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Neuropsychiatric Evaluation of Patients with Acute Delirium

Andy Jagoda, MD

A 31 year old female was brought to the ED by her companion who claimed that the patient had become acutely confused, agitated, with paranoid ideation. The patient had had an uncomplicated appendectomy 9 days prior and discharged from the hospital 4 days prior. The companion noted that the symptoms had begun the day after surgery and had progressed with fluctuations in the patients symptoms. The altered behavior was initially attributed to a possible occult infection for which the surgeon had treated the patient with azithromycin and ciprofloxicin.

There as no past medical history. The patient drank alcohol socially and had experimented with cocaine, marijuana, and intravenous heroin briefly ten years prior. The patient was in a monogamous relationship with another woman for the past year. There was no history of head trauma or psychiatric illness. The patient was a school teacher preparing her thesis for her PhD in literature.

The patient was initially triaged to the psychiatric ED where she was re-triaged to the adult ED for “medical clearance”.

On physical exam the BP was 168/74; P 120, RR 20, T 97, Pulse Ox 98%, blood sugar 110.

The patient was disheveled and agitated. The head exam was atraumatic, pupils were symmetrically 4 mm and reactive. The cardiopulmonary exam was normal. The abdomen exam revealed a well healed incision, no evidence of infection, soft, nontender, and no masses. On neurologic exam the patient's cranial nerves were all intact; motor, sensory, cerebellar, testing were normal; the deep tendon reflexes were +3 and symmetric. The psychiatric exam revealed a labile affect, paranoid ideation, and inattention.

The CBC, electrolytes, BUN, Cr, and liver function tests were normal. The urinalysis, urine pregnancy test, and urine drug of abuse screen were all normal. A head CT followed by a lumbar puncture were both normal. The patient was admitted to medicine for further evaluation.

Key Questions

- What is delirium and how does it differ from other altered mental states?
- What is the differential diagnosis of delirium and how does the differential impact the diagnostic work-up?
- What is the therapy of choice to control acute agitation in the patient with delirium?

Introduction

Delirium is a medical emergency characterized by an alteration in consciousness associated with an acute disturbance of cognition, attention, and perception. (1) The patient's inability to focus, sustain, or shift attention may result in the impairment of other neurobehavioral tasks such as memory. Language and visual spatial skills may also be affected. (2) Changes is the mental status fluctuate considerably during a 24 hour period and tend to be more pronounced at night. Delirium is a manifestation of an underlying process, which must be identified in order to appropriately manage the condition.

The DSM-IVR divides the criteria for diagnosing delirium into categories based on the underlying etiology. (3) There must be evidence from the history, physical examination, and laboratory evaluation that the disturbance is caused by direct consequences of a general medical condition, medication side-effect, substance intoxication, substance withdrawal, or multiple factors. If the etiology is due to substance intoxication, or a medication side-effect or withdrawal, there must be a temporal relationship between use of the substance and onset of the disturbance.

Epidemiology

Most studies on delirium focus on the elderly making it difficult to ascertain the incidence in the general ED population, see below. Certain risk factors for delirium are identified consistently in published studies: Chief among these are advanced age. (4) Medication use, especially polypharmacy, is a strongly associated factor. Medications with anticholinergic properties have been identified as the single most common pharmacologic cause of delirium. (4) Interaction of multiple risk factors, including chronic medical conditions, preexisting dementia, limited ambulation, and social isolation, is an important consideration and put the elderly at increased risk. (5) Intoxication with substances, legal or illicit, is an universal risk. Delirium risk increases for an individual as the number of underlying risk factors increases. Pediatric patients at greatest risk are those hospitalized with acute toxic, metabolic, or traumatic central nervous system disorders.

It has been estimated that 10% of hospitalized patients are delirious at any given time with rates of 30% to 50% in those over age 70. (6) Up to 40% of hospitalized HIV positive patients

develop delirium. (7) One study reported that 24% of elderly patients presenting to the ED had delirium. (8) Two studies have demonstrated that in general emergency physicians fail to recognize acute changes in mental status in the elderly and send home approximately 40% of patients with delirium. (6, 9) Delirious patients have a higher rate of mortality than non-delirious patients with the same underlying medical condition. Mortality rates as high as 74% have been reported in patients admitted to the hospital with delirium. (10)

Delirious patients pose a potential medical-legal risk. They are unable to give informed consent; they are at risk to escape if not supervised; they may display aggressive behavior toward health care personnel; and they are at risk for falls or self injury. They are poorly cooperative with necessary procedures and therapy, frequently pulling out IVs, catheters, drains, and sutures further complicating their underlying medical condition.

Clinical Presentation

There are three broad characteristics of delirium. The first characteristic is disturbance of consciousness. The poorly defined concept of consciousness is generally understood as alertness, awareness of environment, wakefulness, and ability to voluntarily focus, sustain, or shift attention. Delirious patients may present either in a hyper- or a hypo-active state with a blunted response to their environment. They may be passive, mute in response to verbal stimuli or, in the extreme, may be comatose. The passive, quiet patient is easily overlooked and misdiagnosed. At the other extreme are hyper-alert and hyperactive patients. They may be combative, agitated, loud or physically difficult to restrain. These patients attract the most attention, are difficult to manage, and are most likely to be directed to the psychiatric consultant without appropriate medical evaluation. These behaviors are not mutually exclusive with some patients exhibiting both behaviors over the course of their illness. Some drug regimens used to treat underlying medical disorders may alter the level of consciousness and further complicate recognition of behavioral changes.

The second characteristic is disturbance in cognition that is not due to an underlying dementia. The memory disturbance in delirium is primarily due to inattention with a subsequent impairment in registering new information thus affecting recall. Long term memory is generally preserved. Thought processes are disorganized and inconsistent. Patients are unable to direct thoughts to plan actions or solve problems. They are unable to distinguish fact from mental images and cannot relate new information to premorbid knowledge. Illusions or mistaken perceptions of reality may be present. Hallucinations, abnormal perceptions with no basis in reality, are less common and more likely to be found in younger patients with substance intoxication or withdrawal. Mood lability is frequent with rapid shifts among depression, agitation, apathy, fear, and suspiciousness. Disturbed speech ranges from increase to decrease in rate, quantity, and volume and may be rambling or totally incomprehensible. Reading and writing ability may also be affected. Orientation for time and place is usually impaired, while orientation to self often preserved.

The third characteristic, the most important in distinguishing delirium from other mental disorders, refers to the temporal course. Onset is typically sudden, develops over hours or days,

and is often first apparent at night. Symptoms fluctuate in severity during a 24 hour period and are classically worse at night. Marked disruption of the sleep-wake cycle may result in wakefulness, agitation, and hallucinations by night; with napping and drowsiness by day.

By definition, delirium is transient with recovery to the patient's baseline status once the underlying disorder has resolved. If the underlying disease is severe, progressive or unaddressed the patient commonly has a downward course with increasing stupor, coma, and death. After recovery, patients may have no recollection of the episode.

Differential Diagnosis

Delirium must be distinguished from dementia, psychosis, or other psychiatric disorders, see Table 1. Because dementia is a major risk factor for delirium, the patient with acute delirium superimposed on a baseline dementia represents a major diagnostic challenge. Such patients are easily misdiagnosed as having a mere progression of dementia when the acute changes are not recognized. The distinguishing aspects of the history are baseline cognitive function, time frame of new symptom onset, course over 24 hours, and level of consciousness.

Patient Evaluation

An attempt should be made initially to obtain history though in reality the factual history must usually be obtained from family members, friends, or caregivers. The history should focus on causal factors related to the delirium such as intracranial disease including head trauma, systemic disease including metabolic and cardiopulmonary disorders, exogenous toxic agents, and withdrawal from substances of abuse. (11, 12)
The physical exam must include a complete evaluation including a neurologic exam and a psychiatric exam, see Table 2. The physical exam must look for evidence of trauma, cardiovascular disease, "toxidromes", and sepsis. The neurologic exam must look for signs of focal deficits. The Mini-mental status examination (MMSE) is used to test for cognition which include orientation, registration (storing new information so that is can be retrieved later), attention and calculation, recall, and language (including visual-spatial). A high score on the exam makes a cognitive deficit unlikely, however, a low score is nonspecific and not diagnostic of any specific disorder. Therefore, the MMSE must be interpreted with care in delirium since the delirious patient has impairment with attention which interferes with exam performance. The Confusion Assessment Method, see Table 3, has been developed as an easy to use, sensitive, specific, and reliable method which enables nonpsychiatric physicians to quickly detect delirium.(13)

Diagnostic Testing: Laboratory testing is directed by clinical suspicion. Routine testing is individualized and limited initially to blood chemistry studies that assess for electrolytes, glucose, renal and hepatic abnormalities. (12) A complete blood cell count is obtained to assess for anemia or leucocytosis. Routine urinalysis and chest roentgenogram may be considered to rule-out infection. An electrocardiogram is indicated for elderly patients or patients with cardiac history or risk factors. It should also be obtained in patients who might receive haloperidol or

droperidol to assess for QTc prolongation. Additional tests may be indicated if a cause is not found on initial evaluation. For patients with history of falls, suspected trauma; focal findings are an indication for neuroimaging. (14) Examination of cerebrospinal fluid may be useful in febrile, delirious patients when meningitis or encephalitis are suspected but most febrile, delirious patients have other obvious sources of infection and do not require lumbar puncture.

The electroencephalogram (EEG) has limited value in the ED setting but may have some utility when diagnosis of delirium remains in doubt. The EEG lacks specificity but usually shows generalized slowing. (1) These changes do not distinguish between delirium and dementia but are not found in psychosis, in which the EEG is normal. In delirium secondary to psychoactive substance use, the EEG may show excessive fast activity superimposed to the slow activity. The EEG can also be diagnostic in cases of nonconvulsive status epilepticus.

Management and Disposition

Treatment of the underlying disorder: Acute management of identified medical disorders must be initiated using established standards of care for resuscitation, monitoring, medication, and diagnostic procedures. In cases of drug related delirium, the risks and benefits of using antidotes must be weighed: e.g., anticholinergic drug toxicity usually resolves safely with drug withdrawal without exposing the patient to added complications from physostigmine.

Symptomatic treatment: Fever and pain must be controlled directed by the suspected underlying medical disorder by judiciously selecting appropriate antipyretic measures and analgesics. Management of agitation is more controversial. Behavioral manifestations, rather than delirium itself, constitute indications for sedation. Agitated or aggressive patients may be dangerous to themselves and others or may not be able to cooperate with necessary procedures. Although there are no controlled studies demonstrating superiority over other drug regimens, intravenous or intramuscular haloperidol with or without addition of intravenous benzodiazepines is often cited as the optimal pharmacologic management of delirium except in cases that are drug withdrawal related.(1) For delirium related to drug withdrawal, benzodiazepines are the first line agents. (1) Haloperidol has been frequently used because it has few anticholinergic side effects, few active metabolites, and a relatively small likelihood of causing sedation and hypotension. The recent “black box warning” by the FDA has dampened many clinicians’ enthusiasm for droperidol despite many years of successful use. (15, 16) A recent review of the management of acute agitation cites the concerns related to the prolonged QTc associated with droperidol and haloperidol and concludes by recommending that benzodiazepines be chosen as a first line pharmaco-intervention. (17)
The disposition of the patient with delirium depends on age and underlying cause of the presentation. A young patient with delirium secondary to drug ingestion could conceivably be discharged under the supervision of a responsible adult. On the other hand, most of the elderly who present with delirium should be admitted to the hospital for stabilization and careful assessment of the factors that led to the event.

Summary / Recommendation

- Patients, especially the elderly, with suspected altered behavior require a systematic evaluation that includes a Confusion Assessment Method (CAM) score.

- Delirium is a medical emergency; treatment requires that the underlying etiology be identified and managed.

- Failure to properly identify and manage delirium is associated with a high mortality; the elderly are at particular risk.

- The agitated patient with delirium is best managed with intravenous haloperidol with or without a benzodiazepine. Patients with delirium secondary to drug withdrawal are best managed using monotherapy with a benzodiazepine.

- Careful consideration should be given to admitting patients with delirium in order to address the underlying factors that led to the event.

Case Outcome

On the medical floor the patient fluctuated between somnolence and agitation; the periods of agitation required haloperidol for behavior control. On the second hospital day, the thyroid function tests returned: TSH <.01 and the TSH receptor antibodies 65% (normal 0-12%). Final diagnosis was hyperthyroidism secondary to Grave's Disease.

The question remained what was the acute precipitant of the Grave's hyperthyroid state. Review of the events leading to the patient's presentation traced the onset to the surgery nine days prior; ultimately, the association was made between the iodine containing prep and the patient's condition making the final diagnosis of Jod Basedow phenomenon (iodine induced hyperthyroidism).

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Table 1: Differential diagnosis of the patient with altered consciousness

	Delirium	Dementia	Psychosis
Onset	Sudden	Insidious	Sudden (may have past history)
24 hr course	Fluctuating,	Stable	Stable
Consciousness	Reduced	Clear	Clear
Attention	Globally disordered	Normal except in severe cases	May be disordered
Cognition	Globally disordered	Globally impaired	Selectively impaired
Hallucinations	Usually visual	Often absent	Auditory predominant
Delusions	Fleeting, poorly systematized	Often absent	Sustained, systematized
Orientation	Usually impaired, at least for time	Often impaired	May be impaired
Psychomotor	Increased, reduced,	Often normal	Varies-hypo-activity or shifting To hyperactive
Speech	Often incoherent, slow or rapid	Perseveration, difficulty finding words	Normal, slow or rapid
Physical illness or drug toxicity	One or both present	Often absent, especially in Alzheimer's type	Usually absent

Table 2: Evaluating Mental Status

Components of Psychiatric Mental Status Exam for Behavioral Function

Appearance
Motor
Speech
Affect / Mood
Thought content
Thought process
Perception
Insight / Judgment
Impulse control / Safety

The Mini-Mental Status Examination for Cognitive Function

Item	*Score*	
Time orientation (year / month)	5	
Place orientation	5	
Registration of 3 words	3	
Serial 7 (tests of attention)	5	
Recall of 3 words	3	
Naming	2	
Repetition	1	
Comprehension	3	
Reading	1	
Writing	1	
Copy a design	1	
total	*30*	*(24 - 30 = "normal")*

TABLE 3: The Confusion Assessment Method (CAM) Diagnostic Algorithm: The diagnosis of delirium by CAM requires the presence of features 1, 2, and either 3 or 4.

(from Inouye S, Van Dyck C, et al: Clarifying Confusion: The Confusion Assessment Method. Ann Intern Med 113:941, 1990)

Feature 1: Acute Onset and Fluctuating Course

This feature is usually obtained from a family member or nurse and is shown by positive responses to the following questions: Is there evidence of an acute change in mental status from the patient's baseline? Did the (abnormal) behavior fluctuate during the day, that is, tend to come and go, or increase and decrease in severity?

Feature 2: Inattention

This feature is shown by a positive response to the following question: Did the patient have difficulty focusing attention, for example, being easily distracted, or having difficulty keeping track of what was being said?

Feature 3: Disorganized Thinking

This feature is shown by a positive response to the following question: Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?

Feature 4: Altered Level of Consciousness

This feature is shown by any answer other than "alert" to the following question: Overall, how would you rate this patient's level of consciousness? (alert-normal, vigilant-hyperalert, lethargic-drowsy, easily aroused, stupor-difficult to arouse, or coma – unarousable)

Annotated Bibliography

McAllister-Williams R, Ferrier I. Rapid tranquillization: Time for a reappraisal of options for parenteral therapy. Brit J Psych 2002; 180:485-489

This is a review article that tries to give some direction on where to go without droperidol and haloperidol. Neither haloperidol nor droperidol are available on the British market, and this article does a reasonable job reviewing the literature on alternatives. It concludes by recommending benzodiazepines when rapid tranquillization is required pending the availability of newer antipsychotic medications that can be delivered parenterally.

Hustey F, Meldon S. The prevalence and documentation of impaired mental status in elderly emergency department patients. Ann Emerg Med 2002; 39:248-253.

This is a prospective, observational study of 297 patients over the age of 70 who were found in the ED to have some degree mental status impairment. The study reports that 26% of the patients had mental status impairment and that 10% had delirium. The authors report that the emergency physician addressed the mental status impairment in only 18% of those patients who were sent home. The authors stress the importance of a systematic assessment of cognitive function and of altered mental status in the elderly presenting to the ED.

Naughton B, Moran M, Ghaly Y, Michalakes C. Computed tomography scanning and delirium in elder patients. Acad Emerg Med 1997; 4:1107-1110

This study attempted to examine ordering practices in elder patients with altered mental status. The authors report that in all elder patients with altered mental status, those with delirium are most likely to be scanned however no analysis is provided of the findings of these scans nor of the predictors of a positive scan.

American College of Emergency Physicians. Clinical policy for the initial approach to patients presenting with altered mental status. Ann Emerg Med 1999; 33:251-281.

This practice guideline provides a framework to use when evaluating the patient with altered mental status. It emphasizes the historical and physical findings that drive specific actions in evaluating these patients. The clinical policy includes a description of the mini mental status exam, and provides "quick reference" forms that can be used for quality assurance programs and for developing a complaint specific chart.

Wofford J, Loehr L, Schwartz E. Acute cognitive impairment in elderly ED patients: Etiologies and outcomes. Am J Emerg Med 1996; 14:649-653.

This is a descriptive study of ED patients with acute cognitive impairment. It reports that 5% of EMS transports are for patients over the age of 60 with an acute change in mental status. The rate of hospitalization was 75% and mortality was 29%. This paper is one of the earlier studies in the EM literature emphasizing the need for aggressive management of the delirious patient, especially if elderly.

Lewis L, Miller D, Morley J, et al. Unrecognized delirium in ED geriatric patients. Am J Emerg Med 1995; 13:142-145.
This study is a convenience sample of 385 patients over the age of 65 who were not unconscious and who could speak. Patients were evaluated by a nurse trained in geriatric assessments using the CAM score after the emergency physician had done an initial evaluation. 10% of patients were assessed as having delirium; the emergency physician recognized only 17% of these patients however 62% were admitted to the hospital, usually with a diagnosis of sepsis. 37% of the patients meeting criteria for delirium were discharged from the hospital; 3 month mortality was 14% of those patients diagnosed with delirium using the CAM score vs 8% of those without delirium.

American Psychiatric Association. Practice guideline for the treatment of patients with delirium. Am J Psychiatry 1999; 156(suppl): 1-20.

This is an excellent document that provides recommendations on the psychiatric management of patients with acute delirium; environmental interventions; somatic interventions. The experts who wrote this guideline recommended that haloperidol or droperidol be used for the acutely agitated delirious patient while benzodiazepines be used as a monotherapy for delirium caused by withdrawal of alcohol or sedative hypnotics. Interestingly, with the "black box" warning from the FDA, the use of antipsychotics must be readdressed and hopefully the APA is actively working on an updated guideline.

Karas S. Behavioral emergencies: Differentiating medical from psychiatric disease. Emerg Med Practice 2002; 4:1-20.

This is an excellent review of the emergency department approach and management of the patient with an acute change in mental status. The discussions are evidence based and the references are annotated. Clinical pathways are provided that visually present how these patients are managed.

Questions

1. Which is the following is not a characteristic of delirium?

A. Fluctuating course
B. Gradual onset
C. Inattention
D. Altered perception

2. Which of the following is a risk factor for delirium?

A. Age over 60
B. Dementia
C. Polymedication use
D. All of the above

3. What per cent of elderly patients presenting to the emergency department have delirium and what percent of those with delirium are unrecognized as having an acute alteration of mental status and sent home?

A. 10% / 40%
B. 20% / 30%
C. 30% / 20%
D. 40% / 10%

4. What is the recommended medication to manage delirium from drug withdrawal?

A. Haloperidol
B. Resperidone
C. Lorazepam
D. Diphenhydramine

Question Answers

1. B. Delirium is primarily a disturbance of consciousness, attention, cognition, and perception. It can also affect sleep, psychomotor activity, and emotions. The inattention that is frequently seen in delirium makes assessing cognitive function difficult. The onset of delirium is characteristically sudden and does not resolve until the underlying process that precipitated the event is treated.

2. D. Delirium is a medical emergency and its etiology is an underlying medical process. Older age, polymedication use, social isolation, physical stressors such as surgery, and chronic medical conditions are all associated with delirium. Underlying conditions associated with delirium include: central nervous system disorder, metabolic disorders, cardiopulmonary disorders, and systemic illnesses.

3. A. Approximately 10% of all patients over the age of 65-70 who are brought to the ED have delirium. Emergency physicians often fail to recognize that the patient has an acute change in mental status; this is often due to the patients co-morbidities such as dementia. Of those elderly patients coming to the ED with delirium, up to 40% go unrecognized and are sent home. Mortality in elderly patients with delirium has been reported to be as high as 70%.

4. C. According to the American Psychiatric Association, delirium from drug withdrawal is best managed with a benzodiazepine as a monotherapy. The best treatment of agitation in delirium from other medical causes is currently controversial due to concerns of QTc prolongation seen with droperidol and with haloperidol.