Peer Review File

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REVIEWER A

Comment 1: The title needs refining. The present title only focuses on management without mentioning the end-of-life stage.

Reply 1: Thank you for your feedback, based on the reviewer's comment, we have revised the title to focus on the management of end-of-life care.

Changes in the text:

Case Report of Management Challenges at End-of-Life in a Patient with Agitated Delirium and Benzodiazepine Withdrawal at Comprehensive Cancer Care Center

Comment 2: The abstract is too short lacking some vital information, including how this case is unique, what's the primary clinical manifestation, how's the treatment and outcome, and what's the take-away lesson etc.

Reply 2: Thank you for your feedback, based on the reviewer's comment, we have revised the abstract to include additional vital information.

Changes in the text:

Most people have some idea of how they want to live their life; however, an estimated two-thirds of Americans have not completed their advance directives. This becomes an issue when up to 90% of patients develop delirium during their final days of life, at which point we depend on advance directives or surrogate decision-makers. Here, we present a case of terminal delirium in a patient with advanced cancer and a history of alprazolam abuse who had not discussed his end-of-life wishes with the medical team or with his estranged family. Treatment was provided to address reversible causes of delirium, including correcting electrolyte imbalances, urinary retention, and administered antibiotics for purulent otitis media. Hyperactive delirium was managed aggressively with intravenous neuroleptics and benzodiazepine, while keeping a balance between somnolence and control of agitative symptoms. Without knowing the patient's wishes, the family continued to struggle with decision making. However, with multidisciplinary team approach patients and caregivers' symptoms were better managed. Family then requested us to transfer him to a local hospice facility. The patient eventually passed away peacefully surrounded by his family members. This case highlights the importance of advance care planning, addressing emotional distress in estranged family members regarding symptom burden, and developing the appropriate treatment regimen for a delirious patient with a history of

benzodiazepine abuse. Our case serves as a reminder of the support, guidance, and impact that inpatient palliative care teams can offer to both the patient and caregivers

Comment 3: As the whole procedure is complicated, it is recommended drawing a timeline to outline the whole.

Reply 3: Thank you for your feedback, based on the reviewer's comment, we have included a timeline of events (Figure 1).

Changes in the text:

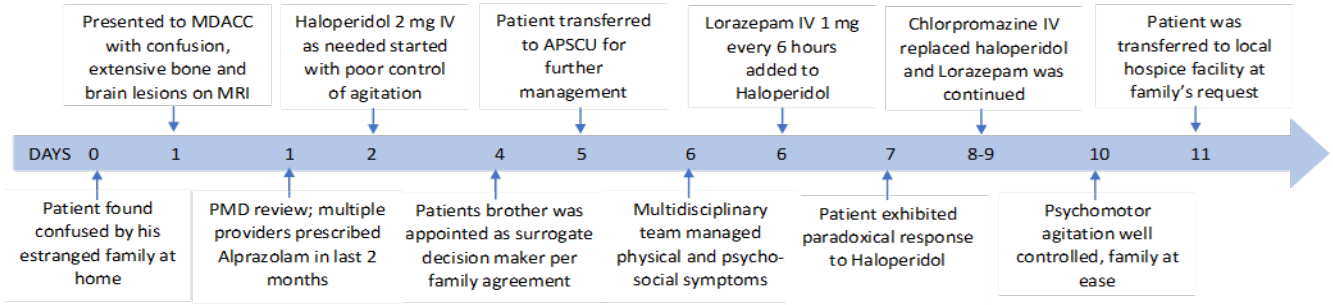

Figure 1: Timeline to show patients clinical course during hospitalization
Abbreviations: MDACC, MD Anderson Cancer Center; PMD; Prescription Monitoring Database; IV, Intravenous; APSCU, Acute Palliative and Supportive Care Unit

Comment 4: What are the strengths and limitations of this case report? Please mention this in the discussion.

Reply 4: Thank you for your feedback, based on the reviewer's comment, we have included a paragraph to highlight the strength and limitations of this case report.

Changes in the text:

Our case is unique because it highlights the challenges experienced by non-compliant and socially isolated advanced cancer patients at the end-of-life. We have also demonstrated the importance of a dedicated inpatient palliative care unit in a comprehensive cancer center, where a multidisciplinary team approach can be utilized to care for such patients and their caregivers. Our case is also unique because it highlights the importance of early detection and effective management of delirium which can be more challenging in the case of benzodiazepine withdrawals. Our findings are limited due to a lack of scientific rigor and inability to generalize to a broader population or in a different clinical setting. Further investigation in determining the optimal drug combination in managing delirium is needed.