Archives of Disease in Childhood 1992; **67**: 302–306

Narcolepsy

M R Allsopp, Z Zaiwalla

Abstract

The symptom of excessive sleepiness in children and adolescents does not necessarily cause great concern to families and professionals involved in their care. Children may deny the symptom and minimise the adverse effects. These factors contribute to an underdiagnosis of narcolepsy in this age group when clinical diagnosis is difficult as associated symptoms may not have appeared or are hard to elicit. In this paper three children whose difficult behaviour contributed to the presentation of their sleep disorder are described.

The narcolepsy syndrome comprises sleep disturbance, cataplexy, sleep paralysis, and hypnagogic hallucinations, although all four symptoms occur only in a minority.[1 2] The sleep disturbance involves excessive daytime drowsiness with intermittent, irresistible naps and a disrupted pattern of nocturnal sleep. Estimates of the prevalence of the condition suggest that between two and nine per 10 000 of the general population are affected.[3] There is a strong link with HLA-DR2.[4] The condition is rarely diagnosed in childhood or early puberty, although single cases have been reported.[5 6] In a large series of patients only 4% of 400 adults had been diagnosed before the age of 15 years,[7] yet Navelet *et al* reported that the families of more than half of adult patients recalled that symptoms had begun by that age.[8]

The apparent under identification of narcolepsy in children and young adolescents is given added significance by the increasing evidence that patients with narcolepsy suffer significant psychosocial adversity and the possibility that early intervention may reduce this.[9 10] Kales *et al* detail the retrospectively self reported psychosocial adverse consequences of excessive sleepiness in childhood or adolsecence.[11] Many patients had school problems and reported that their teachers misinterpreted symptoms as laziness, indifference, or malingering. The authors suggest that these consequences, together with a lack of emotional expressivity cultivated by patients to prevent cataplexy, contribute to the high rate (50%) of minor psychopathology found in this and other studies of adult populations.[12 13]

In this paper we describe three consecutive cases of narcolepsy in childhood presenting to the Park Hospital for Children, Oxford, a specialist centre for childhood epilepsy, sleep disorders, and behavioural disturbance. They illustrate some of the diagnostic issues and management problems that may be encountered.

Park Hospital for Children, Oxford
M R Allsopp
Z Zaiwalla

Correspondence to:
Dr M R Allsopp,
Child and Family Guidance Centre, Wyvern House, Theatre Square, Swindon, Wiltshire SN1 1QN.

Accepted 22 November 1991

Case reports

CASE 1

A boy aged 8 years was referred with a history of daytime sleepiness, irritability, and difficult behaviour. He had become increasingly sensitive, surly, and irritable after the birth of a sister one year earlier. When three months later the family moved home the boy resented the upheaval and found difficulty in settling and making new friends. His parents first noticed problems with daytime sleeping at around this time. Irresistible episodes of sleep, lasting from one to two hours, gradually increased in frequency to three or four times a day. He was often irritable on waking and his behaviour sometimes confused and disorientated. Sometimes he fell asleep while eating or even standing. His nocturnal sleep became restless, he was troubled by vivid dreams, and by a recurrence of nocturnal enuresis. He did not snore. At school he slept in quiet activities in class every day. Noting that during computing and games periods he was able to stay awake, his teachers had made the assumption that he was opting out of activities he disliked. They described him as academically bright and continuing to make good progress in class.

On interview he persistently denied that he slept during the day or had any problem with drowsiness. He gave no history of hypnogogic hallucination, cataplexy, or sleep paralysis. On admission to hospital for investigation the pattern of sleep disturbance and the denial of sleepiness continued. He would often remain standing for long periods during activities in order to prevent sleep. Although generally pleasant and cooperative, he became noticeably aggressive on waking from a daytime nap. Physical and neurological examination was normal. Investigations including thyroid function tests, 24 hour cassette recordings for electroencephalography (EEG), computed tomography, and magnetic resonance imaging (MRI) brain scans were normal. He was found to be of HLA type DR2.

Sleep recordings

All night polygraphic recordings of sleep over two consecutive nights were undertaken.[14] The physiological parameters measured included EEG, eye movements, and electromyelography for sleep staging as well as electrocardiography and periodic leg movements.[15] Simultaneous video recordings of nocturnal sleep and all night oximetry were also carried out. The results of the oximetry supported by video recording enabled obstructive sleep apnoea to be excluded.

The sleep recordings were analysed automatically using the Oxford Medilog sleep stager[16] and rechecked visually. The sleep architecture over both nights was stable with no significant differences in sleep stages. He went into rapid eye movement (REM) sleep within five minutes of sleep onset on both nights of the recording. His sleep was fragmented with frequent brief arousals and awakenings and he spent 16% of sleep time in the awake state or stage one sleep. This increase was at the expense of stage two sleep. Periodic leg movements, although increased, were not responsible for all arousals.

After the second night of recording a multiple sleep latency test was carried out, using standard protocol suggested by Carskadon *et al.*[17] Sleep onset occurred in less than five minutes in all five opportunities given and REM sleep within 10 minutes of sleep onset on four occasions. Taken together these sleep study findings were considered diagnostic of narcolepsy.

Management

After the sleep studies a detailed and age appropriate explanation of the diagnosis of narcolepsy was given to the boy and his parents over several meetings. The father was able to help his son overcome his initial denial and work positively on a management programme once he was discharged from hospital. This was facilitated by supportive family sessions and visits to the boy's school by hospital staff. As he was refreshed and able to concentrate well after a nap, a routine of three to four naps of 15 to 20 minutes' duration at fixed points in the day was established and was designed to help him to be alert in academic periods while minimising interference with social activities. In addition he was encouraged to follow a strict night time sleep routine to consolidate nocturnal sleep and advised not to get out of bed even if waking frequently.

As some daytime sleepiness persisted after these interventions, stimulant medication was prescribed in the form of mazindol 1 mg taken in the morning with food.[18] This produced improvement and 12 months after the diagnosis he continues to do well in school and remains alert during the day. His family report a reduction in irritability on waking and in his angry expression of sibling rivalry. He has not yet reported cataplexy or other associated symptoms.

CASE 2

A boy aged 12 years was referred by his paediatrician for investigation of behavioural disturbance and possible epilepsy. Four years earlier there had been a change in his disposition such that from being a relaxed and happy child he had become withdrawn, surly and truculent, had frequent temper outbursts, and was physically aggressive. On one occasion he struck a passer by who tried to prevent his breaking a shop window with a hammer. Both parents were profoundly deaf and this change in demeanour coincided with an appreciable deterioration in his father's hearing.

Episodes of daytime sleepiness started at 10 years of age. Initially they occurred at home when he was bored but gradually he started to fall asleep in unusual circumstances. He fell asleep during mealtimes and was once found asleep on the pavement outside a neighbour's house. If undisturbed he would sleep for three to four hours and would be irritable, aggressive, and moody if woken. There had been a number of episodes of confusion on waking. He did not snore and there was no definite history of cataplexy or sleep paralysis but he did report frequent nightmares. His appetite and weight had recently increased. At school his sleepiness was thought to be due to disinterest and laziness. His academic attainments had fallen dramatically and he had become withdrawn and socially isolated. Such was the extent of the difficulties in school that it was thought that his educational needs were best met away from mainstream school and transfer to residential special school had been arranged.

At interview he was argumentative and irritable with an abrupt and sullen manner. Although intermittently dozing off, he denied feeling sleepy and became angry when this denial was challenged. His general physical and neurological examination was normal. On admission for investigation his pattern of sleep disturbance and angry, oppositional behaviour in relation to daytime sleepiness was confirmed. Thyroid function tests, 24 hour cassette EEG, computed tomography, and MRI scans were normal. Nocturnal oximetry was normal. There was an increase in periodic leg movements. He was positive for HLA type DR2. Polysomnography showed disrupted sleep architecture consistent over two consecutive nights, with frequent arousals. The boy spent 27% of sleep time in wake or stage one sleep and entered REM sleep within five minutes of sleep onset. In the multiple sleep latency test sleep onset occurred in less than five minutes in all five opportunities given and sleep onset REM sleep occurred on two occasions. These findings were considered compatible with the diagnosis of narcolepsy.

Management

The diagnosis was discussed in detail with the boy and his family. He remained unable to accept the diagnosis or that daytime sleepiness posed any problem for him. He remained uncooperative with any intervention in hospital. With parental permission we discussed the implications with staff from the special residential school that he attended on discharge from hospital who were understanding and keen to help. The structured environment of a residential school allowed for the effective implementation of a strict nocturnal sleep routine and fixed naps to fit into the school day from the onset. At first he continued to deny problems and fought the desire to sleep by excessively argumentative and aggressive behaviour. However with continued support from school staff and the medical team he gradually, over a period of several months, became more amenable.

This allowed other treatment strategies to be employed. As he was overweight, he cooperated

in the introduction of a weight reduction programme. He started a low energy diet that also incorporated the avoidance of pure sugars, which are known precipitants of sleep in narcolepsy,[19] and took up weight lifting with great zeal and success. This considerably reduced daytime sleepiness, which was further helped by a small dose of stimulant drug in the form of mazindol 1 mg in the morning after food. This combined programme resulted in a considerable improvement in his behaviour and level of daytime alertness and he continues to function well 18 months after diagnosis.

CASE 3

A boy aged 9 years was referred by his paediatrician for investigation of disturbed nocturnal sleep, excessive daytime sleepiness, and excessive appetite, all gradually increasing over two years. At the time of referral he was suddenly falling asleep for periods of 15 minutes to one hour, three to four times a day. If undisturbed he awoke refreshed but if aroused was often irritable and aggressive. His noctural sleep was restless with frequent jerkings and awakenings. There was no history of sleep paralysis, hypnagogic hallucinations, or cataplexy. There was considerable concern about his voracious appetite with bingeing, which had resulted in excessive weight gain in the previous year.

Epilepsy had been considered in the differential diagnosis because of an unexplained injurious fall from a bicycle a year previously and non-specific EEG changes in the awake record including excessive slow waves for age. There were also considerable pre-existing psychosocial problems. The boy's parents separated 18 months after his birth because of marital violence. His teenage mother had returned to live with her father and stepmother. The boy's behaviour had become the focus of considerable friction between the adult members of the family. At school he was disruptive in class with poor concentration and was chaotic and aggressive in the playground. He was intelligent but significantly under achieving. He often fell asleep in class and his teacher initially attempted to rouse him without success. He had been referred to a child guidance clinic where a diagnosis of conduct disturbance was made and sleep disturbance was ascribed to psychosocial problems. With the advice of the clinic the boy's behaviour had significantly improved in the months before his assessment for sleep problems.

On admission to hospital daytime episodes of sleepiness and restless nocturnal sleep were confirmed. No behaviour problems were encountered during his stay and he interacted well with peers and staff. His general and neurological examination was normal. He was of HLA type DR2. Investigations, including 24 hour cassette EEG recordings, computed tomography, and oximetry were normal. Polysomnography and the multiple sleep latency test produced a pattern strongly suggestive of narcolepsy with fragmented noctural sleep architecture, a relative reduction in stage two sleep, and rapid entry into REM sleep at night. In four opportunities offered to sleep during the multiple sleep latency test there was an increase in periodic leg jerks but not sufficient to explain the extent of nocturnal arousal.

Management

Repeated explanation of these findings were given to the boy and his family, who found it initially very difficult to accept the diagnosis of narcolepsy. For three years the boy denied problems with daytime sleepiness and his family gave no commitment to a sleep management programme. However, at secondary school teachers construed his periods of sleepiness as 'opting out' and he was placed in a class for children with learning difficulties. The issue of his school progress was raised in a case conference. As a result the boy began to accept the need for active management of his daytime sleepiness. His teachers felt that fixed naps during the day would be impractical in a comprehensive school setting. His programme therefore included a weight reducing diet with avoidance of pure sugars, good nocturnal sleep hygiene, and stimulant medication (mazindol 2 mg) in the morning after food. He took responsibility for compliance and monitoring his own progress. At follow up there has been significant improvement in his level of alertness during the day and his progress in school is encouraging. Two episodes of possible cateplexy occurred about one year after diagnosis when his legs felt unsteady during an outburst of laughter.

Discussion

These cases illustrate many of the considerable difficulties in the diagnosis of narcolepsy in children and young adolescents. Recognition of the problem may be delayed for a number of reasons because children, like adults, find the occurrence of daytime sleepiness embarassing as it is often associated with indolence, incompetence, or social irresponsibility. To avoid teasing or admonition children deny symptoms and develop a variety of strategies to stave off sleep. Some of these strategies may be maladaptive, for example argumentative or disruptive class behaviour. Parental knowledge about normal sleep development is often sparse and in the absence of cataplexy, school failure, or appreciable behavioural difficulty anxiety about daytime sleepiness may be insufficient to bring the matter to medical attention.[8] The same environmental factors influence daytime sleepiness in narcoleptic patients and normal people. As patients tend to fall asleep in quiet lessons and after lunch rather than during periods of physical activity, teachers tend to initially attribute symptoms to disinterest, laziness, or social problems at home. This attribution may inhibit recognition of the problem until symptoms become considerable. Finally, as the condition is relatively rare before puberty few paediatricians or child psychiatrists have much experience of its presentation.

Guilleminault has described the differential

diagnosis of daytime sleepiness in children,[20] and Stores has pointed to confusions concerning sleep disorders and the epilepsies.[21] Though in adult or adolescent patients a clinical diagnosis of narcoleptic syndrome can often be made on the basis of detailed history taking alone, this is rarely the case with children, and in none of this series was it possible. All gave a history of a change in the quality of nocturnal sleep but a history of brief refreshing episodes of daytime sleep characteristic of narcolepsy was not obtained.[1] Rather, the daytime naps were long and unrefreshing perhaps because sleep had been resisted for long periods. On awakening the boys were often irritable and disorientated. It proved difficult also to elicit subjective experiences involved in sleep paralysis, hypnogogic hallucination, or cataplexy.

The short latency before REM sleep with fragmentation of sleep structure by frequent nocturnal arousals seen in the three children is characteristic of narcolepsy. Other causes of a short REM latency are sleep deprivation and depressive illness in adults. An increase in periodic leg movements or nocturnal myoclonus is reported in narcolepsy and was seen in all three children. The frequency of these movements was not sufficient to account for the frequency of nocturnal arousal found. The multiple sleep latency test is an objective measure of daytime sleepiness standardised by Carskadon *et al.*[17] A mean sleep latency of less than five minutes suggests pathological excessive daytime sleepiness and occurs in narcolepsy and occasionally in central nervous system hypersomnia and severe obstructive sleep apnoea. Two or more episodes of REM sleep occurring within 10 minutes of sleep onset (SOREM) on the five opportunities given to sleep during the day is considered diagnostic of narcolepsy. The mean sleep latency in all three children was less than five minutes and all had more than two episodes of SOREM.

The children's denial of symptoms, diagnosis, and problems became the greatest single barrier to effective management. Families found it difficult to accept a diagnosis with life long implications based solely on a sleep disturbance. We found it important to continue to support the family and child with regular follow up sessions. The cooperation of the children's school proved crucial in management. Teachers welcomed contact and explanation of the nature of the problem and when schools took up the suggestion of a nap programme there was undoubted success.[22] All three children required a small amount of stimulant medication to allow effective daytime function. Stimulants were not started until other management strategies had been fully explored. A very small once daily dose (1 or 2 mg) of mazindol given in the mornings after breakfast, on school days only, was found to be sufficient. No adverse effects have been encountered and the drug regimen has been well tolerated but requires continued monitoring.[23]

The behaviour problems exhibited by these boys were at times severe. There were pre-existing psychosocial and familial variables that undoubtedly contributed to them. Problems with conduct, control, and peer interactions were reported by families and schools before the onset of other symptoms in all three cases and may simply have been coincidental factors leading to early referral. However the onset of narcoleptic symptoms was temporally associated with a significant exacerbation of behavioural difficult. A number of mechanisms could be postulated for this. Firstly, there may be an increase in irritability, disinhibition, and disorientation associated with constant excessive drowsiness and periods of 'microsleep'.[24] Secondly, Roth has reviewed the association between narcolepsy and depression.[25] Mood changes might arise from neurobiological mechanisms associated with the as yet unknown aetiology of narcolepsy, or as a reaction to the disabling cognitive, emotional, and social effects of chronic sleepiness.[9 10 26] Although none of the boys met diagnostic criteria for depressive disorder, all tended to be low in mood, irritable, and socially withdrawn. Lastly it is possible that anxiety among the boy's carers after the onset of unusual symptoms led to more inconsistent management of behavioural problems at home, at school, and in hospital.

As narcolepsy is a life long condition early diagnosis would be of value if it could be demonstrated that psychosocial and educational problems could be reduced as a result. This might be achieved both through symptom control and educational approaches. These three cases illustrate some of the difficulties that may lie ahead in any attempt to achieve such a reduction. Research into management and educational strategies specifically for young people is needed. Studies are needed relating outcome in terms of employment and psychosocial factors to age and delay in diagnosis and to medical and educational intervention. With this information a better understanding of the aetiology and management of associated behavioural and mood problems may be achieved. As the number of children with the condition is small it may be necessary for specialist centres with appropriate resources for diagnosis and management to evolve. Difficulties for these patients may best be minimised by greater public awareness of the condition and knowledge of normal sleep development in children.

The authors would like to thank Dr Gregory Stores for his permission to report cases under his consultant care and for his help and advice in the preparation of this paper.

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