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Refractory Delirium in a Hospice Patient

A Case Study

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Delirium affects an enormous number of patients at end of life and entails great physical, emotional, and financial burdens. Existing algorithms approach this phenomenon simplistically with the primary goal of identifying and treating the underlying cause. However, many episodes of delirium are multifactorial and not so easily resolved. Much has been written about controlling for physical and pharmacologic causes, but there has not been much attention paid to the interaction of the care setting in managing delirium. This case study illustrates some of the challenges in caring for a patient with refractory delirium in a skilled nursing facility.

KEY WORDS

agitation, antipsychotics, delirium, safety

Delirium is defined as an acute change in attention and cognition with the hallmark pattern of waxing and waning behaviors. Up to 85% of patients with advanced illness will develop some form of delirium as it is a syndrome that accompanies physiologic stress.[1] Delirium is typically underdiagnosed as the presentation can mimic or coincide with other factors that change a patient's sensorium.[2] Anybody with a preexisting functional or cognitive impairment is at higher risk for developing delirium.[3]

Untreated delirium hampers treatment, increases risk of injury, and contributes to increased length of hospital stays and health care expenses. Patients with delirium have an increased risk of death during the episode and have poorer outcomes after hospitalization when compared with patients without delirium.[4] Cognitive and communication deficits that accompany the syndrome interfere with caregiving and add stress to already burdened families.[5]

A key barrier to managing delirium is lack of recognition. The majority of patients present with a hypoactive delirium. This type is marked by a decrease in cognitive status and motor activity and may go unrecognized by those unfamiliar with the patient's functional baseline.[3] These patients may have preserved social skills that mask disorganized thinking in a casual interaction but may appear irritable or withdrawn.[6] These might also be the patients who simply sleep all day or are "pleasantly confused." Hypoactive delirium is linked to higher mortality, possibly from a delay in the diagnosis.[3]

There are several well-known delirium screening tools that are validated for use in cancer patients. The Confusion Assessment Method and the Memorial Delirium Assessment Scale are just 2 of the many available scales.[1] These instruments may be limited in that they focus on basic patient orientation, which may yet be preserved in delirium.[6] In addition, tools are not always administered consistently and require subjective input.[2] Inouye et al[7] have developed the Confusion Assessment Method–Severity scoring system that goes beyond screening to actually measure not only the severity of the acute episode but also an association with clinical outcomes such as length of stay, functional decline, nursing home placement, or death at 90 days.

About 25% of affected patients will present with hyperactive delirium marked by excessive verbal or motor activity. It may also include irritability, hallucinations and delusions, threats of violence, and actual acts of violence or destruction. Some patients will have a combination of the two, known as mixed delirium.[1] Oftentimes, it is only when a patient's behaviors become bizarre or violent that clinicians recognize and diagnose the delirium.[2]

Troubling as well is the concept that those with delirium are suffering invisibly from a disorder of consciousness, in which patients reported feeling as though they were "trapped in incomprehensible experiences" where past, present, time, and place are mixed together.[8] In 1 study, 53.5% of hospitalized patients with delirium were able to recall their experience afterward. Furthermore, 80% of those patients described the delirium as an extremely distressing experience.[5]

It should also be noted that whichever type of delirium a patient experiences, their family is experiencing distress as well. Families of patients at end of life have spoken of an "early bereavement" when they feel they have lost the person's consciousness despite their loved one's continued physical existence.[1]

Most treatment guidelines focus on treating the underlying cause, decreasing environmental stimuli, and using antipsychotic medications. It is clear from research and anecdotal

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case studies that there is no "one size fits all" approach.[9] The concept of addressing the impact of the potential for post-traumatic effects of "disordered consciousness" of delirium survivors is relatively new.[2] A treatment algorithm that begins with "identify cause and treat" may be sufficient to manage about 50% of patients with delirium,[10] but what of the patient with refractory delirium for whom the standard plan of care is not at all effective? Such was the case with H.G. The following case study illustrates some obstacles in caring for a complex oncology patient suffering with delirium in a skilled nursing facility.

Case Study

H.G. is a 65-year-old man with squamous cell carcinoma of the head and neck with metastasis to the lungs at time of diagnosis. Significant health history includes 30 pack-years of tobacco use, benign prostatic hypertrophy, and depression. He had received chemotherapy and radiation within the previous 6 months. The tumor began to compromise his airway, and he required a tracheostomy. He also had a feeding tube inserted. It was after these interventions that H.G. enrolled in hospice care.

H.G.'s baseline mental status was fully alert and oriented. He was fairly robust despite his illness and independent in most of his care. His active medications upon admission to hospice are as follows: mirtazapine 30 mg at bedtime, warfarin 5 mg daily, dexamethasone 8 mg daily, oxycodone 10 mg as needed, fentanyl patch (100 μg/h) every 72 hours, and a bowel regimen.

Two weeks after hospice election, H.G. developed worsening pain along with swelling of his lower jaw at his initial tumor site. His dexamethasone dose was increased to 16 mg daily.

About 3 days after the steroid was increased, H.G.'s pain lessened, but he then developed weakness and mild confusion. His hospice nurse noted concern for delirium. His wife requested the patient be transferred to a skilled nursing facility as she could no longer meet his needs at home. Hospice admitted H.G. to a contracted skilled nursing facility and provided daily nursing visits as well as a sitter to promote safety.

During the course of the next 3 weeks, H.G. suffered an agitated delirium. He would pace for hours, slept in 1- to 2-hour stretches and was irritable with interaction. He would tug at his tracheostomy and feeding tube. H.G. also began to urinate in inappropriate places despite being continent. He resisted any attempts at social engagement, even with family. The physician ordered scheduled haloperidol along with breakthrough dosing. The hospice team evaluated the factors that could be leading to the patient's delirium.

CONTRIBUTING FACTORS TO DELIRIUM

Medications

Forty percent of delirium episodes can be linked in part to medications.[11] Corticosteroids and opiates are 2 agents that are particular to this case study as H.G. was on dexamethasone, oxycodone, and fentanyl. Corticosteroids have significant adverse effects that may contribute to mental status changes. Exogenous corticosteroids interact at the neurotransmitter level and cause excitatory effects such as euphoria or psychosis.[12]

Psychiatric symptoms related to steroid use are most likely to occur within the first 2 weeks of treatment. It is prudent to reserve steroids for use in which there is no other alternative and use them at lower doses for the shortest period of duration and with frequent monitoring.[12]

Opioids can impact mental status, but so can uncontrolled pain. It may be appropriate to lower the dose or consider a rotation to a different opioid, the goal being good analgesia with fewer adverse effects.[13]

Not specific to this case study but an important consideration is abstinence from other agents. This includes agents such as illicit drugs, alcohol, or tobacco. It also includes abstinence from prescribed medications, especially psychotropics. Patients who were previously on a psychotropic medication will have developed some increased receptor sensitivity. Abruptly discontinuing these medications can alter dopamine and serotonin neurotransmitter transmission, leading to rebound agitation, insomnia, and anxiety.[14]

A host of other agents are implicated in delirium, although not in this particular case, and go well beyond the scope of this article. A pharmacy review may help determine if a patient is on any drugs that are prone to causing changes in mental status and suggest alternatives. Another resource is the American Geriatrics Society BEERS criteria, which list medications and classes that may cause adverse drug reactions in the elderly patient, including confusion.[15]

Blood Chemistry Changes

Malignant conditions can alter the blood chemistry and may worsen delirium. Many laboratory derangements can impair mental status. Of special concern in this case study were hypercalcemia and hyponatremia. Hypercalcemia in particular can affect cognition. Up to 30% of all patients with advanced cancer develop hypercalcemia.[10] H.G. was at higher risk of developing hypercalcemia as head and neck cancers are often squamous cell tumors. These tumors increase bone resorption, which affects serum calcium levels.[16] Hypercalcemia is amenable to ongoing treatment with bisphosphonates and hydration.[10] Sodium levels also affect mental status and should be evaluated. H.G. was a risk for sodium derangement as he was dependent on tube feeding and could not respond to normal thirst because of dysphagia. H.G. had normal calcium and sodium levels when they were drawn. Uremia and

elevated ammonia levels can cause confusion as well. H.G. did not have a history of renal insufficiency, but a renal function panel was checked and found to be normal. He had no evidence of liver failure, and liver enzyme concentrations were within reference ranges when checked as part of the complete metabolic panel; therefore, a specific ammonia level was not obtained.

Other Contributors to Delirium

Brain metastasis can effect behavioral changes in patients by destruction of areas that control inhibition and organization.[16] Similarly, edema from gamma knife or whole-brain radiation will structurally affect brain functioning.

Other potential contributors for delirium would be infection and constipation. H.G. was at high risk for infection, given his artificial airway, enteral feedings, and steroid use. The patient was on an aggressive bowel regimen and was having regular bowel movements.

The hospice team assessed for contributing factors to H.G.'s delirium. His pain regimen was optimized. Dexamethasone was reduced to 8 mg. Laboratory workups were within normal limits. His most recent brain imaging did not show metastatic lesions. The tracheostomy and jejunostomy sites were free from infection. We discouraged overstimulation and limited changes in caregivers.

Initial Management of H.G.

Managing H.G.'s medication regimen proved challenging. He would refuse medications at times. At other times, nursing felt the patient to be too aggressive to approach. Newer nurses were fearful of the patient and resisted "bothering" him for scheduled medications when he was calm. H.G.'s behaviors would then escalate as his antipsychotics wore off, requiring higher doses to regain control. This would often lead to oversedation, and the cycle would start over. An interdisciplinary meeting convened with facility and hospice staff.

It was recommended to try a depot antipsychotic to bypass the dosing issues. Use of depot agents in treatment of mental illness is common and well accepted. They have been in use since the 1960s.[17] The team chose haloperidol over other agents as the patient already met many of the criteria set out for safe use. He was not naive to haloperidol and had not had any adverse effects, and the drug had been effective when dosed appropriately. Haloperidol can prolong the Q-T interval, but that was not the case with H.G.

Haloperidol decanoate can be injected every 28 days and has a half-life of 21 days. Some effect on symptoms can be noted within 5 to 7 days. Breakthrough medications can be used concurrently.[17] The scheduled oral haloperidol was set on a downward taper to anticipate the onset of the depot injection. Breakthrough haloperidol remained in place. Within the week, H.G.'s behaviors seemed to be improving.

Despite the observed improvement, one morning H.G. suddenly became violent, lashed out, and injured 2 staff members. The decision was made to transfer him to the hospital for a more thorough workup for his delirium. The hospice team had requested to the emergency medical services that H.G. be taken to the tertiary care hospital where he had been receiving care. Instead, he was taken to a local community hospital. There, he was restrained and sedated. Results of his laboratory tests were normal, and he was discharged back to the skilled nursing facility a few hours later as the emergency room felt he was no longer a danger.

The nursing home administration expressed concern for H.G.'s escalating behaviors and the safety of staff and other patients. The clinical staff began to lose sight of H.G. as a person and focused on his potential for violence. There was a sense that the patient was a "hospice problem" and that the facility could defer all care and problem solving to hospice. While this facility cared for many people with behavioral challenges, most were frail elderly and unlikely to have the capacity to inflict serious injury.

The skilled nursing facility was not able to manage his needs despite hospice support, but no other care setting seemed viable. His pain and symptoms could have been managed on a hospital medical floor, but his overt psychotic symptoms might not receive the treatment they needed. He was also not a candidate for a psychiatric admission because of his clinical status. Returning the patient to his home was not a safe option. Also considered was a transfer to a local hospice inpatient facility, but there were no available beds.

Three days after this most recent trip to the emergency room, H.G.'s behavior radically escalated again. He struck several staff members and his wife. He attempted to break the window in his room. Finally, he wrestled his adult daughter to the bed and behaved in a manner that suggested he planned to sexually assault her. This required the intervention of 3 male staff members to separate them. Emergency services were contacted, and the patient was transferred, with police escort, to the tertiary care center.

The patient remained at the hospital on a medical floor followed by medicine, psychiatry, and the inpatient palliative care service. The same cyclical nature of agitation noted during his stay in the skilled nursing facility continued to impact his treatment at the hospital. He was discharged home after a prolonged hospitalization.

He was lost clinically to follow-up. One of the hospice staff members ran into Mrs H.G. later, who reported that the patient had since died while under the care of another hospice. It is unknown whether his delirium recurred. The etiology of H.G.'s delirium was never

fully identified. After a prolonged period without contact, it did not feel appropriate to contact Mrs H.G. about her feelings regarding the care H.G. had received.

Pharmacologic Management

Antipsychotic medications are considered the standard of care to address the presenting behaviors while concurrently searching for and treating the underlying cause. Generally, all antipsychotics show efficacy over placebo. Some studies favor certain medications over another, but there is no consensus on the most effective.[18] Second-generation medications alone did not show greater efficacy than first-generation ones on symptom management or recall of episode.[19] At least 1 small study shows that combining scheduled quetiapine and as-needed haloperidol caused an overall decrease in the number of days of delirium.[20]

Both first- and second-generation drugs have potential for extrapyramidal syndrome and Q-T prolongation. Second-generation medications may cause more cardiac adverse effects.[21] A large study that involved 33 604 patients found that mortality was the highest in the first 30 days of treatment with haloperidol when compared with newer agents, but that all agents had the same level of risk at 120 days of treatment.[22] This article focused on longer-term use in patients with dementia, rather than patients with delirium.

Both types of drugs come with US Food and Drug Administration black-box warnings.[22] Despite widespread use, research still lags on efficacy and safety of both generations.[18,23] All of the antipsychotics discussed in this article are used off-label when treating delirium.[18]

Common adverse effects of all antipsychotic agents are sedation, extrapyramidal symptoms, anticholinergic effects, and cardiovascular effects. Longer-term use may see the development of alterations in weight gain, metabolic changes, and hyperlipidemia. Clinicians should tailor the profile to the individual's symptom load, availability of route, anticipated length of treatment, and acceptability of adverse effects.[24]

Clinicians should consider the patient's and family's goals of care as well as risks and benefits of the particular medications when implementing and reviewing the antipsychotic regimen. Risks, including the black-box warning, should be explained to the family, and their understanding and acceptance of the plan should be documented. For example, the potential of cardiac arrhythmia may be worth the risk for a delirious patient who is close to death. H.G. was not felt to be close to death and did not have a history of cardiac arrhythmias, and his most recent electrocardiogram showed a normal QT interval. Cost is also important to hospice programs, and haloperidol is less expensive than alternatives.

Meticulous assessment and medication reconciliation will help identify needs related to issues such as infection, uncontrolled pain, abstinence from tobacco or alcohol, or previously used psychotropic medications. If H.G.'s delirium were related to any of these items, the plan of care would have expanded to include the appropriate treatments.

Nonpharmacologic Management

An environment that provides structure, predictability, and appropriate levels of stimulation will help the patient cope more effectively. This starts with caregiver and staff education. Staff should promote normal circadian rhythms by utilizing principles of good sleep hygiene.[6] Avoid tethering the patient to the bed with restraints, continuous intravenous lines, and Foley catheters. Patients should be allowed mobilization as soon as safely possible.[3]

H.G.'s care began at home, but with the initial symptoms of delirium, his wife requested his transfer to a facility. Most people would prefer to be at home, rather than institutionalized, but the workup and management of delirium may require urgent clinical input.[21] Delirium adds another level to the physical and emotional stress and prevents many family members from providing care through death in the home.[1]

Health care providers need to enlist the help of the family in maintaining the best environment for the patient. Education will help family members understand the plan of care and

TABLE Old Beliefs and New Behaviors in Managing Delirium

Issues	• Ineffective beliefs and processes	• Adapted processes
Complacency	• Assessment only with acute agitation	• Assessment of all patients across course of care
	• Experiential guidance only	• Ongoing review of best practices
	• Internal resource use	• Inclusion of external resources such as pharmacy and psychiatry
Environment of care	• Assuming adequate educational competency and comfort level regarding delirium among staff	• Ongoing support and education
	• Safety is the responsibility of facility	• Education about management
		• Shared focus on staff and patient safety
Transitions in care	• Verbal report and written records sent with patients	• Hospice nurse accompanies patient and provides face-to-face handoff along with written records

increase compliance with environmental support.[1] A comprehensive care plan should have been developed for H.G. and distributed to caregivers. This would have helped staff to provide a consistent approach and reduce environmental stressors.

Another way to decrease stress is to focus on staff and patient safety. On 2 separate occasions, the patient was able to strike staff members hard enough to cause injury. Prior to that, he had made threatening gestures, threw things, or physically pushed caregivers away. At the first sign of aggressive posturing, the team should have reviewed basic safety principles such as using a "buddy system," arranging his room so that staff could more easily exit the space, and keeping the door to the room open if at all possible.[25] H.G. was not this facility's first patient with violent behavior and likely not the last. All health care facilities need to have a plan to address this issue that includes ongoing education and an ethos that staff and patient safety are equally important.[26] H.G.'s medication regimen might have been dosed more effectively had staff felt safer in providing care. Effective staff education, support, and care coordination are vital in treating a refractory case of delirium.

CONCLUSIONS

Delirium research provides a growing body of work to provide evidence-based practices for the management of these complex patients. If clinicians are more successful at treating delirium, it behooves us to identify treatment goals as it seems merely addressing the motor activity does not quell the psychological distress. There is still no magic potion or protocol to "fix" these individuals, but there are resources to help guide providers. This experience has provided some hard lessons and new processes (Table).

The experience with H.G. has provided an opportunity to look beyond our collective experience of what had been successful in the past to develop new, evidence-based practices so that hospice patients with complex delirium can be more effectively and safely managed.

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