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CASE REPORT

A rare case of Paediatric Narcolepsy in Malta

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Narcolepsy is a lifelong disorder that is usually diagnosed in early adulthood, however most often symptoms begin in the childhood years. It is characterized by excessive day time sleepiness (EDS) and features of rapid eye movement (REM) sleep. It is under diagnosed in both children and adults due to the clinical heterogeneity. We report a case of a child presenting with excessive day time sleepiness, who was diagnosed with narcolepsy, which although is a rare disease, is very treatable, and early intervention will reduce its psychosocial impact.

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Introduction

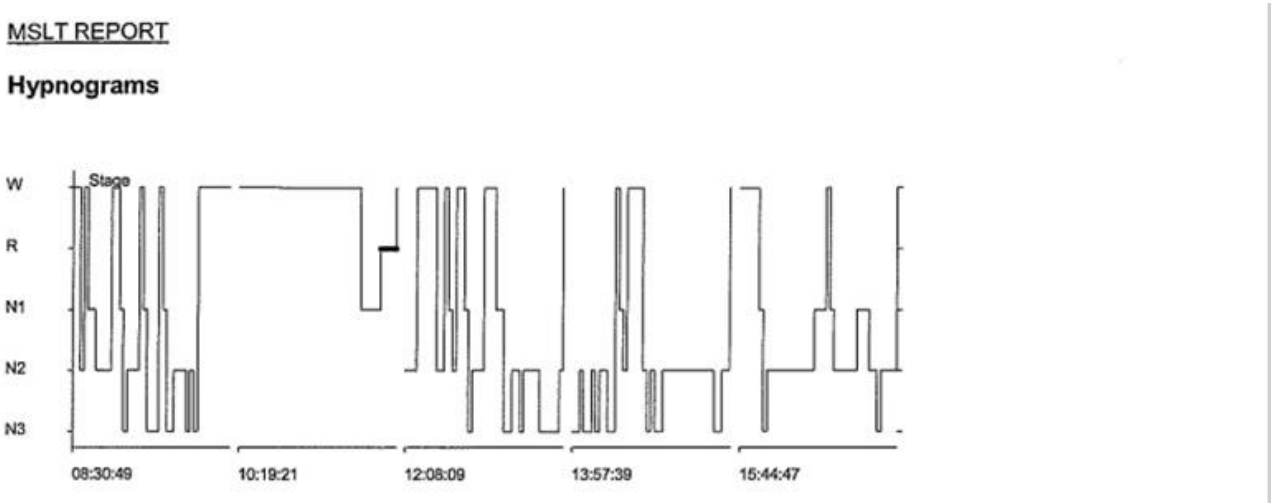
Narcolepsy is a lifelong disorder that is usually diagnosed in early adulthood, however most often symptoms begin in the childhood years.[1]It is characterized by excessive day time sleepiness (EDS) and features of rapid eye movement (REM) sleep. It is under diagnosed in both children and adults due to the clinical heterogeneity. We report a case of a child presenting with excessive day time sleepiness, who was diagnosed with narcolepsy, which although is a rare disease, is very treatable, and early intervention will reduce its psychosocial impact.

Case

A previously healthy nine-and-a-half-year-old girl was referred to the children's outpatient department with a 10-month history of increasing daytime lethargy and sleepiness which started at age 8. She was sleeping well at night for an average of ten hours, but she was still complaining of feeling tired during the day, with frequent episodes of sleeping during school hours. After returning home from school, she would sleep again for another three hours. According to her mother her academic performance and concentration were being affected because of this. She had an Epsworth sleepiness scale of 14.

She was never noted to snore at night or mouth breath. Her systemic examination was unremarkable, and her height and weight were on the 50th percentile with a Basal Metabolic Index (BMI) of 19 kg/m^2. She was investigated thoroughly with blood tests which excluded iron deficiency anemia, and showed normal thyroid, renal and liver function tests, and a normal cortisol response of 958 nmol/L after a short synacthen test. Magnetic Resonance imaging of the brain was reported as normal. A polysomnography study was performed and the patient had a mean sleep latency of 3 minutes 48 seconds, one sleep onset rapid eye movement (SOREM) of 2 minutes 30 seconds on the multiple sleep latency test (MSLT), and at least one SOREM of less than 20 minutes in the preceding overnight polysomnography study (Fig 1). Her oxygen saturation and carbon dioxide levels were normal during sleep. The MSLT and polysomnography findings were suggestive of narcolepsy. HLA-DQB1*06:02 was found to be positive which further confirmed the diagnosis.

Figure 1: Multiple Sleep Latency Test (MSLT)



She was started on low dose methylphenidate at 5 mg twice daily for a week then increased to 10mg in the morning and 5 mg in the afternoon. She improved rapidly, with resolution of her daytime sleepiness, requiring no naps throughout the day, sleeping for ten hours at night, and she also resumed extracurricular activities such as art lessons. She was also referred for psychological assessment and support.

Discussion

EDS and cataplexy, associated with sleep paralysis and hypnagogic and hypnopompic hallucinations, are typical characteristic features of narcolepsy.[2] EDS is the most common presenting feature and may be reported as tiredness or lack of energy by the patient or carers.[3] EDS can be the result of a wide range of sleep disorders and other conditions, and it may affect the child's health and general wellbeing.[4] Causes of EDS include insufficient sleep duration, broken or fragmented sleep, illness which increases sleep requirements and circadian misalignment. When assessing a child presenting with features of EDS it is important to quantify the total sleep time and the impact of EDS on overall function of the child. Whilst narcolepsy is rare in childhood, its incidence has increased since 2009 and this is thought to be due to the administration of adjuvanted H1N1 vaccine and viral infections.[5] The prevalence of narcolepsy in children between ages five to nineteen years is 0.83 per 100,000.[6]

Onset of narcolepsy is described as having a bimodal distribution with 2 peaks at ages 15 and 35. EDS in children may cause change in behaviour of the child, with increased irritability and aggression, and this may lead to delay in diagnosis. Children might find the occurrence of day time sleepiness embarrassing as it might be mistaken for laziness, and the patient might deny their symptoms. Furthermore, since this condition is uncommon in prepubertal children, health care professionals may dismiss these symptoms.[7] The diagnosis of narcolepsy in children is made by a history of EDS, together with nocturnal polysomnography and a multiple sleep latency test. The diagnostic criteria in adults and children are identical. The International Classification of Sleep Disorders, Third Edition, requires two criteria to make a diagnosis of type 1 narcolepsy (NT1): 1) at least a 3 month history of excessive day time sleepiness and 2) the presence of one or both of i) cataplexy and a mean sleep latency of less or equal to 8 minutes and two or more SOREM on an MSLT (A SOREMP (within 15 minutes of sleep onset) on the preceding nocturnal polysomnogram may replace one of the SOREMPs on the MSLT); and ii) CSF hypocretin concentration which is less than or equal to 110pg/mL.[8] NT1 is also known as narcolepsy with cataplexy. On the contrary, type 2 narcolepsy (NT2), also called narcolepsy without cataplexy, is clinically distinguished from NT1 by the absence of cataplexy symptoms. However, patients diagnosed at onset with NT2 can be reclassified as having NT1 after development of cataplexy symptoms, usually within 5 years of diagnosis but this can also be delayed by up to twenty years especially among at-risk children for example those with low CSF hypocretin-1 levels.[9]

Use of MSLT is limited in children less than 8 years of age, as baseline MSLT values are not known for this age group. NT1 is a thought to be an autoimmune condition linked to both an underlying genetic susceptibility, and environmental factors in predisposed individuals, precipitating cell loss that destroys the hypocretin producing neurons in the dorsolateral hypothalamus. Hypocretin is a neuropeptide transmitter and is required for wakefulness and it inhibits REM sleep.

There is a strong association between NT1 and HLA-DQ6 (DQB1*06:02) and its presence is sometimes used to support the diagnosis together with

characteristic symptoms and findings of MSLT or polysomnorgraphy.[10] Genetic factors also play a role as there have been reports of familial narcolepsy in the literature. Environmental risk factors that play a role in development of narcolepsy include H1N1 infection or specific H1N1 vaccination (specifically Pandemrix), and upper respiratory tract infections such as *Streptococcal* infection. Other neurological illnesses may also be associated with NT1 such as traumatic brain injury, Guillan Barre syndrome and Multiple Sclerosis.[9]

An association between narcolepsy in prepubertal children and endocrine diseases such as precocious puberty and obesity has been observed in some studies, however the exact causation is unknown. [11]

There is no curative treatment for narcolepsy as destruction of hypocretin producing neurons is irreversible,[12] thus management is symptomatic and includes both behavioral modification and pharmacotherapy. Use of cognitive and behavioural modification therapy is encouraged to decrease the negative impact of this disease on the patient's quality of life, as well as increase adherence to medication. The importance of sleep hygiene must be emphasized, and regular sleep-wake schedules enforced. Children should be encouraged to exercise to increase daytime alertness and decrease day time sleepiness attacks. If the child requires naps, these should be planned at appropriate times, for example after coming home from school. Furthermore, naps should be timed and should not last longer than 30 minutes.[13] It is advisable that the child and parents complete a sleep diary. Teenagers must be counselled about the risks of driving and use of alcohol, which will worsen the symptoms.[6] Cognitive behavioural therapy was found to not only improve patient's quality of life, but also decrease symptoms of EDS[14]. Pharmacotherapy treatment is based on the individual's symptoms. In children with increased daytime sleepiness, wake promoting agents such as Modafinil and Armodafanil or traditional stimulants such as Methylphenidate are recommended. These are used off license, but they are commonly used in split doses in the paediatric population[13]. Split doses have been shown to have an improved effect on EDS. Side effects include headaches, irritability and appetite loss.[6] Low doses are initially started, then they are titrated according to clinical response to allow for effective daytime functioning. Sodium oxybate is used off license to treat cataplexy in childhood and is given in two divided doses at night. Randomised controlled trials on use of sodium oxybate in the paediatric population, with symptoms of both narcolepsy and cataplexy, have shown a similar safety profile to that of adults.[15-16]

This disorder commonly affects the child's behaviour and relationship with their peers, as well as their mental health and academic performance, hence psychosocial support is a crucial part of its management.

Conclusion

Childhood narcolepsy has a major impact on the child's quality of life and academic performance, hence prompt diagnosis and treatment is essential to limit morbidity. Difficulties in diagnosis may arise as the occurrence of EDS can cause embarrassment to the child or may be misinterpreted as laziness and such symptoms can be denied. These issues can be minimized by greater public awareness of the condition. Untreated narcolepsy may affect the child's safety, as well as their social development. This case report highlights the need for further evaluation of EDS in paediatric population and the importance of knowledge of normal sleep development in children.

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