Delirium

Geriatrics Interests Group
September 18, 2007
Laurence Solberg, MD
Geriatrics, VUMC
Outline

• Definition
• Epidemiology
• Pathogenesis
• Risk Factors
• Clinical Presentation
• Differential Diagnosis
• Assessment
• Testing
• Treatments
• Outcomes
DEFINITION AND TERMINOLOGY — The American Psychiatric Association's Diagnostic and Statistical Manual, 4th edition (DSM-IV) lists four key features that characterize delirium:

- Disturbance of consciousness
  - reduced ability to focus, sustain, or shift attention.
- Change in cognition or development of a perceptual disturbance
  - not better accounted for by a preexisting, established, or evolving dementia.
- Disturbance develops over a short period of time and tends to fluctuate during the course of the day.
- There is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by a medical condition, substance intoxication, or medication side effect.
Additional features

• Psychomotor behavioral disturbances
  • Hypoactivity or hyperactivity
  • impairment in sleep duration and architecture.

• Variable emotional disturbances:
  • Fear
  • depression
  • euphoria
  • perplexity
Delirium by any other name...

- acute confusional state
- acute brain syndrome
- toxic or metabolic encephalopathy
- Confusion
EPIDEMIOLOGY — Delirium in the hospital setting

- Older medical patients experience delirium during hospitalization (30 percent)
- In older surgical patients, the risk for delirium varies (15 to greater than 53 percent)
- Higher figures are associated with frail patients
- High rates of delirium have been demonstrated in intensive care units (up to 87 percent)
- Hospice units (42 percent)
- Postacute care settings (60 percent)
**PATHOGENESIS**

- **Neurobiology of attention** — Disorder of attention is a universal feature of delirium. Short summary of the neurobiology of attention.
  - Arousal and attention may be disrupted by brain lesions involving the ascending reticular activating system (ARAS) from the mid-pontine tegmentum rostrally to the anterior cingulate regions.
  - Attention in both right and left aspects of extrapersonal space is governed by the "nondominant" parietal and frontal lobes. Thus with inattention, there is typically some disruption of the integrated function of these regions.
  - Insight and judgment are dependent on intact higher order integrated cortical function. Insight into perceptions is often reduced with delirium and confusional states.
Cortical versus subcortical mechanisms — Studies using electroencephalography (EEG) in acutely ill patients established that delirium was a disturbance of global cortical function. Characterized by slowing of the dominant posterior alpha rhythm and the appearance of abnormal slow-wave activity. These are so consistent that EEG can be used to resolve uncertainty in patients if the diagnosis of delirium is in doubt. The results of brainstem auditory evoked potential, somatosensory evoked potentials, and neuroimaging studies have supported an important role for subcortical (e.g., thalamus, basal ganglia, and pontine reticular formation) as well as cortical structures in the pathogenesis of delirium. These findings correlate with clinical reports that patients with subcortical strokes and basal ganglia abnormalities (including Parkinson’s disease) have a higher susceptibility to delirium.
Neurotransmitter and humoral mechanisms — Acetylcholine plays a key role in the pathogenesis of delirium.

Anticholinergic drugs cause delirium when given to healthy volunteers and are even more likely to lead to acute confusion in frail elderly persons.
  - This effect can be reversed with cholinesterase inhibitors such as Physostigmine (Eserine – used only in anticholinergic overdose).

Further support for the role of acetylcholine is derived from observations that medical conditions precipitating delirium, such as hypoxia, hypoglycemia, and thiamine deficiency, decrease acetylcholine synthesis in the central nervous system (CNS).

Alzheimer's disease, which is characterized by a loss of cholinergic neurons, increases the risk of delirium due to anticholinergic medications.
Risk factors

- Delirium is a multifactorial disorder.
- Factors that increase the risk for delirium:
  - those that increase baseline vulnerability
    - advanced age and sensory impairment.
  - those that precipitate the disturbance
    - polypharmacy (particularly psychoactive drugs), infection, dehydration, immobility (including restraint use), malnutrition, and the use of bladder catheters.
The most commonly identified risk factors are underlying brain diseases:

- Dementia
- Stroke
- Parkinson's disease

(These are present in nearly one-half of older patients with delirium.)
CLINICAL PRESENTATION

• **Disturbance of consciousness**
  • A change in the level of awareness and the ability to focus, sustain, or shift attention.

• **Change in cognition**
  • Delirious individuals have cognitive and perceptual problems, including memory loss, disorientation, and difficulty with language and speech.

• **Temporal course**
  • Delirium develops over hours to days and typically persists for days to months.

• **Elderly patients**
  • Patients with delirium are sick by definition. However, older patients with delirium often do not look sick apart from their behavioral change.

• **Other features**
  • A variety of other clinical manifestations that are not diagnostic features may be present, including psychomotor agitation, sleep-wake reversals, irritability, anxiety, emotional lability, and hypersensitivity to lights and sounds.
Differential Diagnosis

• **Sundowning:** Behavioral deterioration seen in the evening hours, typically in demented, institutionalized patients who may be suffering the effects of impaired circadian regulation in the institutional environment.

• **Focal syndromes:** A number of lobar or focal neurologic syndromes may mimic delirium.
  
  • **Temporal-parietal:**
    - Patients with Wernicke's aphasia may appear delirious in that they do not comprehend or obey and seem confused.
  
  • **Occipital:**
    - Anton's blindness (Anton-Babinski syndrome) of cortical blindness and confabulation might be confused with delirium. However, the patient will betray his or her lack of vision, if one is observant.

  • **Frontal:**
    - Patients with bifrontal lesions (eg, from tumor or trauma) often show akinetic mutism, lack of spontaneity, lack of judgment, problems with recent or working memory, blunted or labile emotional responses, and incontinence.
Nonconvulsive status:

- Nonconvulsive status epilepticus (NCSE) requires an EEG for detection and continuous EEG for management. No classical ictal features, but features that suggest the possibility of seizures:
  - prominent bilateral facial twitching
  - unexplained nystagmoid eye movements during obtundated periods
  - spontaneous hippus (spasmodic, rhythmic dilating and contracting of the pupil)
  - prolonged "post-ictal state"
  - automatisms (lip smacking, chewing, or swallowing movements)
  - acute aphasia or neglect without a structural lesion
  - when the etiology of a confusional state remains obscure
Dementia:

- Dementia may sometimes be confused with delirium or confusion. Characteristic differences in progression and cognitive features distinguish these disorders.
  - **Alzheimer's** — Cognitive change is typically insidious, progressive, without much fluctuation, and occurs over a much longer time (months to years). Attention is relatively intact, as are long term memories in the earlier stages.
  - **Lewy bodies** — Dementia with Lewy bodies (DLB) is similar to Alzheimer's disease but can be more easily confused with delirium, because fluctuations and visual hallucinations are common and prominent.
**DIFFERENTIAL DIAGNOSIS**

- **Primary psychiatric illnesses:**
  - Depression. Associated with poor sleep and difficulty with attention or concentration. Agitated depression may be especially problematic. Depression is associated with dysphoria, and there is less fluctuation than in delirium.
  - Mania. Can be confused with hyperactive delirium with agitation, delusions, and psychotic behavior. However, mania is usually associated with a history of previous episodes of mania or depression.
  - Schizophrenia. The delusions are usually highly systematized, the history is longer, and the sensorium is otherwise clear.
EVALUATION

• There are two important aspects to the diagnostic evaluation of delirium:
  • 1. Recognizing that the disorder is present
  • 2. Uncovering the underlying medical illness that has caused delirium.
• **Recognizing the disorder:**
  • Clinicians often fail to recognize delirium
    • This happens in more than 70 percent of cases.
    • Behavioral problems or cognitive impairment may be wrongly attributed to the patient's age, to dementia, or to other mental disorders.
  • Determining that cognitive impairment is not due to a prior dementia requires knowledge of the patient's baseline level of functioning.
Assessment

• **Confusion Assessment Method (CAM):**

  1. Acute onset and fluctuating course  [yes] [no]
     (Is there evidence of an acute change in mental status from the patient’s baseline? Did this behavior fluctuate during the past day, that is, tend to come and go or increase and decrease in severity?)

  2. Inattention  [yes] [no]
     (Does the patient have difficulty focusing attention, for example, being easily distractible, or having difficulty keeping track of what is being said?)

  3. Disorganized Thinking  [yes] [no]
     (Is the patient’s speech disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?)

  4. Altered level of consciousness  [yes] [no]
     Overall, how would you rate this patient’s level of consciousness? Alert (normal), Vigilant (hyperalert), Lethargic (drowsy, easily aroused), Stupor (difficult to arouse), Coma (unarousable)

• The diagnosis of Delirium requires a “yes” answer for criteria 1 and 2 and either 3 or 4.
Investigating medical etiologies

- Fluid and electrolyte disturbances (dehydration, hyponatremia and hypernatremia)
- Infections (urinary tract, respiratory tract, skin and soft tissue)
- Drug or alcohol toxicity
- Withdrawal from alcohol
- Withdrawal from barbiturates, benzodiazepines, and selective serotonin reuptake inhibitors
- Metabolic disorders (hypoglycemia, hypercalcemia, uremia, liver failure, thyrotoxicosis)
- Low perfusion states (shock, heart failure)
- Postoperative states, especially in the elderly
Medication review

• Drug toxicity accounts for approximately 30 percent of all cases of delirium.
• Most important initial step is a medication review.
• Do not forget over-the-counter agents
• Look for drugs prescribed by other physicians, or drugs belonging to other household members.
• Ask a family member to clean out the medicine cabinet and bring the contents for review.
LABORATORY TESTING

• Serum electrolytes, creatinine, glucose, calcium, complete blood count, and urinalysis
• Drug levels should be ordered where appropriate. (digoxin, lithium, or quinidine)
• Toxin screen of blood and urine
• Blood gas determination is often helpful
• Thyroid function and vitamin B12 levels
Neuroimaging

- Head CT should be used selectively rather than routinely for most patients with delirium.
- MRI is more sensitive than head CT for acute stroke, posterior fossa lesions, and white matter lesions.
- However, neuroimaging is necessary, if no obvious cause of delirium is apparent on first evaluation.
- In patients with delirium of unknown cause and negative head CT, MRI may be useful to exclude acute or subacute stroke and multifocal inflammatory lesions (eg, as seen in reversible posterior leukoencephalopathy and acute disseminated encephalomyelitis).
EEG testing

• Electroencephalography (EEG) is useful in patients with altered consciousness in order to:
  • Exclude seizures, especially nonconvulsive or subclinical seizures
  • Confirm the diagnosis of certain metabolic encephalopathies or infectious encephalitides that have characteristic EEG patterns
  • EEG evaluation should be obtained for any patient with altered consciousness of unknown etiology
Treatments

• SUPPORTIVE CARE:
  • An interdisciplinary approach to delirium should focus upon maintaining adequate hydration and nutrition, enhancing mobility and range of motion, treating pain and discomfort, preventing skin breakdown, ameliorating incontinence (seen in over half of delirious patients), and minimizing the risk of aspiration pneumonitis.
• MANAGING BEHAVIORS
  • Managing disruptive behavior is the most challenging aspect of delirium therapy.
  • Mild confusion and agitation may respond to interpersonal and environmental manipulations
  • Frequent reassurance, touch, and verbal orientation from familiar persons lessen disruptive behaviors.
Treatments

- Physical restraints should be used only as a last resort.
  - Lead to increased agitation and create additional morbidity.
  - Constant observation, preferably by someone familiar to the patient, is less traumatic.
  - Constant observation, by avoiding further complications, may be more cost-effective in the long run than restraining or sedating the patient.
Treatments

• **PSYCHOTROPIC MEDICATIONS:**
  • Prompt symptom control is occasionally necessary to prevent harm or allow evaluation and treatment.
  • A cautious trial of psychotropic medication is warranted in these circumstances.
  • The newer atypical antipsychotic agents, quetiapine, risperidone, and olanzapine have fewer extrapyramidal side effects.
  • They appear to have similar efficacy to haloperidol.
  • These medications are more costly.
  • Concerns have been raised about a possible small increase in risk for cerebrovascular adverse events and mortality when used to treat agitation in patients with dementia.
  • **Benzodiazepines have a more rapid onset of action (five minutes after parenteral administration) than the antipsychotics, but they commonly worsen confusion with sedation and/or agitation.**
Outcomes of Delirium

• Delirium has an enormous impact upon the health of older persons.
• Patients with delirium experience prolonged hospitalizations, functional decline, and are at high risk for institutionalization. (43% at 6 months post admission)
• Signs of delirium may persist for 12 months or longer, particularly in those with underlying dementia. (25% had persistant delirium.)
• Thus, although delirium is considered potentially reversible, it is often a predictor of future problems for frail, elderly persons.
• Delirium was an independent marker for mortality at 6 or 12 months after hospitalization. (Risk Ratio of 2.24)