**Dementia and Delirium:**
*A Neurologist’s Approach to Altered Mental Status*

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**Case 1**

- An 80yo woman presents to your office for the evaluation of recent short-term memory loss
- Her husband states she often forgets her keys and asks repetitive questions
- She no longer takes care of the family finances (2 yrs prior) and is seldom left alone
- The pt and husband believe this is “old age”

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**Which of the following evaluations is your next step?**

A. TSH, B12, RPR  
B. Head Imaging  
C. Formal Neuropsychiatric testing  
D. No testing, begin donepezil  
E. Test screening labs for delirium

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**The Major Dementias**

<table>
<thead>
<tr>
<th>Name</th>
<th>Anatomy</th>
<th>Pathology</th>
<th>First Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer’s Disease</td>
<td>Hippocampus</td>
<td>Amyloid Plaques, Tau tangles</td>
<td>Memory Loss</td>
</tr>
<tr>
<td>Frontotemporal Dementia (FTD)</td>
<td>Frontal and Temporal Lobes</td>
<td>Tau inclusions</td>
<td>Apathy, Behavior, Anxiety</td>
</tr>
<tr>
<td>Dementia with Lewy Bodies (DLB)</td>
<td>Hippocampus and Posterior Parietal</td>
<td>Lewy Bodies</td>
<td>Visual Hallucinations, Parkinsonism</td>
</tr>
<tr>
<td>Vascular Dementia</td>
<td>Diffuse or focal</td>
<td>Gliosis</td>
<td>Executive Slowing</td>
</tr>
</tbody>
</table>

*Mixed AD and vascular “strangely” common*
Alzheimer’s Therapy

- Cholinesterase Inhibitors
- Memantine

Continuing therapy in advanced disease

- 295 patients with moderate to severe AD (SMMSE 5-13) already taking donepezil
- Randomized for 1 year to continuation of donepezil, stopping donepezil, adding memantine, or replacing with memantine
- Those who stopped donepezil did significantly worse than those continuing by nearly 2 points on the MMSE
- Combination therapy did not help*


Alzheimer’s Therapy

- Cholinesterase Inhibitors
- Memantine
- Behavioral Therapies lacking
  - Antipsychotics?
  - Cholinesterase Inhibitors?
- Current Trials
  - Mainly amyloid-directed
    - Likely start way too late

Alzheimer’s Diagnosis: New Frontiers of Accuracy

- CSF Biomarkers
  - Aβ 1-42/phosphorylated tau levels
  - “AD signature”: 95-100% sensitivity
    • Found in 1/3 of cognitive normal individuals
- Serum Biomarkers
  - Maybe just as good?
  - Cognitive reserve association demonstrated

De Meyer G Arch Neurol 67:949, 2010
Yaffe K JAMA 305:261, 2011
Alzheimer’s Diagnosis: New Frontiers of Accuracy

• PET imaging with PiB and other compounds

• April 2012: FDA approval for one of these compounds…Florbetapir

Mild Cognitive Impairment (MCI)

• NOT normal aging
• Preservation of function with abnormal cognitive complaints and/or symptoms
• Amnestic MCI becomes AD 10% per year
• Is there anything we can do to prevent AD?
  – Vitamin E?
  – Ginkgo?
  – Cholinesterase Inhibitors?

Case 2

• A 71 year-old previously healthy woman comes to the ER with two days of new progressive confusion according to her family. She has no PMH and takes no meds.
• General physical exam is normal except for a T=38.8. Neurologic exam is notable for disorientation, confusion, and visual hallucinations.

What is the most likely etiology of the patient’s AMS?

A. Heroin overdose
B. Stroke
C. UTI
D. Seizure
E. DKA
Delirium Defined

(DSM-IV-TR) criteria for delirium

(a) Disturbance of consciousness (that is, reduced clarity of awareness of the environment, with reduced ability to focus, sustain, or shift attention)
(b) A change in cognition (such as memory deficit, disorientation, language disturbance) or the development of a perceptual disturbance that is not better accounted for by a pre-existing established or evolving dementia
(c) The disturbance developed over a short period of time (usually hours to days) and tends to fluctuate during the course of the day

Delirium: Really Defined

• Relatively acute onset (hours to days)
• Cognitive change
  – Attentional deficit the hallmark
  – All domains may be impaired
• Fluctuations
• Associated symptoms that may be present
  – Hallucinations, delusions, altered sleep-wake cycle, changes in affect, autonomic instability

Clinical Spectrum of Delirium

• Hyperactive Subtype
  – Classically with alcohol withdrawal
• Hypoactive Subtype
  – Classically with narcotic or benzodiazepine administration
  – More likely to be missed by clinicians
  – Associated with a worse outcome?
• More accurately a spectrum of presentations

Delirium vs. Dementia

• “This distinction is easy”:
  • Not so easy…
    – Dementia is the major risk factor for development of delirium
    – Some degenerative illness can present with symptoms resembling delirium
Dementia with Lewy Bodies (DLB)
• Common Neurodegenerative disorder
• Parkinsonism
• Dementia
• Fluctuating Course
• Prominent Visual Hallucinations
• Extremely sensitive to antipsychotics
• Cholinergic Deficit:
  – TREATMENT WORKS!!!

Delirium: A Stress Test for the Brain

Common Etiologies of Delirium
• Drugs
  – Especially those with anticholinergic properties
• Infection
  – Systemic infections more common than CNS
• Metabolic Disturbances
  – Electrolytes, renal and liver failure, endocrine
• Vascular (Rarely)
• And many others

Risk Factors for Delirium
• Patient characteristics
  – Increasing age
  – Baseline cognitive impairment
  – Baseline vision, hearing or functional impairment
  – Previous episode of delirium
  – Dehydration
  – Fever or hypothermia
• In-hospital characteristics
  – Sensory overload
  – Isolation
  – Bladder Catheterization
  – Physical Restraints
  – Adding three or more new medications
Evaluating the Delirious Patient

- **Initial Laboratory Tests:**
  - CBC, BUN/Cr, Lytes, Ca/Mg/Phos, LFTs
    - Seemingly small abnormalities (i.e. Na=130) can contribute
  - ABG
  - Utox
  - CXR, blood cultures, urine cultures for systemic infection
- **Initial Imaging with CT or MRI**
- If no etiology found consider…
  - LP
  - EEG

Treatment of Delirium

- Treat underlying precipitant first!
  - Correct lytes, treat infection, remove offending medications, etc…
- Then use environmental methods proven to help in delirium management
  - Turn off lights to establish sleep-wake cycles at night
  - Remove all physical restraints (key contributor in multiple studies of delirium)
  - D/C unnecessary monitors and catheters
  - Provide reorientation frequently
  - Maintain adequate hydration
  - Daytime mobilization and exercise
  - Make sure hearing aids, glasses used at home are present
  - Familiar pictures, objects, visitors can help

Treatment of Delirium: Evidence for These Simple Measures

A MULTICOMPONENT INTERVENTION TO PREVENT DELIRIUM IN HOSPITALIZED OLDER PATIENTS

Randomized trial showed that these simple measures decrease incidence of delirium in hospitalized elderly

Treatment of Delirium

- As last resort, consider medical management
  - Antipsychotics common first-line (caution with risk of death in elderly recently demonstrated)
    - Start with low qhs dosing
  - Avoid benzodiazepines
- Formal studies of drugs to boost cholinergic tone underway
Case 3

- A 50 year-old woman is brought in to the ED by his girlfriend with several days of paranoia and unusually aggressive behavior.
- General physical exam is normal. Neurologic examination shows a disoriented woman threatening the staff.
- Labs: Lytes, CBC, BUN/Cr, LFTs, ABG, Utox all Normal
- CT head negative, CXR negative, U/A negative

What is the next test you would like to order?

A. MRI Brain  
B. LP  
C. Blood Cultures  
D. Urinary Porphyrins  
E. EEG

Lumbar Puncture

- Opening Pressure 19 cm H₂O  
- 18 WBCs (94% Lymphocytes)  
- CSF Protein 58  
- CSF Glucose 70  
- Gram stain negative

- Empiric treatment begun

HSV-1 Meningoencephalitis

- Diagnosis  
  - CSF lymphocytic pleocytosis (can be normal)  
  - EEG (can be normal)  
  - MRI (can be normal)  
  - CSF HSV PCR  
- If suspected, start IV acyclovir 10-15mg/kg q 8 hours
**Lumbar Puncture in AMS Workup**

- Perform immediately after imaging if any CSF infection suspected
- Useful information:
  - Inflammatory Conditions (e.g. CNS vasculitis)
  - Neoplastic Conditions (e.g. CNS lymphoma)
  - Hepatic Encephalopathy
- Likely should occur in any patient with an unexplained delirium after initial workup

**Case 4**

- A 45 year-old woman with a PMH only of gastric bypass 6 months earlier presents with 3 days of confusion and inability to walk.
- General physical exam is normal. On neurologic examination the patient is somnolent but arouses to voice. She has deficits in attention and is oriented only to person. Her gait is ataxic.
- Labs: Lytes, CBC, BUN/Cr, LFTs, Utox all nl
- CT head negative, CXR negative, U/A negative

**Deficits of Attention**

- Neuropsychologic hallmark of delirium
- Diffuse localization
- Diagnose during the history
  - Tangential speech, fragmented ideas
- Test at bedside with digits forward task
  - Four digits or less signifies lack of attention
- MMSE often not helpful

**Wernicke’s Encephalopathy**

- Caused by thiamine deficiency leading to interruption of mammillothalamic tract
- Classically in alcoholics, now seen mainly in vitamin deficient states
- Triad: confusion, ataxia, ophthalmoparesis
- Thiamine 100mg IV daily if even suspected
  - Consider in any case of unexplained delirium
Case 5

- An 86 year-old woman with a history of stroke presents with 2 days of confusion.
- General physical exam is normal. On neurologic examination the patient is somnolent and will not arouse to voice. The rest of the neurologic examination is normal except for fine nystagmus in all directions of gaze.
- Labs: Lytes, CBC, BUN/Cr, LFTs, Utox all nl
- CT head negative, CXR negative, U/A negative

What is the next test you would like to order?

A. MRI Brain
B. LP
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Seizure-Related AMS

- Non-convulsive status epilepticus
- Post-ictal states that may be prolonged
  - Coma
  - Focal Neurologic Deficits (Todd’s phenomena)
  - Psychosis
  - Confusion
- Can only diagnose with EEG

Case 6

- A 30 year-old man with no PMH presents with 6 hours of stupor. He is on no medications.
- General physical exam is normal. On neurologic examination the patient is unarousable. He has vertical bobbing movements of both eyes. He does not spontaneously move any extremities
- Labs: Lytes, CBC, BUN/Cr, LFTs, Utox all nl
Structures involved in coma

- Either localizes to…
  - Brainstem (reticular activating system)
  - Bilateral hemispheres
- Coma exam focuses on brainstem
  - Pupils, corneals, oculocephalic, gag, cough, etc.

Basilar Artery Thrombosis

- Carries a high mortality
- Common from cardioembolic disease or vertebral artery dissection (in young)
- Embolectomy successful out to 12-16 hours
- Clues on exam
  - Coma with cranial nerve abnormalities
  - Asymmetric cerebellar signs

Take-Home Points

- Delirium signifies a serious underlying disorder and should be viewed as heralding the onset of a neurologic disease
- Spinal fluid examination (LP) is underutilized and should be obtained frequently
- Thiamine 100mg IV should be initiated in AMS nearly always

Take-Home Points

- EEG can rule out rare causes of AMS
- Structural brainstem disease can lead to AMS and clinicians should have a high index of suspicion
- Treatment for AD (and likely FTD) will likely change dramatically over the next few years