

Refractory delirium in palliative care sitting

Igbal Abdelati MD¹, Sami Ayed Alshammary, MD^{2*}, Savithiri Ratnapalan MBBS, PhD³

¹Palliative Care Unit, Comprehensive Cancer Centre, King Fahad Medical City, Riyadh

²Palliative Care Unit, Comprehensive Cancer Centre, King Fahad Medical City, Riyadh and Centre for Postgraduate Studies in Family Medicine, Ministry of Health, Riyadh, Saudi Arabia

³Department of Paediatrics and Dalla Lana School of Public Health, University of Toronto

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ABSTRACT

This paper describes the management of a 65 years old male patient transferred to the palliative care ward from the Intensive Care Unit, with brain metastasis and infarction admission, epilepsy, neurological dysfunction, cognitive impairment and a history of previous delirium episodes. We discuss four delirium assessment methods and possible collaborative multidisciplinary approaches to manage persistent delirium in palliative care patients.

* Email: drsamiayed@gmail.com.

CASE HISTORY

A 66 years old male developed metastatic thyroid cancer, post total thyroidectomy, and radioactive iodine five years ago was treated with external beam radiation of the neck and was transferred to the palliative care team. This patient had been treated using cyberknife (9 lesions were treated) and craniotomy twice for metastatic brain lesions 3 years ago. He was admitted to hospital with loss of consciousness, intubated and transferred to the intensive care unit (ICU) of our hospital. Initial Glasgow Coma Scale was 9/15, with unequal pupils, and he was found to have a new Left posterior MCA infarction on top of brain metastasis. He had

poor prognostic factors and was not considered a candidate for further neurosurgical intervention.

In ICU patient was agitated and self-extubated but was stable and able to maintain the airway and have normal oxygen saturation in room air. ICU delirium screening tool as part of ICU routine screening identified cognitive impairment and referred him to the psychiatric services. The psychiatric team found his Mini-Mental Screening Exam (MMSE) score to be 16 points (of a possible 30 points) with deficiencies in orientation, recall, and attention and confirmed cognitive impairment and delirium secondary to medical conditions. As such, the patient was transferred to the palliative ward.

In the palliative ward, the patient was confused and was not cooperative. The patient's son and nurse described bouts of confusion, disorientation, impaired memory, difficult speech, and visual hallucination. He also had worsened sleep and was awake the whole night, and obvious. No history of fever, cough, pain, or change of bowel habits. Son stated that before admission with loss of consciousness, his father was alert, continent, ambulatory, no vision or hearing problems, and was independent in his activities of daily living. His has had multiple admissions under oncology with confusion and seizures. He was discharged on Quetiapine 12.5mg twice a day and haloperidol 0.5mg every 12 hours, Levetiracetam 1000mg every 12 hours and Dexamethasone 4mg after his last admission in addition to thyroid supplements. There was no family history of memory loss, psychiatric, or neurologic disorders. He was unemployed but had a very has a supportive family.

Physical examination reveals patient was confused, disorientated in time, place, and person, with mood, and behavior changes, agitated pulling at intravenous (IV) line and urinary catheter, aggressive and uncooperative, speaking incoherently and having visual hallucinations.

Delirium Prevalence in Palliative Care Patients

Delirium is common comorbidity in patients with advanced chronic diseases with prevalence rates ranging from 13.3% to 42.3% upon admission to palliative care units or hospices, 3% and 45% after admission and 58.8-88% before death [1]. It is characterized by disturbances in the level of alertness, attention, thinking, perception, cognition, psychomotor behavior, mood, and sleep-wake cycle" [1]. Although delirium is a reversible process, it may not be reversible in the advanced disease and may be a sign of imminent death [1]. Different types of

delirium identified: hyperactive (patient agitated), hypoactive (patient drowsy and inactive), and mixed subtypes [2]. Due to high prevalence in palliative care inpatients, routine screening to be considered for early detection of any reversible cause of delirium and better management of distressing symptoms [3].

Delirium Assessment Tools

The most common instrument used for the assessment of impaired cognition is the Mini-Mental Status Examination (MMSE), the screening test for cognitive impairment. Although MMSE is a sensitive indicator of cognitive impairment, it is not specific for the diagnosis of delirium or dementia [3]. MMSE can be used to document the progression of a patient's illness over time. Of a possible 30 points, a total score of 20-24 points generally indicates mild impairment, 18-19 points indicate moderate impairment, and 15 points or less indicates a severe deficit. Designed to assess broad cognitive impairment, but has some limitations, it takes time for administration time and scoring influenced by culture and education levels [3].

Delirium screening tools can be helpful and effectively screen for delirium and may improve delirium detection rates [3]. Four assessment tools are described below.

The Confusion Assessment Method (CAM) a four-question version, can be used as a screening and diagnostic tool for delirium. CAM is brief and widely used in a patient with advanced illness after training physicians to do it [3]. CAM takes about 5 minutes to complete and is validated in palliative care [4-5]. CAM is positive if confusion has an acute onset or fluctuating course, and the patient has inattention, and either has disorganized thinking or an altered level of consciousness.

The Nursing Delirium Screening Scale (Nu-DESC) is a five-item observational screening tool that can be administered by nurses and can be completed quickly (in one minute), has sensitivity and specificity similar to the Memorial Delirium Assessment Scale [3]. It is designed for continuous screening, symptom monitoring, and severity rating [2]. It is useful but lacks validity in palliative care [6]. Single Question in Delirium (SQiD) asks caregivers and others to interact with the patient if the patient has been more confused recently [2]. It is useful but lacks validity in palliative care [6].

Severity assessment tools are used as severity assessment tools and help clinicians in operationalizing DSM-IV criteria [3]. Some examples are: The Memorial Delirium Assessment Scale (MDAS), a ten items rated tool for clinician use in delirium severity assessment, has been validated in palliative care settings [6]. Delirium Rating Scale-Revised-98 (DRS-R-98) is 16 items clinician-rated tool [2]. That is potentially useful but lacks validity in palliative care [6].

According to the United Kingdom (UK) National Institute of Clinical Excellence (NICE) guidelines; if delirium indicators are detected, a clinical assessment based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria or short CAM should be performed to establish the diagnosis [7,8]. Please see Table 1 for a list of possible tools that can be used to assess delirium

Risk Factors for Delirium in Cancer patients

Delirium occurs when simultaneous physical impairments, act on a physiologically vulnerable brain, leading to confusion, changes in perceptions, and altered behaviors [7]. As in our patient's case, a severely ill, older patient with pre-existing cognitive impairment decrease the brain's ability to overcome delirium [8].

Metastatic brain tumor and infarction predisposed to delirium [9] Delirium risk factors include old age visual and hearing impairment, the severity of illness, cognitive impairment, depression, alcohol abuse, previous episodes of delirium [10]. Precipitating factors include new environment excessive hot and cold stimuli, wet sheets, uncontrolled symptoms (pain, constipation, urinary retention.), dehydration, infection which electrolyte imbalance hypercalcemia, hyponatremia, drug withdrawal (alcohol, nicotine) benzodiazepine, corticosteroid poor sleep and previous brain radiation, brain metastases and infarction [10]. Potentially reversible causes in advance illness include dehydration, borderline renal function, infections, metabolic disturbances, drug withdrawal, and psychoactive medications, e.g. opioids [3].

Investigations should be done to rule out predisposing factors and underline causes mentioned above and to treat revisable causes. Blood test for electrolytes, metabolic, and hematological abnormalities. Blood cultures midstream urine specimen to rule out sepsis. Serum urea nitrogen/creatinine ratio for dehydration assessment. Liver and renal function tests if impairment, thyroid function patient had total thyroidectomy on the replacement. All results within a normal range.

OUR PATIENT

Electroencephalography was performed to exclude Non-convulsive epileptic status (NCES), and medications for seizure control were optimized. We carried out a clinical assessment to confirm the diagnosis based on the CAM method. The acute onset and fluctuating course, inattention, disorganized thinking, and altered level of consciousness confirmed the diagnosis.

A multidisciplinary team in under the guidance of the Palliative care consultant planned for

nonpharmacological and pharmacological management. Nonpharmacological methods started with explanations about the conditions and collaborative with family members [10]. The family needed education about cognitive impairment, possible causes for the patient's confusion, the possibility that delirium may not be reversible, and management of the patient's behavior during the delirious state. The family was advised not to be forceful when contradicting him [10]. Nurses were educated to explain to the patient in advance of any procedures or administration of drugs [8]. We handled the patient gently and strived to provide a safe, private environment with reduced stimuli, frequent orientation, and ongoing monitoring for his confusion status [8]. All our rooms in palliative wards are single bedroom with good lightening. We had a calendar that showed prayers time and a clock, easily visible for orientation of the patient to time and day. Each nurse is assigned two patients due to staff shortage, and the majority are Non-Arabic speakers. As such, family members play a significant role in regular and repeated cues to improve the patient's orientation and reporting any status change [8]. The social worker facilitates visits from family and friends who can help to calm the patient.

Although we generally avoid physical restraints, catheterization, nasogastric tube (NGT) where possible [8], we had to use restraints (two points mittens) because patient was agitated and aggressive with nurses. He needed an NGT because he was not taking food or fluids orally. We encouragement normal sleep-wake cycles by minimizing procedures and disturbances during night and stimulate wakefulness and mobility during the day.

The patient required antipsychotics when verbal and non-verbal de-escalation techniques failed and he became very restless and agitated. He was already on haloperidol 0.5mg every 12 hours and

Quetiapine 12.5mg twice a day for one week. The psychiatric team recommended increasing Quetiapine to 25mg twice a day and added haloperidol 0.5mg every 2 hours as needed in addition to regular doses.

Experts from different specialties have been involved:

Radiation Oncologist said there was no role for radiation therapy as his previous image had shown radiation necrosis lesions. Neurosurgery team recommended dexamethasone intravenous 4 mg later increased to 6mg for brain edema [11,12]. Neurology recommended an increase of Lacosamide doses to continue the same phenytoin and Levetiracetam doses and to add lorazepam 1mg as needed.

The patient continued to deteriorate, and haloperidol and Quetiapine were titrated cautiously according to symptoms and with close monitoring for extrapyramidal side effects. [11] and lorazepam 1mg intravenous every two hours as needed was added [11].

The patient removed the NGT, and the swallowing assessment was not completed as he was agitated, refused an assessment, and closed his mouth. As such, the team suggested not feeding him orally as there was a risk of aspiration. Gastrostomy tube insertion was cancelled due to colonic interposition between the stomach and the abdominal wall precluding safe percutaneous access.

At this point, haloperidol was 20mg per day and Quetiapine 50 mg twice a day. We tapered down haloperidol gradually and increased Quetiapine till dose of 100mg twice a day as it was atypical antipsychotic with sedative action [10]. Unfortunately, the patient aspirated (family fed him at night upon his request) and died from aspiration pneumonia despite treatment with antibiotics and bronchodilators. Both the staff and the family members experience significant

distress and grief after the death of the patient. The team arranged for a brief psychological support to all with guided mourning therapy.

Suggestion for Managing Palliative Patients with Delirium

The use of the Diagnostic and Statistical Manual of Mental Disorders-IV criteria gives the best results for delirium diagnosis [1].

A disturbance of consciousness, a change in cognition, short and fluctuating chronology, and the presence of an underlying medical condition are components of hyperactive delirium secondary to a medical condition [1]. NCS occurs in association with complex metabolic disorders, result in altered consciousness manifesting with delirium [3]. It occurs in 5% of the cancer patient and probably higher in patients with brain metastases, should be included in the differential diagnosis of delirium, dementia, psychiatric disorders, or coma, EEG can confirm diagnosis it identifies epileptiform activity [10].

Multi-disciplinary Collaborative Care:
Physiotherapist to encourage mobilization if

possible. If bed-bound physiotherapy for passive range of mobilization (PROM) with limbs stretching sitting with support and transfer to chair or wheelchair, and to help for spasticity management

Occupational therapist for possible hand splints, because redness may be noted in the area around mittens, soft hand splint can be applied instead of mittens to prevent pressure sores on the joints.

“Relatives of the seriously ill thus have higher levels of depression and anxiety than the general population” [3]. Multiple family meetings may need to be held as part of counseling to give a chance for them to ask questions, to understand the situation, and to be updated.

Psychologist and social worker should be involved to help in relieving the family distress and anxiety. The social worker, in collaboration with a volunteer, can arrange to gather with other patient and their families to share feelings and exchange experiences and support each other. Social workers can also help the family to utilize hospital resources optimally. The psychologist can help validate and acknowledged their stress and fear of empathetic and good communication.

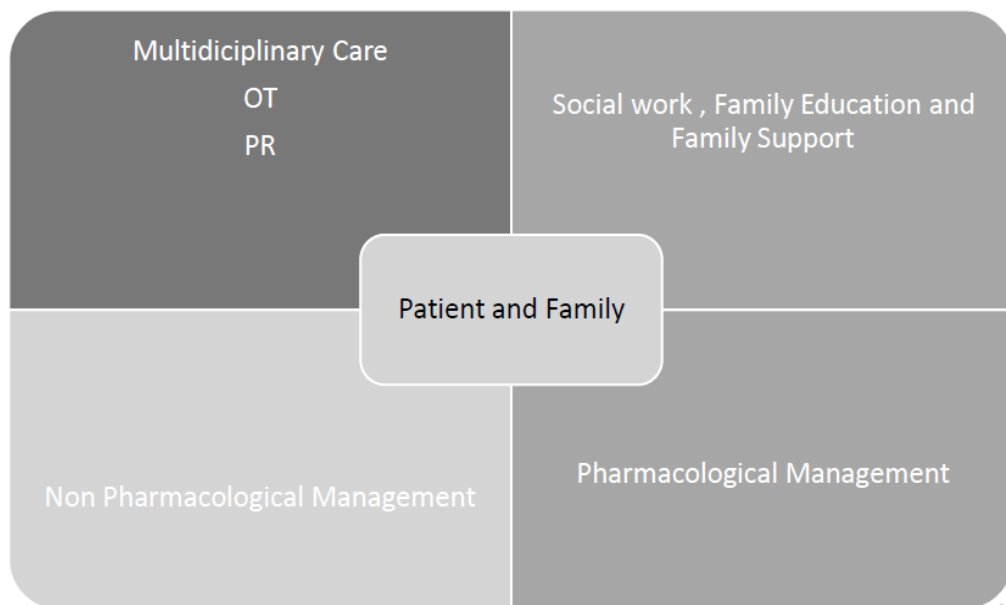


Table 1

Characteristics of Delirium Tools Used in Palliative Care Populations

Category	Scale	Dimensions	Items	Score	Administration Time (min)	Characteristics
Delirium screening	CAM	Nine operationalized criteria based on DSM-III-R, classified as four features	9	Observational	5 ^a	Required for diagnosis: Features 1 (acute onset and fluctuating course) and 2 (inattention) þ either Feature 3 (disorganized thinking) or 4 (altered level of consciousness)
	Nu-DESC	Four items from the CRS þ psychomotor Retardation	5	0-10 Cut off: > 2	1	<ul style="list-style-type: none"> _ Three-point scale: 0e2 _ Observational scale _ Higher score ¼ positive Delirium
	SQID	Third party perception of patient's confusion	1	Yes/no	20-30	<ul style="list-style-type: none"> _ Simple single question _ Perception of family member/friend
Delirium severity	DRS-R-98	13 Severity items (including five cognitive domains) Three diagnostic items	16	0-39 (Severity) 0-6 (total) Cut off: 15.25 (severity) Cut off: 17.75 (diagnostic)	20-30	<ul style="list-style-type: none"> Items rated from zero (normal) to three (severely impaired) Symptoms rated over 24 h Higher score ¼ increased severity 13-Item severity section can be scored separately from three-item diagnostic section Total scale can be scored initially to enhance differential diagnosis.
	MDAS	Based on DSM-IV, DSM-III, and ICD-9 criteria: Arousal and LOC Cognitive functioning Psychomotor activity	10	0-30 Diagnostic cut off: 7-13	10	<ul style="list-style-type: none"> Four-point scale: 0-3 Higher score increased severity
Neuropsychological assessment of delirium for research purposes	CTD	Orientation, attention memory, vigilance, and comprehension		0-30 Cut off: <19	20	Lower score –lower cognitive function

DSM-IV = Diagnostic and Statistical Manual of Mental Disorders-IV; CAM =Confusion Assessment

Method; Nu-DESC = Nursing Delirium

Screening Scale; SQID = Single Question in Delirium; DRS-R-98 = Delirium Rating Scale-Revised;

MDAS = Memorial Delirium Assessment Scale;

CTD = Cognitive Test for Delirium.

A single question assesses for nonspecific feature of “confusion.”

Table 2
Representativeness of Delirium Domains

Domain (DSM-IV Criteria)	Dimensions	CAM	Nu-DESC	SQid ^a	DRS-R-98	MDAS	CTD
Consciousness	Altered level of consciousness	✓					✓
	Inattention	✓			✓		✓
Cognition	Inappropriate behavior		✓		✓		✓
	Decreased psychomotor activity	✓	✓		✓		✓
	Increased psychomotor activity	✓	✓		✓		✓
	Sleep-wake cycle disturbance	✓	✓		✓		✓
	Disorientation	✓	✓		✓		✓
	Memory deficit	✓	✓		✓		✓
	Perceptual disturbance	✓	✓		✓		✓
	Language disturbance (speech)				✓		✓
	Delusions				✓		✓
	Impaired digit span				✓		✓
	Decreased visual-spatial ability				✓		✓
	Decreased comprehension				✓		✓
	Vigilance				✓		✓
	Disorganized thinking		✓	✓			✓
Onset	Acute onset	✓			✓		
Course	Fluctuating course	✓			✓		
Physical disorder related to disturbance					✓		
Affect	Liability of affect						

DSM-IV Diagnostic and Statistical Manual of Mental Disorders-IV; CAM Confusion Assessment Method; Nu-DESC Nursing Delirium Screening Scale; SQid Single Question in Delirium; DRS-R-98 Delirium Rating Scale-Revised; MDAS Memorial Delirium Assessment Scale; CTD Cognitive Test for Delirium.
^aSingle question assesses for nonspecific feature of "confusion."

CONCLUSION

Specific tools for delirium evaluation, especially in palliative care patients, are limited, and MMSE is suboptimal for evaluating and assessing delirium as it focuses mainly on cognitive impairment. Relieve distressing symptoms is one of palliative care elements, and we may be unable to relieve symptoms of delirium sometimes at it happened with our patients.

We believe more awareness and coordinated non-pharmacological management with minimal drug use coupled with the social worker and family education and ongoing support, may alleviate distress to both patients and families.

We plan to collaborate with other departments to train staff, implement CAM for our patient assessments for early identification of delirium, and to evaluate the outcome.

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