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Brief communication

The use of citalopram in resistant cataplexy

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Abstract

Background: Cataplexy is a disabling component of the narcolepsy tetrad that is sometimes resistant to standard treatment.

Case reports: Three of our patients with narcolepsy, including one who had post-traumatic narcolepsy, suffered from intractable cataplexy with failure of treatment with established drugs due to unacceptable side-effects.

Results: We explored the use of citalopram (Celexa), the newest and most specific of the serotonin reuptake inhibitors, and were successful in treating cataplexy without significant side-effects. Stimulant drugs remained necessary for controlling symptoms of excessive drowsiness.

Conclusions: Citalopram was effective in relieving the symptoms of resistant cataplexy in out patients.

Keywords: Cataplexy; Citalopram; Post-traumatic narcolepsy

1. Introduction

The narcolepsy tetrad comprises excessive daytime sleepiness (EDS), cataplexy, hypnagogic hallucinations, and sleep paralysis. While most cases are idiopathic and in the Caucasian population associated with HLA DR2, narcolepsy is a rare consequence of head trauma [1–3]. The most common presenting symptom of narcolepsy is excessive daytime sleepiness (EDS), which usually responds well to stimulant medication, but disability may persist because cataplexy may be difficult to control. Tricyclic antidepressants such as imipramine, and more recently, serotonin reuptake inhibitors (SSRI) such as fluoxetine [4] have been shown to be efficacious but side-effects, may be intolerable in some cases. We report three patients whose cataplexy failed standard treatment because of unacceptable side-effects, whom we successfully treated with citalopram.

2. Case reports

Patient 1: a 51-year-old white male, had post-traumatic narcolepsy. He presented to us for excessive daytime sleepiness with sleep attacks occurring several times a week. The frequency of these attacks was decreased by napping regularly, twice a day or so for 15 min to a few hours. He also experienced buckling of the knees and legs without completely losing tone 4–5 times a week and occasional buckling of his arms while writing. These episodes were precipitated by strong negative emotions. He also experienced sleep paralysis at the time of awakening on a daily basis. He reported frightening and violent dreams while falling asleep every other night, including one in which people threw insects at his left shoulder and

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strange experiences while drowsy that he described as 'almost psychedelic'.

These problems began at age 43 years, a few hours after a closed head injury with a fall backwards from a chair. He was unconscious for 5–15 min, and was taken to a hospital where he recounts that on an X-ray table, he was unable to move although fully awake. He soon started to have vivid dreams and over the next few days he developed symptoms of memory loss, difficulty reading with 'letters mixed up', leg weakness and excessive sleepiness whereby he could fall asleep 'any time, any place'.

His medical illnesses included renovascular hypertension, allergic rhinitis and depression. His wife reported snoring and pauses in breathing during sleep associated with gasping and choking. Physical examination showed moderate obesity (height 68 inches, weight 208 pounds, BMI 32.7 kg/m^2), inflamed nasal mucosa, enlarged uvula and low soft palate. Neurological examination was normal.

Nocturnal polysomnography (NPSG) showed sleep latency of 5.5 min, REM latency of 88 min, sleep efficiency of 89% and sleep maintenance of 90%. Sleep architecture was disrupted because of frequent arousals (arousal index 22.3/h), with 8% spent awake, 6% in Stage 1, 47% in Stage 2, 10% in Stages 3 and 4, and 29% in REM. Moderate snoring was noted and the respiratory disturbance index was 11 with six obstructive apneas, and hypopneas in both REM and NREM sleep mainly in the supine position, with basal oxygen saturation of 95.4% and 14 desaturations to 90.8%. Periodic limb movement of sleep (PLMS) index was 21.5/h causing 0.8 arousals/h. No bruxism or other parasomnias were noted.

The degree of sleepiness and associated symptoms suggested coexistent narcolepsy. Multiple sleep latency test (MSLT) performed the following morning showed a reduced sleep latency of 1.6 min over five naps and REM sleep on three of the five naps.

NPSG was repeated after treatment with clonazepam 1 mg, and on CPAP of 4 cms, with a Respironics mask and five spacer, which was sufficient to eliminate sleep apnea, snoring and desaturation. RDI was reduced to 2/h, arousal index 28.2/h mainly due to spontaneous arousals unrelated to PLMS or respiratory events. PLMS index was 18.8/h with 0.7 arousals/h due to PLMS. MSLT performed the following morning showed a reduced sleep latency of 1.87 min over four naps and REM sleep on each of the four naps with the patient reporting dreams in three of four naps.

Magnetic resonance imaging (MRI) and MRI angiogram of the vertebrobasilar system were normal. HLA DR2 typing was negative. Neuropsychological testing performed 3 years after the onset of the symptoms showed mild deficits in attention and concentration with intact speech, reading, cognition, intelligence and memory, moderate anxiety and depression and dysthymia.

A mandibular repositioning device was attempted to alleviate his mild sleep apnea and Neurontin 300 mg was prescribed for his PLMS. The EDS was initially resistant to treatment with methylphenidate and amphetamine with poor response at low doses and intolerable anxiety at higher doses, but responded well to a combination of methylphenidate 20 mg SR b.i.d. and modafinil 200 mg daily. The frequency of sleep attacks was further decreased by scheduled naps. Cataplexy was more difficult to treat. Treatment with multiple drugs including various anti-depressants and stimulants met with little success due to unacceptable side-effects. Several drugs including fluoxetine at a dose of 20 mg, protryptiline 10 mg twice a day, clomipramine 25 mg, sertraline 25 mg, and venlofaxine 37.5 mg were tried and were unsuccessful because of anxiety with SSRI drugs, and drowsiness with tricyclics, and lethargy or effects on cognition which he described as a sense of 'feeling spaced out'. Finally, he was placed on citalopram 20 mg with improvement in mood, with sustained benefit for the last 8 months in the symptoms of cataplexy with rare attacks (1–2 mild attacks/month), and elimination of sleep paralysis and hypnagogic hallucinations. Modafinil and methylphenidate with citalopram proved to be the most efficacious and best tolerated combination of drugs for relief from symptoms in this atypical patient.

Patient 2: a 45-year-old female, had daytime sleepiness since adolescence, worsening over time. She would fall asleep as often as ten times a day, for a few minutes each time, sometimes unexpectedly and inappropriately, for example, while taking a shower or while standing and talking or while working at a simultaneously boring and pressured job. She would sometimes fall in and out of sleep repeatedly over a few hours. Each sleep attack, which she describes as a

'power nap', energizes her and improves her mood. When engaged, such as during singing rehearsals or during emergency response to an earthquake (her present job), she has no difficulty staying awake, even without medication.

Embarrassment and even embarrassing thoughts, or stressful times when there was no escape, would precipitate cataplectic attacks, during which she felt like a jellyfish from head to toe and on rare occasions, fell to the ground. She would remain conscious but unable to keep her eyes open or speak. These attacks occurred 2–3 times a day and were not longer than a few minutes. During some of these attacks, she would feel extremely sleepy, and if it were possible, she would sleep. On one occasion, while looking at healing sutures on her hand after peeling off a band-aid, she felt shocked, and experienced a cataplectic attack in which she slept for 2 h. She recalls not having felt pain at the time and also stated that she was able to cheerfully tolerate having the sutures applied the previous week.

She has had automatic behaviors, especially while driving or while working on the computer when she would lose track of what she was doing. She occasionally experienced hypnagogic hallucinations and stated that she would 'dream while awake' and carry on conversations and respond to questions while in a dream state.

She incurred mild head trauma without loss of consciousness at age 13 years, and had staring spells in childhood during which she was unresponsive. These spells were thought to be seizures, and have spontaneously resolved. She suffered from chronic depression. Past surgical history was remarkable for a tumor of the pancreas removed as age 20 due to which she had hypoglycemic attacks.

Physical examination was remarkable only for mild obesity (weight 174 pounds, height 67 inches, BMI 28.3). The upper airway and chest was normal. Neurological examination was normal. NPSG showed a sleep efficiency of 88%, sleep maintenance of 92%, arousal index 10/h, with sleep onset latency of 19 min and REM latency of 116 min, without snoring, apneas or desaturations. MSLT showed a reduced sleep latency of 3.9 min over five naps and REM sleep on the fourth nap. Narcolepsy was considered the most likely diagnosis given normal NPSG and the presence of associated symptoms. Electroencephalography (EEG) showed interictal epileptiform activity over the left temporal region without clinical change and drug screen showed the presence of caffeine.

Pemoline 37.5 mg was effective in alleviating the EDS. The cataplexy and depression were treated initially with sertraline, which caused her to gain weight. Fluoxetine caused anorexia, severe weight loss and dizzy spells. A skin rash erupted on Paxil. Fluvoxamine caused anxiety at doses adequate to control the cataplexy. Citalopram (20 mg daily), completely controlled cataplexy, without side-effects and has been effective for more than 10 months.

Patient 3: is an 86-year-old female with sleep attacks several times a day since the age of 12 years. She could fall asleep without warning, typically with a spoon half way to her mouth, while eating with her family while seated at the table. In adolescence, she would fall asleep even while standing. She often complained of fatigue following these attacks. She was diagnosed with cataplexy at age 62 years when she developed sudden muscle weakness while playing cards with her grandchildren. She appeared to 'pass out', with her neck falling forward and was unable to keep her eyes open. However, she was conscious and able to hear what was said to her but unable to speak or communicate expect for a few sounds. This lasted 30 min, and recurred several times in the next few months while laughing especially when watching sit-coms on television, or when angry or crying. She fell several times due to cataplectic attacks that occurred while she was standing, and as a result sustained broken teeth, rotator cuff injury, fracture of the hip, and knee injuries requiring surgery. She denied sleep paralysis or hypnagogic hallucinations. She reported difficulty both in falling asleep and in staying asleep at night and her husband noted that she twitched and jerked her legs in sleep. Family history was significant for the diagnosis of narcolepsy in her mother.

Her other medical problems include cerebellar degeneration and peripheral neuropathy secondary to chronic alcoholism, essential tremor, transient right hemiparesis lasting 48 h at age 81 years, hypothyroidism, polycythemia vera, osteoporosis with collapsed T12 vertebral body, mild scoliosis, arthritis, gout, hypertension, and myocardial infarction at age 66 years. Medications include mysoline 50 mg at bedtime for the tremor, hydroxyurea (500

mg) daily, lactulose (20 mg) tid, trazodone (50 mg) at night for sleep onset and sleep maintenance insomnia, Voltaren (50 mg) bid, vitamin D, Procardia (20 mg/day), and synthroid (0.2 mg daily).

Neurological examination was remarkable for mild gait ataxia, inability to walk in tandem or turn rapidly, and decreased vibratory sense, position sense and absent ankle reflex in the lower extremities. NPSG showed sleep onset and maintenance insomnia and periodic leg movements. Sleep efficiency was 41%, and sleep maintenance 42%. Sleep latency was 0 min, and REM latency 313 min. Sleep architecture was fragmented with 228 min, with the patient awake after sleep onset (58%), 74 min spent in stage 1 (19%), 72 min in stage 2 (18%), 18 min in stage 3 and 4 (5%), and 2.5 min in REM (1%). Sleep time was reduced to 167 min, 142 arousals on EEG and 17 arousals longer than 2 min, with an arousal index of 51/h. RDI was 1 with two events of obstructive hypopnea and four central apneas, and mild snoring. PLMS index was 71, 43% associated with arousals. MSLT performed the following morning supported the diagnosis of narcolepsy with an average sleep latency of 5.3 min and REM at sleep onset (0.1–0.5 min) in three of four naps, and with two REM periods in the first nap. MRI scan showed degenerative changes in the cerebellum, in particular the vermis. EEG showed no abnormal epileptiform discharges.

On methylphenidate 20 mg SR and imipramine 100 mg, she no longer had sleep attacks but did have rare cataplectic attacks, every 3–4 months. While on this treatment, she complained of dry mouth, and developed fatigue and complained of feeling dizzy. She also reported two episodes of brief loss of consciousness, when she felt faint and hot, and fell forwards bruising her face in the process. There were no tonic or clonic jerks observed. She recovered quickly and was aware of her surroundings. These complaints were evaluated and she was diagnosed with bradycardia without orthostatic hypotension, due to heart block at the atrio-ventricular node, for which a pace-maker was implanted. Citalopram (20 mg) replaced the imipramine, which may have contributed to the cardiac arrhythmia. In the 8 months since starting the patient on citalopram, there have been two cataplectic attacks at times of major stress, e.g. hospitalization of her husband. She has had only one sleep attack in the past year at a moment of quiet inactivity, and reports no side-effects from the medication.

3. Conclusion

Citalopram was effective and well tolerated in three of our patients with cataplexy who had difficulty tolerating other drugs. Citalopram has proven to be efficacious and safe for the treatment of depression [5,6]. The serotonin reuptake inhibitors differ subtly in their clinical profile, especially with regard to side-effects, with varying influences on appetite and anxiety. Citalopram now merits further evaluation as treatment for cataplexy.

References

[1] Lankford DA, Wellman JJ, O'Hara C. Post-traumatic narcolepsy in mild to moderate closed head injury. Sleep 1994;17(8):S25–S28.

[2] Francisco GE, Ivanhoe CB. Successful treatment of post-traumatic narcolepsy with methylphenidate: a case report. Am J Phys Med Rehab 1996;75(1):63–65.

[3] Maeda M, Tamaoka A, Hagashi A, et al. A case of HLA DQw1 negative post-traumatic narcolepsy. Rinsho Shinkeigaku 1995;35(7):811–813.

[4] Frey J, Darbonne C. Fluoxetine suppresses human cataplexy: a pilot study. Neurology 1994;44(4):707–709.

[5] Kyle CJ, Petersen HE, Overo KF. Comparison of the tolerability and efficacy of citalopram and amitryptiline in elderly depressed patients. Depress Anxiety 1998;8(4):147–153.

[6] Montgomery SA. The antidepressant efficacy of citalopram. Int Clin Psychopharmacol 1996;11(Suppl 1):29–33.