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•Case report•

Case report of narcolepsy in a six-year-old child initially misdiagnosed as atypical epilepsy

Jinquan ZHOU*, Xi ZHANG, Zaiwen DONG

Summary: This report describes a case of first-onset narcolepsy in a six-year-old female that was misdiagnosed as atypical epilepsy and other diagnoses at eight different hospitals over a period of 10 months before the correct diagnosis was made. The diagnosis of narcolepsy is more difficult in children because very few of them experience all four cardinal symptoms of narcolepsy – paroxysmal sleep, cataplexy, hypnagogic hallucination, and sleep paralysis – and they often have a more prolonged onset and diverse symptoms. To decrease the time lag between initial presentation and accurate diagnosis, we recommend that in all cases in which children report excessive sleep of unknown etiology – regardless of the associated symptoms – that sleep monitoring and sleep latency tests be conducted to rule out the possibility of narcolepsy. The case highlights the wide variety of presentations of uncommon psychiatric conditions, particularly in children, and the need for clinicians to be aware of the atypical presentations of these conditions when collecting medical histories.

Keywords: narcolepsy, hypnagogic hallucinations, misdiagnosis, epilepsy, children, China

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1. Background

Narcolepsy is a chronic neurodegenerative disease caused by autoimmune destruction of hypocretin-producing neurons.[1] Its primary clinical manifestations are excessive daytime sleep and cataplexy -- loss of muscle tone which is typically triggered by strong emotional stimuli. Less common symptoms include hypnagogic or hypnopompic hallucinations, sleep paralysis, vivid dreams and frequent nocturnal awakening, behavioral changes, obesity, and cognitive impairment.[2] About 10% of individuals with narcolepsy have the four core symptoms of narcolepsy: paroxysmal sleep, cataplexy, hypnagogic hallucination, and sleep paralysis.[3-4] Because narcolepsy is relatively rare, it is often misdiagnosed, particularly in primary care hospitals. Misdiagnosis of children with narcolepsy can interfere with their normal growth and puts them at increased risk of life-threating accidents.

2. Clinical history

The patient was a 6-year old female who was hospitalized with the written consent of her parents because of visual hypnagogic hallucinations and other symptoms that had gradually exacerbated over the last 10 months.

She reported initially seeing various ghosts when falling asleep at night; on some nights she shouted, was agitated, and was unable to fall asleep. After one month of these nocturnal symptoms other symptoms started to occur during the day; her teacher found her asleep in class and she sometimes collapsed when standing, walking, watching television, or eating. Her parents initially attributed these daytime symptoms to her poor sleep. Then other symptoms started while she was sleeping: 2 to 10-minute episodes during the night when she was unresponsive and her limbs were flaccid followed by agitation when she woke.

The Second People's Hospital of Dali prefecture, Dali City, Yunnan Province, China
* correspondence: zhoujinquan@sohu.com

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The number of these episodes gradually increased to 10 times per day so her parents sought treatment at the general medical and neurological departments of eight different hospitals before coming to our hospital. A wide range of tests and examinations were conducted at these hospitals and many diagnoses were considered, but in most cases she was diagnosed as having some form of atypical epilepsy that did not have EEG evidence. She was treated with anti-epileptics but her symptoms gradually worsened. Over the course of time she became more irritable and less active. She gained 7kg within 10 months despite having a normal diet and normal elimination.

On admission to our hospital the family reported no prior mental disorder and no family history of mental disorders. She was 112cm tall and weighed 23kg. On mental status examination she was irritable and had difficulty concentrating but was fully conscious and orientated. Her behavior was appropriate and well-coordinated. She had normal intelligence and insight appropriate for a 6-year-old child. She reported no current hallucinations or delusions at the time of the examination. She had slurred speech and at times during the examination her eyes closed and she was not responsive to loud noises.

Blood tests including complete blood count, blood chemistry, blood concentration of sodium valproate, and assessment of muscle enzymes were normal. Cranial CT, chest radiograph, electrocardiogram, cardiac ultrasound, and spinal fluid pressure examinations were also normal. Skull MRI demonstrated that the right hippocampal sulcus was slightly widened.

Video-EEG while awake identified occasional low amplitude Beta activity in the background of irregular 5-8Hz 20-80uv intertwined Alpha and Theta activity. The two hemispheres were symmetrical. Hyperventilation and visual responses were normal. Sleep-wake cycle was disordered. No epileptiform discharges were found. Nocturnal polysomnography (PSG) showed reduced average sleep latency at 6 to 8 minutes, increased number of awakenings, disturbed sleep-wake cycle, shortened REM latency (the patient entered REM sleep immediately), and increased proportion of REM. After getting enough sleep (≥6h), daytime the Multiple Sleep Latency Test (MSLT) revealed two incidents of sleep-onset REM periods with reduced sleep latency.

Children with narcolepsy usually show shortened average sleep latency on their EEG and sleep onset REM periods. The video EEG of this patient showed disturbed sleep-wake cycles. Based on her medical history, PSG results, and MSLT results she was diagnosed as having narcolepsy and was given methylphenidate 5mg/d for 5 days. Her symptoms resolved and her diurnal sleep was significantly reduced, particularly at school. At 1-year follow-up, she had no significant difficulties in daily life or attending school.

3. Discussion

According to the American Academy of Sleep Medicine (2005),[5] symptoms of narcolepsy with cataplexy include: (a) recurrent daytime naps or lapses into sleep that occur almost daily for at least three months and; (b) sudden bilateral loss of postural muscle tone in association with intense emotion- cataplexy. Administering the Multiple Sleep Latency Test (MSLT) after overnight polysomnography (PSG) can assist in making the diagnosis of narcolepsy with cataplexy. The presence of one or both of the following confirms the diagnosis: (a) a mean sleep latency of ≤8 minutes and two or more sleep onset REM periods (SOREMPs) based on MSLT performed after at least six hours of sleep during the previous night. (A SOREMP on the preceding nocturnal PSG may replace one of the SOREMPs on the MSLT.) (b) Hypocretin-1 concentration, measured by immunoreactivity of either ≤110 pg/ml or <1/3 of the mean values obtained in normal subjects with the same standardized assay. Finally, the symptoms are not explained by other sleep disorders, nervous system diseases, mental disorders, or drug or substance abuse.

Based on reports from other countries, the prevalence of narcolepsy is about 0.2 to 0.9% with no discernible male-female differences. Most cases have their first onset after 10 years of age. Cases with onset before 10 years of age account for about 5% of all cases. Some patients have a family history. Studies have shown that the lack of orexin (hyopcretin) or the dysfunction of its receptors in the brain may lead to narcolepsy.[6] Other reports suggest that narcolepsy is related to hypofunction of the ascending reticular activating system or hyperfunction of the caudal pontine reticular nucleus. The cardinal symptoms include paroxysmal sleep (100%), cataplexy (70%), hypnagogic hallucination (25%), and sleep paralysis (5%).[6-8] Usually, patients experience some, but not all, of these four symptoms. About two-thirds of patients experience transient paroxysmal sleep only, and one-third of patients have one of the other three symptoms in addition to paroxysmal sleep. It is accompanied by nocturnal sleep disturbances or mood problems in some patients. Pathophysiological changes of narcolepsy mainly include sleep-wake cycle disturbances, and shortened REM latency (<8 minutes after falling asleep).[6-8]

The patient reported here initially presented with hypnagogic hallucination but no dreams. Her diurnal sleep increased and she experienced cataplexy. Her EEG demonstrated disrupted sleep cycles, and her PSG indicated shortened sleep latency. In addition, she had obvious weight gain (7kg within 10 months) and personality changes, symptoms that are sometimes seen in patients with narcolepsy.[4] It was not difficult to make the diagnosis based on these typical clinical manifestations and the results of the polysomnography and EEG monitoring.

The diagnosis of narcolepsy is more difficult in children because very few of them experience all four cardinal symptoms and they often have a more prolonged onset and more diffuse symptoms. The initial or prodromal symptoms may be atypical which can result in delayed diagnosis and treatment. Lack of clinical awareness about the different presentations of narcolepsy in children can result in misdiagnosis, as occurred at eight different hospitals in this case. The financial and emotional costs for the patient and the family of such a protracted process of arriving at the correct diagnosis can be substantial.

To decrease the time lag between initial presentation and accurate diagnosis, we recommend that in all cases in which children report excessive sleep of unknown etiology – regardless of the associated symptoms – that sleep monitoring and sleep latency tests be conducted to rule out the possibility of narcolepsy. In this case the initial presentation of hypnagogic hallucinations and clinicians' failure to understand the relevance of the patient's reports (and her parents' report) of excessive sleep lead to the repeated incorrect diagnosis of different types of atypical epilepsy and to inappropriate treatment with antiepileptic medications, despite the absence of EEG evidence of epilepsy. Accurate diagnosis and treatment depends on taking detailed medical histories and being sensitive to the atypical presentations of uncommon psychiatric conditions, particularly in children.

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Conflict of interest

The authors declare that they have no competing interests.

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Informed consent

The patient's parents signed an informed consent form and agreed to the publication of this case report.

1 例发作性睡病的 6 岁孩子最初误诊为不典型癫痫的病例报告

周锦泉，张溪，董再文

概述：本文报告 1 例 6 岁女童首次发生发作性睡病被误诊为不典型癫痫。之后 10 个月在 8 家不同医院被误诊为其他疾病，最后才得以确诊。发作性睡病的诊断在小儿中比较困难，因为睡眠发作、猝倒、入睡前幻觉和睡眠麻痹四个主要症状都存在的病例在儿童中极少见到。患儿往往发作期更长、症状多样化。为了缩短从首次发病到确诊的时间，我们建议对所有不明原因过度睡眠的患儿监测睡眠并进行睡眠潜伏期试验，以排除发作性睡病的可能，而不论其相关症状如何。该病例凸显出罕见精神障碍的表现可以是多种多样的，特别是儿童。这就需要临床医生在采集病史时要充分考虑这些病例的非典型表现。

关键词：发作性睡病，入睡前幻觉，误诊，癫痫，儿童，中国

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Jinquan Zhou obtained his bachelor's degree in Clinical Medicine from Kunming Medical School in 1993. He is a chief psychiatrist and director of the Department of Psychiatry at the Dali Prefecture Second People's Hospital. He is responsible for clinical care, teaching, research, and health care management. He also serves as the secretary of the second party branch of the Communist Party at the hospital. He has won the Level Two Award of the State Government Scientific and Technological Progress Award once and the Level Two Award of the Dali Health System New Technology Projects twice.