Case 1

"I've Fallen … and I Can't Get Up"

Sundowner Syndrome

Mr. S is an 80-year-old gentleman with a significant medical history of a kidney transplant, diabetes, hypertension, hyperlipidemia, gastroesophageal reflux disease (GERD), atrial fibrillation, obstructive sleep apnea, and hypothyroidism. He was living at home with his wife when he had a nighttime fall with loss of consciousness. The fall resulted in a lumbar spinal burst fracture that required spinal fusion surgery. His post-op course was complicated by delirium in the intensive care unit (ICU). He would become disoriented and agitated and throw himself from his bed to the floor. He was referred to geriatric psychiatry for consultation due to concerns about his agitated behavior since his arrival at hospital two weeks prior. He had poor nutritional intake with a 30-pound weight loss. This led to a PICC line placement for total parenteral nutrition (TPN). Before discharge TPN was stopped and Mr. S had a G-tube placed for nutritional support. He was in acute rehab for nine weeks before being transferred to long-term care.

The family reported that the patient was often irritable. He had increased confusion and agitation in the evening and continued to occasionally throw himself out of bed. He had had several urinary tract infections (UTIs) over the three months prior to long-term care.

The nursing staff informed his medical provider that the patient would yell at anyone involved in his care, including physical therapists and nurses. They said he would purposely throw himself out of his wheelchair or bed when his requests were not responded to promptly. He would not engage in social activities at the facility and complained of poor energy and always feeling tired.

Mr. S had no significant psychiatric history and had never been under the care of a psychiatrist before. His sleep was described as poor. He would sleep throughout the late morning and early afternoon and not sleep well at night. He still seemed to enjoy watching baseball games at times.

His mental status exam described his mood as sad, with poor eye contact and a mostly logical and linear thought process. He was also described as irritable during portions of the interview and cooperative at other times. He was oriented to person but was not oriented to place or time. He was unable to identify his wife's sister or name his two children.

The medical provider recommended routine bloodwork and a repeat urinalysis to check for potentially reversible causes of subtle delirium. He was put on trazodone 50 mg qhs for sleep and 25 mg twice daily as needed for anxiety or agitation.

At the time of follow-up two weeks later, Mr. S was found to be mostly unchanged. He continued with regular displays of agitation and aggression toward care staff and family members that seemed to become more pronounced in the late afternoon and early evening hours. His appetite continued to be poor and his mood was mostly described as

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irritable. He slept a bit better at night but would wake up in the early morning hours asking to get out of bed into his wheelchair, at which time he would be brought close to the nurse's station where he would often yell at staff.

The provider started the patient on sertraline 25 mg daily, which was soon increased to 50 mg daily. The physician recommended that the patient be brought out of his room and encouraged to participate in activities during the daytime instead of being allowed to stay in his room and sleep. Care staff were encouraged to bring Mr. S to the dining room for meals instead of allowing him to take his meals in his room. This was to encourage more socialization, combat boredom, and encourage the normalization of day/night cycles. Melatonin 5 mg qhs was also started.

At a four-week follow-up visit, Mr. S was found to be doing somewhat better. His mood was described as less irritable and he was more cooperative with care. His nutritional intake improved, and his weight loss started to level off. It was noted that care staff were taking the patient outdoors when the weather was good and he seemed to enjoy this. His family was pleased with his improvements in neuropsychiatric symptoms and encouraged by his increasing willingness to participate in therapies, with the goal of Mr. S being able to participate adequately enough in his care to potentially move back home with his family.

Teaching Points

"Sundowner syndrome" refers to a constellation of neuropsychiatric symptoms, usually accompanied by agitation that occurs late in the day in a patient with a major neurocognitive disorder (MNCD). In addition to agitation, anxiety, aggressiveness, increased confusion, and even visual or auditory hallucinations are common. Second only to wandering, sundowning is reported to be one of the most common disruptive behaviors in long-term care settings [1]. Symptoms usually emerge later in the day, classically in the late afternoon or early evening at the time of sunset. This neuropsychiatric syndrome can be very challenging for caregivers. Sundowning is a common reason for those with MNCDs to be moved from home to a long-term care facility. It is also one of the more common reasons for consultation with a geriatric psychiatrist in the long-term care setting.

Sundowning and delirium share some similarities with regard to underlying causes. Both are strongly associated with MNCDs. One key difference between sundowning and delirium is the time of day in which symptoms occur. Sundowning typically occurs and recurs in the late afternoon or evening hours whereas delirium can occur at any time of the day or night.

The treatment of delirium focuses on the identification and treatment of underlying medical issues or medications that may be contributing. In contrast, the treatment of sundowning focuses on altering environmental factors that can contribute to the condition.

The pathophysiology of sundowner syndrome is not fully understood, but there are several theories about the underlying mechanisms. These theories are not mutually exclusive.

One theory is that sundowning may be related to changes in the body's internal clock or circadian rhythm regulation. These rhythms are regulated by the suprachiasmatic nucleus (SCN), which responds to light and dark stimuli to help regulate sleep–wake cycles and other physiological processes. In individuals with dementia or other cognitive

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impairments, the SCN may be disrupted, leading to changes in sleep patterns and other circadian rhythms. This disruption may contribute to the development of sundowning symptoms in the late afternoon or evening.

Another theory is that sundowning may be related to pain or fatigue that becomes more pronounced in the late afternoon or evening. Individuals with dementia or other cognitive impairments may have difficulty communicating their discomfort, leading to increased agitation or confusion as a way of expressing their discomfort.

There is also evidence to suggest that sundowning may be related to changes in neurotransmitter levels, particularly concerning the neurotransmitter acetylcholine. Individuals with Alzheimer's disease or other forms of MNCD have a loss of acetylcholine-producing neurons in the brain, which contributes to changes in cognitive function and behavior [1].

Sensory deprivation can also play a role in sundowner syndrome. Seniors in long-term care are often lacking in stimulating daytime activities. A multidisciplinary approach to creating individualized care plans for seniors with MNCD is important. These care plans should allow seniors to have regular social interactions, physical activity, family-style mealtimes, time outdoors, and religious activities.

The treatment of sundowning depends on the acuity of symptoms. All patients should have a thorough examination of environmental factors that could be contributing to late-day confusion and agitation and changes made to improve those environmental factors. Medications that could be contributing to confusion should also be identified and removed.

At the time of this writing, there has been relatively recent approval from the US Food and Drug Administration (FDA) of the atypical antipsychotic brexpiprazole for treating agitation due to Alzheimer's disease[2]. There are several other pharmacologic options for the treatment of agitation in the setting of MNCDs. For mild symptoms, several studies have demonstrated improved outcomes for those with sundowner syndrome with melatonin [1]. Melatonin levels are deficient in those with MNCDs (especially Alzheimer's disease). Melatonin is generally well tolerated and may be worth trying in those with mild symptoms. In those patients with more severe symptoms, including severe agitation or psychosis, a trial of a second- or third-generation antipsychotic may be warranted [1]. Antipsychotics are used off-label and should be used with caution and in the smallest dose for the shortest possible duration. Regular efforts to decrease the dosage of antipsychotics are also needed once symptoms are controlled. Cholinesterase inhibitors such as donepezil are known to improve behavioral disturbances in patients with dementia but there are conflicting data on the effect of cholinesterase inhibitors on sundowner syndrome [1].

Take-Home Points

- Sundowner syndrome refers to a constellation of neuropsychiatric symptoms, usually accompanied by agitation that occurs late in the day in a patient with an MNCD. In addition to agitation, anxiety, aggressiveness, increased confusion, and even visual or auditory hallucinations are common.
- Mild symptoms may respond well to melatonin 5 mg in the late afternoon. In those patients with more severe symptoms, including severe agitation or psychosis, a trial of a second- or third-generation antipsychotic may be warranted.
- All patients should have a thorough examination of environmental factors that could be contributing to the late-day confusion and agitation and changes made to improve those environmental factors. Medications that could be contributing to confusion should also be identified and removed.

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– Antipsychotics are used off-label and should be used with caution and in the smallest dose for the shortest possible duration. Regular efforts to decrease the dosage of antipsychotics are also needed once symptoms are controlled.

References

1. Canevelli, M., Valletta, M., Trebbastoni, A., Sarli, G., Tariciotti, L., & Bruno, G. (2015). Sundowning in dementia: Clinical relevance, pathophysiological determinants, and therapeutic approaches. *Frontiers in Medicine*, 3. https://doi.org/10.3389/fmed.2016.00073
2. Grossberg, G. T., Kohegyi, E., Mergel, V., Josiassen, M. K., Meulien, D., Hobart, M., Slomkowski, M., Baker, R. A., McQuade, R. D., & Cummings, J. L. (2020). Efficacy and safety of brexpiprazole for the treatment of agitation in Alzheimer's dementia: Two 12-week, randomized, double-blind, placebo-controlled trials. *The American Journal of Geriatric Psychiatry*, 28 (4), 383–400.

Further Reading

Ahmad, F., Sachdeva, P., Sarkar, J., & Izhaar, R. (2022). Circadian dysfunction and Alzheimer's disease: An updated review. *Aging Medicine*, 6 (1), 71–81. doi: 10.1002/agm2.12221. PMID: 36911088; PCMID: PMC10000289.

Carrarini, C., Russo, M., Dono, F., Barbone, F., Rispoli, M. G., Ferri, L., Pietro, M. D., Digiovanni, A., Ajdinaj, P., Speranza, R., Granzotto, A., Frazzini, V., Thomas, A., Pilotto, A., Padovani, A., Onofrj, M., Sensi, S. L., & Bonanni, L. (2020). Agitation and dementia: Prevention and treatment strategies in acute and chronic conditions. *Frontiers in Neurology*, 12. https://doi.org/10.3389/fneur.2021.644317

Desai, A., & Grossberg, G. (2018). *Psychiatric Consultation in Long-Term Care. A Guide for Healthcare Professionals.* 2nd ed. (Cambridge University Press.)

Guu, W., & Aarsland, D. (2022). Light, sleep–wake rhythm, and behavioural and psychological symptoms of dementia in care home patients: Revisiting the sundowning syndrome. *International Journal of Geriatric Psychiatry*, 37 (5). https://doi.org/10.1002/gps.5712

Lin, L., Huang, Q. X., Yang, S. S., Chu, J., Wang, J. Z., & Tian, Q. (2013). Melatonin in Alzheimer's disease. *International Journal of Molecular Sciences*, 14 (7), 14575–14593. doi: 10.3390/ijms140714575. PMID: 23857055; PMCID: PMC3742260.

Menegardo, C. S., Friggi, F. A., Scardini, J. B., Rossi, T. S., Vieira, S., Tieppo, A., & Morelato, R. L. (2019). Sundown syndrome in patients with Alzheimer's disease dementia. *Dementia & Neuropsychologia*, 13 (4), 469–474. https://doi.org/10.1590/1980-57642018dn13–040015

Sharma, A., Sethi, G., Tambuwala, M. M. A., Aljabali, A. A., Chellappan, D. K., Dua, K., & Goyal, R. (2021). Circadian rhythm disruption and Alzheimer's disease: The dynamics of a vicious cycle. *Current Neuropharmacology*, 19 (2), 248–264. https://doi.org/10.2174/1570159X18666200429013041

Todd, W. D. (2019). Potential pathways for circadian dysfunction and sundowning-related behavioral aggression in Alzheimer's disease and related dementias. *Frontiers in Neuroscience*, 14. https://doi.org/10.3389/fnins.2020.00910

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