



PALLIATIVE CARE CASE OF THE MONTH

“When All Else Fails” by Wajeeha Rasool, MD

Volume 24, No. 139

Introduction: Paraneoplastic syndromes present diagnostic and therapeutic challenges. They present with a myriad of debilitating symptoms, necessitating aggressive disease-modifying and palliative management options. Here we highlight the role of palliative sedation for end-of-life symptom management in a patient with neuro-storming (a pattern of recurrent bursts of dysregulated sympathetic activity resulting from severe brain injury) secondary to anti-NMDA receptor antibody encephalitis refractory to conventional therapies.

Case: A 43-year-old female with a history of bipolar disorder presented to the hospital with confusion, agitation, and hallucinations. She was found to have a left adnexal cystic teratoma and anti-NMDA receptor antibody encephalitis. She underwent bilateral salpingo-oophorectomy and later received immunochemotherapy with intravenous immunoglobulin, plasma exchange, steroids, rituximab, and cyclophosphamide. Her hospital course was complicated by seizures, tardive dyskinesia, neuro-storming and respiratory failure requiring mechanical ventilation and tracheostomy. Her tardive dyskinesia was managed with Botox injection to the bilateral masseter muscles and tooth extractions. She required intermittent propofol, midazolam, and fentanyl for symptoms related to neuro-storming. The patient stayed in the hospital for 215 days without significant improvement in her condition. After multiple multidisciplinary family meetings, her husband decided to opt for comfort measures, and she was transferred to the inpatient hospice unit. An aggressive medication regimen of hydromorphone and midazolam with intermittent ketamine and dexmedetomidine was tried for symptom management without success. As a last resort, palliative sedation using propofol was considered. However, UPMC pharmacy guidelines do not approve the use of propofol infusion in non-mechanically ventilated patients. The inpatient unit team advocated on her behalf considering the unusual circumstances and got approval. She was subsequently started on propofol sedation with adequate symptom control and later passed away peacefully.

Discussion: Anti-NMDA receptor encephalitis is an autoimmune encephalitis characterized by complex neuropsychiatric features and the presence of antibodies against the NMDA receptors in the central nervous system (CNS). It comes with a huge symptom burden and an uncertain prognosis. Symptoms include memory loss, cognitive and behavioral decline, abnormal, uncontrollable, involuntary movements, full body spasm, catatonia, tardive dyskinesia, coma and central hypoventilation.¹ Our patient had severe, uncontrolled movements of her whole body which were painful to watch, causing distress in family and medical staff.

She also had tardive dyskinesia for which she had her teeth extracted and Botox injections to the masseter muscles so that she would not have tongue bites. It was also proposed that her tongue or her jaw be sutured so that she would not be able to injure herself. However, the family was troubled by the idea and declined.

Neuro-storms (Paroxysmal Sympathetic Hyperactivity) is a pattern of recurrent bursts of dysregulated sympathetic activity resulting from severe brain injury. It is characterized by tachycardia, hypertension, tachypnea, diaphoresis, hyperthermia, tonic posturing and agitation.²⁻⁴ For our patient, the involuntary movements and tonic posturing could not be stopped despite using a myriad of medications, which caused immense distress among the staff. Thus, palliative sedation was considered using propofol, and her symptoms improved dramatically.

Palliative Sedation:

Palliative sedation is a measure of last resort and is defined as a procedure used to treat refractory symptoms at the end of life by inducing a state of decreased or absent awareness.^{5,6} It is also known as sedation at the end of life or total sedation.

What are the indications to consider palliative sedation?

We consider palliative sedation when a patient's symptoms are not controlled despite the use of a standard treatment regimen. In other words, these are the symptoms that cannot be adequately controlled in a tolerable time frame despite aggressive use of usual therapies.⁷

According to a systematic literature review, the most common refractory symptoms that are managed by palliative sedation in cancer patients are delirium, dyspnea, pain, vomiting and psychological distress.⁸

Which medications are used?

Medications are chosen for their indication, side effect profile, care setting, route of administration and monitoring requirements. Other medications like opioids, which were already used for symptom relief are usually continued.

- Benzodiazepines are usually the mainstay of treatment. One of the short acting benzodiazepines, midazolam, is most commonly used to induce palliative sedation. Its short half-life which allows rapid titration, and it can be used in conjunction with opioids and haloperidol.⁸⁻¹⁰ Lorazepam is another benzodiazepine which can be used especially in home settings since it is longer acting and is available in concentrated oral solutions.^{11,14,16}
- The antipsychotic chlorpromazine is a good option for delirious patients.^{7,11-14}

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Discussion: (Continued)

- Phenobarbital can be considered if a simultaneous anticonvulsant effect is needed. It can also be useful for patients who have developed tolerance to the effects of benzodiazepines.^{7,11,14}
- Propofol is another option if benzodiazepines are not effective. It has a very rapid onset of action and is short lived, allowing for quick titration. However, it can cause respiratory depression and may require closer monitoring.^{7,11,14,17,18}
- The NMDA antagonist ketamine is a dissociative sedative agent, although its use is not well studied in palliative sedation. There are case reports which highlight its importance in emergency palliative sedation when respiratory depression is a concern.^{19,20}
- Dexmedetomidine appears to hold great potential for use in palliative sedation due to its analgesic and opioid sparing properties.²¹ Unlike other sedatives, it has limited effect on respiratory drive and upper airway patency and based on observation, patients sedated with it seem to be generally more arousable. However limited evidence exists for its use in palliative sedation.

How to support the family during Palliative sedation?

The idea of palliative sedation at the end of life can be distressing to the family and thus their continuous involvement in the process is imperative. The following measures should be taken to ensure minimizing family distress.¹⁶

- Consent should always be obtained from the patient, preferably in the presence of the family so that they are part of the decision-making process.
- The family should be reassured that all other means of alleviating symptoms have already been tried and that palliative sedation is being used as a measure of last resort.
- They should be reassured that palliative sedation is unlikely to hasten death.
- They should be updated regularly about the patient's condition and what to expect.

What are the ethical considerations?

Palliative sedation is a widely practiced and accepted procedure for alleviation of physical symptoms at the end of life^{22,23} and is supported by legal precedence.^{20,21} Clinicians who are involved in palliative sedation should be aware of the potential for harm from abusive, injudicious, or unskilled use of sedation.

The use of palliative sedation for existential distress, like feelings of helplessness, hopelessness, and fear of death is still controversial. Thus, palliative sedation should be considered with extreme caution in these patients.^{25,26}

Conclusion:

Palliative sedation is an extreme but useful management option for refractory pain and neurological symptoms. There is a need for discussion and subsequent policy revision regarding provision of propofol infusion for palliative sedation purposes.

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