CLINICAL VIGNETTE

Narcolepsy without Cataplexy – Often a Delayed Diagnosis

Roman Culjat, MD

A 30-year-old man presented with excessive daytime sleepiness. The problem started about 10 years but he does not remember details of initial presentation. He easily falls asleep when around loud music. He can fall asleep while at a red light or while driving. He has had 2 auto accidents. Now whenever he feels sleepy while driving he pulls over. He feels as though there is something that he cannot control. Coffee does not help keep him awake even after 2-3 cups, and now he just drinks it for the taste. He gets about 7-9 hours of sleep per night. It does not matter how much sleep he gets at night as he still falls asleep easily during the day. On a typical night he sleeps from 12 midnight to 8 AM. He feels fine after 6 hours of sleep. He feels energetic after naps. He denies snoring, waking up gasping for air, waking up for unexplained reasons, or witnessed apneas. No paralysis when falling asleep and no hallucinations when waking up or falling asleep. No cataplexy episodes, weakness triggered by anger or laughter. He has no significant past medical or past surgical history. He does not take any medications. He was born in Turkey and has lived in the US for several years. He works in data management from 1130 AM to 730 PM 5 days per week. He may sleep for 10 minutes during a break. On rare occasions he has made mistakes at work, and rarely in a briefing has to take a nap. At most he has a couple of alcoholic beverages per month. No tobacco or illicit drug use. About 7 years ago in his home country of Turkey he had a CT scan and MRI of the brain which were apparently unremarkable. The details of the remainder of the work up in Turkey are not known. After a clinical evaluation he had an in lab overnight polysomnogram (PSG) followed by a multiple sleep latency test (MSLT) the next morning. During the PSG he fell asleep in 5 minutes and reached REM sleep in 58 minutes.

There was no evidence of obstructive sleep apnea with an apnea hypopnea index (AHI) of less than 1. He then did the full day MSLT, falling asleep during all 5 naps with an average sleep latency of 3.9 minutes and going into REM sleep during 3 of the 5 naps. This was an abnormal MSLT consistent with hypersomnia. He was diagnosed with narcolepsy without cataplexy. The patient was started on armodafinil 150 mg by mouth every morning, and scheduled naps were recommended. It was also recommended that he register with the Narcolepsy Network. At 3 month follow up he reported that he was doing much better. He was no longer falling asleep during the day and his friends noticed a major difference in staying awake when he was with them. He was able to stay awake during the day, and drive for 2-hours without feeling sleepy. For the first 10 days of treatment he felt that he had a problem focusing, but after 10 days this focusing problem resolved. He has not had any other side effects from the medication. He initially scheduled daily naps for the first month, but since then he has been scheduling naps about 50% of days.

Chronic excessive daytime sleepiness along with recurrent episodes of hallucinations and sleep paralysis, lack of cataplexy, and the absence of psychiatric conditions point at the diagnosis of narcolepsy without cataplexy (NT2).[1] Daytime naps are usually refreshing and often include dreaming.[1] Hypnagogic or hypnopompic hallucinations are present in around 30% of NT2 cases, and sleep paralysis occurs at an average of 3 times per month in series including patients with NT2.[1] In addition, sleep fragmentation may also be common in NT2 patients.[1] Other sleep conditions and causes of hypersomnia must be ruled out, and the mean sleep latency test (MSLT) must show a mean sleep latency of 8 minutes or less and two or more sleep onset REM periods (SOREMPs).[2] This patient had chronic excessive daytime sleepiness with refreshing naps. He did not have any hallucinations, sleep paralysis, cataplexy, or psychiatric conditions. His overnight polysomnogram (PSG) was unremarkable, but the MSLT showed a mean sleep latency of 3.9 minutes and 3 out of 5 SOREMPs. His condition was consistent with narcolepsy without cataplexy (NT2).

Some patients with narcolepsy without cataplexy (NT2) may develop cataplexy years later and be reclassified as narcolepsy with cataplexy (NT1).[1] Approximately 50% to 60% of patients with narcolepsy have episodes of cataplexy, an abrupt loss of muscle tone induced by a strong emotion (e.g., laughter, anticipation, anger).[3] The presence of cataplexy distinguishes the two subtypes of narcolepsy: narcolepsy with cataplexy (narcolepsy type 1 – NT1) and narcolepsy without cataplexy (narcolepsy type 2 – NT2).[3] This patient had narcolepsy without cataplexy (NT2).

Since the majority of the epidemiological studies included patients with both NT1 and NT2,[4] there are no valid data relating the prevalence of NT2. Its challenging detection, due to lack of awareness of the condition, nonspecific criteria, and lack of pathognomonic features such as cataplexy, may result in under or over diagnosis of the disorder.[4] Delayed diagnosis among narcolepsy patients is a well-described clinical problem as patients often receive the diagnosis years after symptom onset.[3] This patient was diagnosed with narcolepsy without cataplexy at least 10 years after experiencing symptoms.

The main medications for narcolepsy without cataplexy are stimulants and sodium oxybate. A 2007 review article[4] mentioned that the traditional stimulants are considered mainstays for treatment of sleepiness associated with narcolepsy. These

are highly controlled substances and require monthly prescriptions that the patient must take to the pharmacy. Modafinil and armodafinil have become much more popular. Modafinil 200 mg BID or 400 mg in AM was better than modafinil 200 mg in AM in terms of afternoon sleepiness. Taking 200 mg BID seemed to work better than 400 mg in AM. Armodafinil, the R-enantiomer of racemic modafinil, with a longer half-life, was also recently approved by the Food and Drug Administration (FDA) for excessive daytime sleepiness associated with narcolepsy. Importantly, the R-enantiomer of modafinil has a half-life of 10 hours to 15 hours, which is longer than that of the S-enantiomer of modafinil (3–4 hours).[5] Armodafinil comes in 150 mg and 250 mg doses. Sodium oxybate, a different treatment for narcolepsy taken at bedtime and again 2.5 to 4 hours after bedtime. It demonstrated improvement in subjective sleepiness and reduction in inadvertent naps or sleep attacks with doses 6 or 9 gm per night. It was more effective in the 9 gm dose.[4] Scheduled sleep periods are helpful only for those narcolepsy patients who remain profoundly sleepy despite treatment with stimulant medications.[4] The 2007 AASM Practice Parameters [6] supported the use of modafinil and sodium oxybate. Armodafinil as mentioned is now supported as well. Also supported are amphetamine, methamphetamine, dextroamphetamine, and methylphenidate. This patient is currently on armodafinil 150 mg daily. He fortunately responded well to the lower dose of this medication alone and does not need to take daily naps while on the medication. Many patients require the addition of sodium oxybate as well as scheduled daily naps, and they often must modify their work schedules.

REFERENCES

1. **Pérez-Carbonell L, Leschziner G.** Clinical update on central hypersomnias. *J Thorac Dis.* 2018 Jan;10(Suppl 1):S112-S123. doi: 10.21037/jtd.2017.10.161. Review. PubMed PMID: 29445535; PubMed Central PMCID: PMC5803059.
2. **American Academy of Sleep Medicine.** International classification of sleep disorders. 3rd edition. In: Diagnostic and coding manual. Westchester, IL: American Academy of Sleep Medicine, 2014.
3. **Maski K, Steinhart E, Williams D, Scammell T, Flygare J, McCleary K, Gow M.** Listening to the Patient Voice in Narcolepsy: Diagnostic Delay, Disease Burden, and Treatment Efficacy. *J Clin Sleep Med.* 2017 Mar 15;13(3) 419-425.doi:10.5664/jcsm.6494. PubMed PMID: 27923434; PubMed Central PMCID: PMC 5337589.
4. **Wise MS, Arand DL, Auger RR, Brooks SN, Watson NF;** American Academy of Sleep Medicine. Treatment of narcolepsy and other hypersomnias of central origin. *Sleep.* 2007 Dec;30(12):1712-27. Review. PubMed PMID: 18246981; PubMed Central PMCID: PMC2276130.
5. **Takenoshita S, Nishino S.** Pharmacologic Management of Excessive Daytime Sleepiness. *Sleep Med Clin.* 2017 Sep;12(3):461-478. doi:10.1016/j.jsmc.2017.03.019. Epub 2017 Jun 7. Review. PubMed PMID: 28778242.
6. **Morgenthaler TI, Kapur VK, Brown T, Swick TJ, Alessi C, Aurora RN, Boehlecke B, Chesson AL Jr, Friedman L, Maganti R, Owens J, Pancer J, Zak R;** Standards of Practice Committee of the American Academy of Sleep Medicine. Practice parameters for the treatment of narcolepsy and other hypersomnias of central origin. *Sleep*. 2007 Dec;30(12):1705-11. Review. Erratum in: *Sleep.* 2008 Feb 1;31(2):table of contents. PubMed PMID: 18246980; PubMed Central PMCID: PMC 2276123.

Submitted April 19, 2018