NARCOLEPSY WITH CONCOMITANT FEATURES OF OBSTRUCTIVE SLEEP APNEA

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A 17-year-old man presented with daytime sleepiness, episodic attacks of sleep and probable cataplexy. His EEG showed rapid eye movements and central sawtooth waves at sleep onset, and supported the clinical impression of narcolepsy. He improved with methylphenidate but died suddenly, and had cardiomegaly, right ventricular enlargement, and pulmonary hypertension at autopsy. These findings suggested concomitant features of sleep apnea which were not evident by history or examination.

Central apneas have been frequently described in the sleep of narcoleptic patients. Few patients have had indications of obstructive or mixed apneas. This patient's course suggests that ventilation during sleep should be included in the polygraphic assessment of patients with suspected narcolepsy, as the agents used for treatment of narcolepsy may aggravate the cardiac complications of sleep apnea.

Although narcolepsy and sleep apnea are both characterized by daytime sleepiness and nighttime sleep disturbance, they have been clearly differentiated clinically and polygraphically.[1] A number of patients with features of both sleep disorders have been described,[2-9] but those with narcoleptic symptoms have had ventilatory disturbances during sleep that were considerably less prominent than their narcolepsy, and have shown either central impairment of ventilatory drive during sleep or the pickwickian syndrome of obesity and hypoventilation when asleep or awake. This report describes a young man with well-defined narcoleptic symptoms who died suddenly and had pathological changes usually associated with the systemic complications of obstructive sleep apnea, in the absence of known waking or sleep hypoventilation during life.

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Case Report

A 17-year-old, right-handed black man was referred to Duke University Medical Center for evaluation of daytime somnolence and frequent sleeping in school. He had lived for several years at a state training school, and was considered educably retarded. He had a long history of intermittent hyperactivity, misbehavior, and fighting, for which he was occasionally treated with thioridazine (Mellaril). For the previous five years he had been often felt uncooperative and inattentive at school. During the two years prior to evaluation, he had often been sluggish and drowsy during daytime activities, reported himself "too tired" to participate in school functions, and frequently took naps in the classroom and on the playground. Despite this, he often fell asleep in class and, on at least two occasions, fell asleep while standing in line or while eating. On the latter occasion, his head fell into his plate, and he was awakened by the merriment of his classmates. He denied nighttime sleep disturbance and was reported by school personnel to sleep well and without snoring or unusual activity. He denied hypnagogic hallucinations or sleep paralysis. He said that he often became angry at school. At such times he felt weak and tremulous and, on a few occasions, had fallen to the ground. His past medical history was otherwise unremarkable. His family history was noncontributory, although it was incompletely known because he had been orphaned at an early age.

His general physical examination was unremarkable except for short stature and obesity; he was normotensive, had an unremarkable cardiac and chest examination, and had normal physical development and head circumference. His neurologic examination was remarkable only for dull

mentation. An electroencephalogram (EEG), during which the patient promptly fell asleep and was not observed to have abnormal respiration or frequent awakening, showed normal waking background but frequent transitions between wakefulness and sleep. The patient's sleep was characterized by rapid eye movements and central saw-tooth waves, suggestive of REM sleep, at onset.

He was begun on methylphenidate (Ritalin) 5 mg twice daily, and the dose was gradually increased to 10 mg. Little change was reported in his aggressive behavior, but he became more alert in school. Several months later, he was found dead in his bed by school personnel, no unusual events having been noted during the previous night. At autopsy, cardiomegaly and right ventricular enlargement were found, along with changes of pulmonary hypertension. The remainder of the autopsy was unremarkable, although permission to examine the brain was not received.

DISCUSSION

This patient described the onset in the second decade of life of sleepiness, episodic irresistible sleep, and emotionally induced weakness which probably represented cataplexy. His EEG showed rapid eye movements and central saw-tooth waves at sleep onset. These features were characteristic of narcolepsy, and his symptoms improved on methylphenidate. Aside from mild obesity, he had neither signs nor symptoms of sleep apnea. He died suddenly, however, and at autopsy had cardiopulmonary changes characteristic of obstructive sleep apnea. These findings suggest that the patient had a similar ventilatory disturbance, which was not evident by history or examination. His sleep EEG findings support this contention, as frequent transitions between sleep and waking are often seen in patients with obstructive sleep apnea.

The association of narcoleptic symptoms and ventilatory impairment during sleep was described by Sieker et al,[2] who reported a patient with obesity and pickwickian syndrome who had sleep attacks characterized by REM sleep. Subsequent studies have demonstrated primarily central apneas in narcoleptic patients. Kuhlo[3] and Lugaresi and co-workers[4] reported several nonobese patients who had daytime somnolence without other narcoleptic manifestations whose episodic sleep was characterized by central apnea. Kurtz and associates[5] observed central apnea in several patients with more clearly described narcoleptic symptoms. Guilleminault et al[6] studied two patients with narcolepsy including cataplexy and found central apneas of 20 to 90 seconds' duration during stages I, II, and REM. Central apneas were found in all sleep stages in a single patient studied by Lugaresi and associates[7]; the central apneas were associated with cardiac dysrhythmias which required a pacemaker and persisted after the narcoleptic symptoms were treated. Kales and coworkers[8] reported a narcoleptic patient who was unable to tolerate methylphenidate therapy because of cardiac dysrhythmias, and who had 30 to 70 central apneic episodes of mean duration 20 seconds prior to successful therapy with propranolol, which suppressed narcolepsy, cataplexy, and apnea in subsequent follow-up.

Obstructive sleep apnea has been much less frequently noted in association with narcolepsy. Lugaresi et al[9] described an additional narcoleptic patient who had intermittent daytime somnolence and attacks of sleep without other symptoms, which disappeared after weight loss. This patient showed central apneic episodes during stages III and IV of sleep, which persisted after weight loss and resolution of daytime somnolence. He had further apneic episodes of both mixed and purely obstructive type during REM sleep, which were associated with demonstrable alveolar hypoventilation and which remitted along with the somnolence when weight reduction was accomplished. Kales and associates[10] studied 50 adults with narcolepsy and cataplexy, and found histories of snoring in 34 and additional complaints suggestive of sleep apnea in 6; only one patient showed obstructive sleep apnea on polysomnography.

There is thus clear evidence that ventilatory drive may be reduced in patients with narcolepsy, and an indication in a smaller number of patients that the narcoleptic syndrome may coexist with features of obstructive sleep apnea. The patient described here demonstrates such an association, and suggests that the risks of cardiopulmonary complications and sudden death, presumably from cardiac dysrhythmias during sleep, are no less in such patients than in those with obstructive sleep apnea. These risks may in fact be potentiated by the use of systemic stimulants in the management of sleepiness and cataplexy. The small but increasing number of patients with well-characterized

narcolepsy and associated ventilatory disturbances suggests that polygraphic studies for suspected narcolepsy might be expanded to monitor respiration during sleep.

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INTRAOPERATIVE HYPOTHERMIA IN A PATIENT WITH COLD AGGLUTININ DISEASE

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A patient with cold agglutinin disease developed significant hemolysis after surgery because of intraoperative hypothermia. Convective heat losses from exposed viscera may be more significant than realized. A combination of cold-induced shivering heat loss, cold fluids, and long operations in which large surfaces are exposed can cause cardiac arrhythmias. The elderly patient is particularly susceptible to cold exposure and its consequences during surgery. In this situation of a patient with cold agglutinins, and in others with anitbody-related hemolytic disease, control of temperature during surgery is clearly very important.

Among pediatric surgeons, there is a healthy respect for the importance of body temperature control in infant patients during surgery. However, during adult surgical procedures, temperature is often overlooked. In the specific case of a patient with cold agglutinin disease, room and body temperatures must be carefully regulated to prevent postoperative hemolytic crises.

Cold agglutinins are complement-fixing antibodies which can provoke severe hemolysis at temperatures below 37°C. These autoantibodies, specific for Ii group erythrocyte antigens, can occur after mycoplasmal infection or as monoclonal antibodies in the absence of previous disease. Most naturally occurring cold agglutinins are anti-I and usually are not significant due to low titers.[1,2]

We present a patient with high-titer anti-I antibody who developed severe hemolysis after elective abdominal surgery.

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CASE REPORT

History

A 67-year-old white woman had a 3-month history of "crampy" abdominal pain. She denied