

Delirium at End of Life: The Dying Brain

Carmen L. Johnson, MD

CFPC, FCFP, (CAC Palliative Care), CCEP

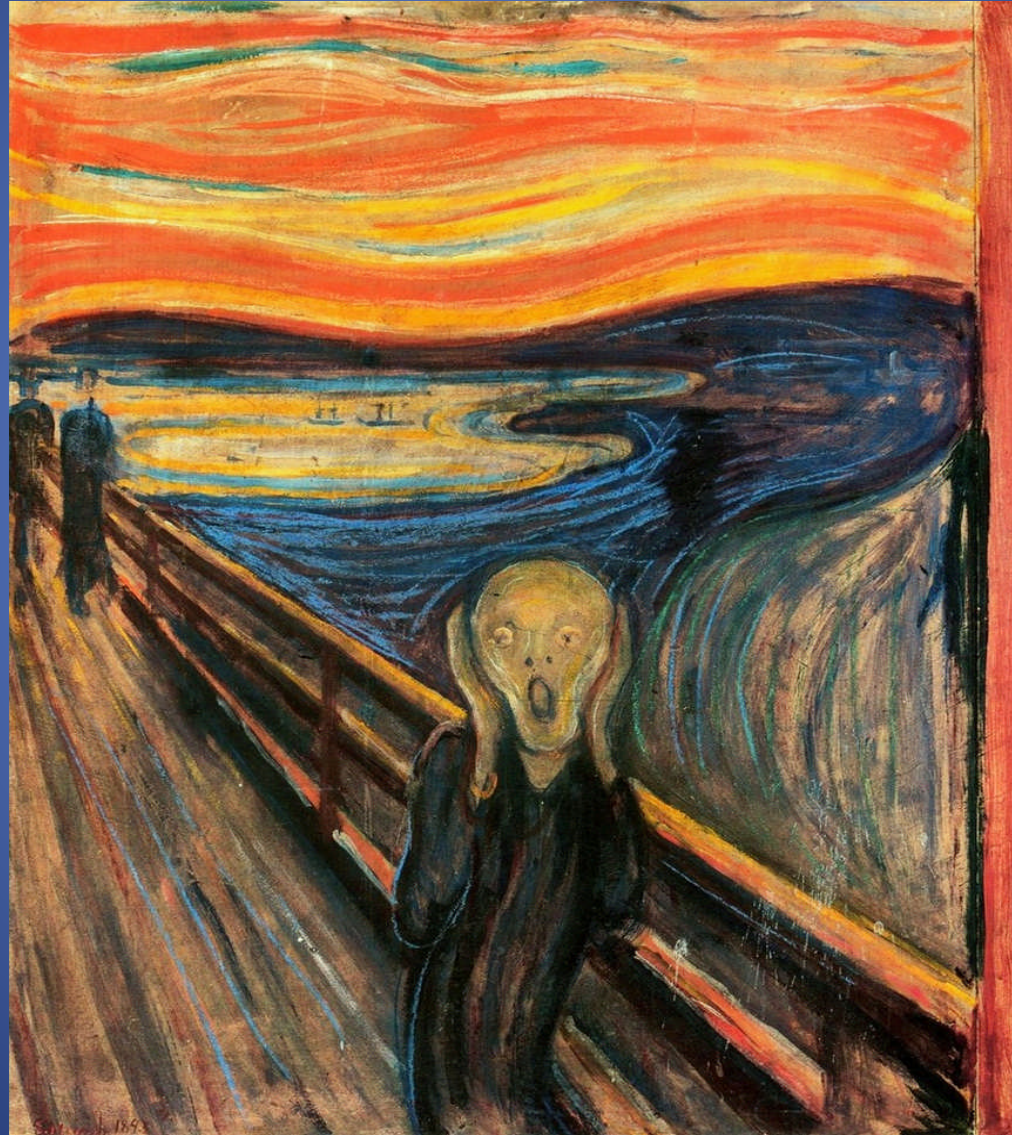
ABFP (Pain Medicine, Addiction Medicine), AAHPM, ABAM, FASAM

Medical Director, Palliative Care Services

Regina Area, Saskatchewan Health Authority

Delirium

“The Scream” by Edvard Munch 1893



Delirium

Learning objectives:

- Understand new insights into the delirium experience
- Examine neurotransmitter derangement in the delirious brain
- Understand clinical screening questions
- Differentiate clinical signs

Delirium

Previously believed that patients were not distressed
when in delirium

Studies suggest otherwise

More understood over last decade

Better data and imaging

Delirium

2009

Bruera - Palliative Patients

- 99 patient/family caregiver dyads

73 patients (74%) remembered

- 59 of 73 (81%) distressing
- Higher distress in caregivers than patient
- Nurses and physicians – much lower levels of distress
- <https://www.ncbi.nlm.nih.gov/pubmed/19241420#>

Delirium

2015

203 patients – General Medicine

Delirium experience

- one third (35%) could recollect the delirium
- majority (86%) were distressed by these experiences

– Clin Neurosci 2015; 27:139–146; doi: 10.1176/appi.neuropsych.13110329

Delirium

Delirium - “Acute Brain Failure”

Most common surgical complication - older adults

- Incidence: 15-25% major elective surgery
- Incidence: 50% after high-risk procedures
 - hip fracture repair, cardiac surgery
- Marcantonio ER. NEJM; 377(15):1456

Delirium

Delirium - “Acute Brain Failure”

Delirium extremely common; hospitalized older adults:

- 1/3 of general medical patients who are 70 or older have delirium during hospitalization
- Decreased visual acuity, presbycusis
- Noisy environment, constant lights– poor sleep

Delirium

Delirium - “Acute Brain Failure”

Not easy to identify

- Hyperactive delirium only 25% of cases
- Others hypoactive (“quiet”) delirium
- Marcantonio ER. NEJM; 377(15):1456

Delirium

Delirium = “Acute Brain Failure”

Leading Causes for Delirium

- Dementia leading risk factor for delirium
 - 2/3 of cases of delirium occur in patients with dementia. Inouye SK. NEJM. 2006;354:1157-1165
- Age related brain atrophy - reticular activation system (RAS)

Delirium

JS

Admit March 29, 2014

84-year-old female admitted from home; increased confusion over 2 weeks

Adenocarcinoma of the lung – dx one year ago

Medical history

- Hypertension, Macular degeneration
- Renal insufficiency, Pacemaker

Delirium

JS

Social History

- Psychosocial team very familiar with JS; husband died 1 year earlier
- Lives alone; good support-one daughter
- “Someone everyone would want as a grandma”
- Very loving, very sweet and kind

Delirium

JS

- Reduced oxygen saturation – 88%
 - resolved with 2L oxygen
- Chest x-ray report
 - no obvious pneumonia
 - ? mild CHF
- Pain in left leg – no known pathology

Delirium

JS

- KUB – marked fecal loading
- Palliative constipation score 12/12
- Unenhanced CT
 - Unable to use contrast – renal function
 - No brain lesions, edema, blood or midline shift

Delirium

JS

Labs

- WBC 11.2 (4.0 – 10.0 x 10⁹/L)
- Urea 15.1 (3.0 – 7.1 mmol/L)
- Creatinine 166 (60 – 130 mmol/L)
- Albumin 33 (35 – 50 g/L)

Patient drinking and eating well, encouraged fluids

Delirium

JS

U/A suggested UTI – bacteriuria

- Amoxicillin – cover most community infections
- No culture – costs \$80.00

Nurse progress note: 3/29/14

- Patient appears anxious, asking a lot of questions and very forgetful, not oriented to time and place

Delirium

JS

3/31/14

- Disimpacted for very large amount hard stool; aggressive bowel care continued for a few days
- Constantly moving
- Patient aware of her confusion
 - not seen in dementia patients*

Delirium

JS

3/4/14

- Frequent haloperidol; agitation poorly controlled

So, what are we seeing?

- A) akathisia - haloperidol (low dopamine state)?
- B) agitation (high dopamine state)?

Delirium

JS

4/4/14

- Healthy appearance
- Up independently; constantly wandering
- Pain not an issue
- No O₂ needed
- Hallucinations – singing bird

Delirium

JS

11/4/14

- Delirium/agitation continues
- Repeat U/A – no bacteriuria

Delirium recovery may take weeks
Gradual improvement during treatment

Not the case here !!!

Delirium

JS

16/4/14

- Nurse withheld scheduled morning antipsychotic
- Patient alert, “pleasantly confused”, non-agitated
- 3 hours later
 - Significant agitation, difficult to settle
 - Left order not to hold scheduled antipsychotics

Delirium

JS

16/4/14 – Night Shift

- Methotrimeprazine ineffective for agitation

17/4/14

- Midazolam given to settle - effective
- Clonazepam started po/pr

Delirium

JS

19/4/14

- Phenobarbital added
- Palliative sedation continued

25/4/14

- JS died peacefully

6 weeks - suffering end of life delirium!

Delirium

Case highlights

- Patient may have normal labs and imaging; no reversible causes found
- Patient can look healthy; eating and drinking well
- End of life delirium can last weeks

Delirium

- D** Drugs
- E** Eyes, ears, and other sensory deficits
- L** Low O₂ states (e.g. heart attack, stroke, and pulmonary embolism)
- I** Infection
- R** Retention (of urine or stool)
- I** Ictal state
- U** Underhydration/undernutrition
- M** Metabolic causes (DM, post-operative state, sodium/calcium)
- (S)** Subdural hematoma

Palliative Prognostic Index (PPI)		
Palliative Performance Scale	10 – 20	4.0
	30-50	2.5
	≥ 60	0
Oral Intake	Severely Reduced (≤mouthfuls)	2.5
	Moderately Reduced (>mouthfuls)	1.0
	Normal	0
Edema	Present	1.0
	Absent	0
Dyspnea at Rest	Present	3.5
	Absent	0
Delirium	Present	4.0
	Absent	0
Maximum possible		15

- Score greater than 6 – 3 weeks survival – sensitivity 80% - specificity 85%
- Score 4 or less – 6 weeks survival – sensitivity 80% - specificity 77%

Delirium

Pathophysiology in Brain

- Reticular Activating System (RAS)
 - Brainstem (pons, medulla, midbrain)
 - Thalamus
 - Wakefulness
 - Our ability to focus
 - Fight-flight-freeze response

Delirium

Reticular Activating System (RAS)

- How we perceive the world
 - our consciousness
 - gatekeeper of information
- Age related atrophy of RAS
- Elderly at increased risk for delirium

Delirium

Reticular Activating System (RAS)

Neurotransmitters

- Acetylcholine, serotonin, norepinephrine, dopamine, histamine, and hypocretin
- Input to RAS
 - Visceral
 - Somatic
 - Sensory systems

Delirium

Delirious Brain

- Unable to produce adequate gamma aminobutyric acid (GABA)
- GABA (inhibitory neurotransmitter) - 80 % of brain function
- Diminishing GABA – increases glutamate release (stimulatory neurotransmitter)

Delirium

Delirious Brain

- Excess glutamate symptoms:
 - Hyperalgesia, allodynia (pain amplification)
 - Anxiety
 - Restlessness
 - Inability to focus
 - Prolonged high excitation - excitotoxicity (nerve death)

Delirium

Delirious Brain

- Increased glutamate increases dopamine
- Dopamine excess in mesolimbic pathway
 - Agitation, paranoia, delusions
 - Distressed behavior, unsettled
 - Confusion, hallucinations
 - *positive symptoms of schizophrenia

Delirium

Delirious Brain

- Acetylcholine - major transmitter in RAS and parasympathetic system
- Acetylcholine inhibited by dopamine
- Symptoms anti-cholinergic nature
 - Urinary retention, constipation, confusion, etc

Delirium

Delirious Brain

- Acetylcholine
 - Theory – retrograde inhibition of parasympathetic system via bladder innervation - effects on RAS
- Infection
 - Reduction in cholinergic activity peripherally
 - Alters parasympathetic acetylcholine levels; RAS
 - Increased sympathetic tone; urinary retention, constipation

Delirium

Delirious Brain

- Norepinephrine
 - Elevated dopamine levels increases production of norepinephrine
- Norepinephrine adverse effect on CNS
 - Leads to delirium (animal models)
 - May augment effect of glutamate

Delirium

Delirious Brain

- Serotonin
 - Inhibitory function; inhibits dopamine release
 - Synthesis dependent on tryptophan in blood
 - Serum tryptophan levels drop – surgery, trauma, alcohol withdrawal, severe illness
- Less serotonin - more dopamine

Delirium

Delirious Brain

- Histamine
 - Neurotransmitter regulation
 - Sleep-wake cycle
 - Motivation, addictive behaviors
 - Satiety, feeding, taste
 - Memory
 - Stress
 - Goal seeking
 - Pain
- Hypocretin – “symphony conductor in background”

Delirium

Three subtypes:

- Hyperactive delirium: heightened arousal; can be restless, agitated or aggressive (25%)
- Hypoactive delirium: characterized by people who become withdrawn, quiet and sleepy
- Mixed: Hypoactive and hyperactive

Delirium

Pre-delirium Screening Questions

- Sleep wake cycle disturbance: Did you sleep well?
Any weird or vivid dreams?
 - Can not sleep
 - Restless sleep
 - Bad, horrifying dreams
- Restlessness: Do you feel restless inside? Do you feel anxious and don't know why?

Delirium

Pre-delirium Screening Questions

- Hallucinations: Tell patient why you are asking!
Normalize question, “these are common symptoms”
 - Visual – seeing things that no one else is seeing?
 - Perceptual – think someone in the room with you and when you look no one is there?
 - Tactile – do you ever feel someone has touched you and you look and there is no one there?

Delirium

Universal Screening – High Level of Suspicion

- Patient with excellent MMSE, MOCCA or SLUMS may still have delirium symptoms!!!
 - 36 year old , alert, pleasant female, PPS 40
 - Pink hippopotamus at the foot of the bed
 - Knew it was not real
 - Passed the time talking to it and it to her

Delirium

Clinical Presentations

- Fine rapid tremor hands/feet – Autonomic nervous system hyperactivity
- Allodynia - Pain resulting from a stimulus (light touch of the skin) which would not normally provoke pain.
“Patient seems peaceful until we touch him”
- Hyperalgesia - Abnormally heightened sensitivity to pain; extreme response to painful stimuli

Delirium

Clinical Presentations

- Alert patient, “Doc, I hurt all over”. Cannot localize pain. (Patient has no history of generalized pain disorder)
- Pain not responsive to analgesics
- Pain will usually improve/resolve with antipsychotic

Delirium

Goal – Identify and Treat Early Stages

- Inform patient and family of the significance of delirium, especially if it does not resolve with treatment of possible underlying causes
- Palliative Performance Index – Delirium score of 4
Total score over 6; sensitivity 80%, specificity 85%

Delirium

Medical Emergency

- Needs aggressive treatment
- Patient suffering
- Family distress; emotional trauma, complicated grief
- Staff safety
- Recommend to treat with scheduled and prn medications

Delirium

Learning objectives:

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- Neurotransmitter derangement in the delirious brain
- Clinical screening questions
- Clinical signs

Delirium

References

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Delirium

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Delirium

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Delirium

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Delirium

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