnostic for narcolepsy; however, SOREMPs become less frequent and sleep latency increases with advancing age. Consequently, the MSLT may be less helpful in the diagnosis of narcolepsy in elderly patients.

Cataplexy, as the second most important

phenomena in narcolepsy, is the sudden loss of muscle tone after strong emotions such as joy, anger and fear. The most prominent is in the antigravity muscles and the patient is unable to stand up from a sitting position, but the procedure and other muscles, which are causing lower eyelids, loss of facial expression, inability to speak clearly. It lasts for a few seconds to a few minutes usually begins in the muscles of the head, and then on the trunk and extremities, which allows the patient to sit. During cataplexy awareness and memory of the event are preserved.

Hypnagogic hallucinations are usually vivid and abnormal visions just before or after sleep paralysis.

Narcolepsy affects all spheres of the life. Many activities, such as walking, driving, cooking are potentially very dangerous. Environment, which usually has little knowledge of the existence of this disease has no understanding, at work they are usually considered as lazy workers, half of the day is spent napping, with the frequent occurrence of difficulty of recalling memories. Private life, especially at the married couples, also suffers

because of excessive sleepiness which often leads to impotence. All this alteration affects the psychologically the patient, which usually leads to the depression, anxiety, alcoholism.

Treatment of this disease is lifelong. Treatments include the application of drugs (antidepressants and stimulants of the central nervous system), because hypocretin itself is too unstable to be administered as a pill or injection. Modafinil is a medication of choice to treat excessive daytime sleepiness caused by certain sleep disorders. These sleep disorders are narcolepsy, obstructive sleep apnea/hypopnea syndrome (OSAHS), and shift work sleep disorder (SWSD). Cataplexy and other related symptoms are treated with γ -Hydroxybutyric acid (GHB), tricyclic antidepressant and inhibits serotonin uptake. Treatment also involves changing the regime of sleep and wakefulness (advised more short breaks during the day to sleep usually 3 or more scheduled "naps"), psychiatric support of the patient and his family, as well as actions to increase the knowledge of the public through the media about the existence of this for a lot of people unknown but not so rare disease.

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L.Radulović, S.Vujišić, N.İvanović, S.Vodopić

Montenegro Kliniki Mərkəzi, Podgorica

НАРКОЛЕПСИЯ

Л.Радулович, С.Вужисич, Н.Иванович, С.Водопич

Монтенегро Клиники Мяркузи, Подгорица

Redaksiyaya daxil olub: 03.09.2012

Çapa tövsiyə olunub: 18.09.2012

Rəyçi: R.K.Şirəliyeva, t.e.d. prof.