

LESSONS LEARNED AT THE INTERFACE OF MEDICINE AND PSYCHIATRY

The Psychiatric Consultation Service at Massachusetts General Hospital (MGH) sees medical and surgical inpatients with comorbid psychiatric symptoms and conditions. Such consultations require the integration of medical and psychiatric knowledge. During rounds, Dr. Stern and the chief resident discuss the diagnosis and management of conditions confronted. These discussions have given rise to rounds reports that will prove useful for clinicians practicing at the interface of medicine and psychiatry.

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Psychotic Symptoms in the Elderly

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Have you ever encountered an older patient who developed paranoia, hallucinations, or other psychotic symptoms? Have you ever wondered how to evaluate the etiology of those symptoms and to create a better diagnostic framework for understanding them?

These questions frame our discussion of an elderly woman who presented with paranoia and agitation. Her case report will highlight the diagnostic complexities of late-life psychosis and allow us to address issues of diagnosis, management, and treatment.

Case Report

Ms. A, an 81-year-old woman with a history of coronary artery disease and hypertension, was admitted to the hospital for evaluation of mental status changes and for behavioral management. During the week prior to admission, Ms. A had become suspicious of her neighbors and her daughter. She accused her daughter of trying to steal her fiancé (who did not exist) and accused her neighbors of entering her apartment at night and stealing her belongings, although she was unable to state what was missing. On the day of admission, Ms. A's daughter became concerned when Ms. A called her to say, "I'm getting married to Bill this afternoon and then going on my honeymoon." When Ms. A's daughter went to stop Ms. A from leaving, Ms. A began punching, scratching, and biting her.

Medical evaluation at the hospital revealed laboratory test results within normal ranges (including blood count; comprehensive metabolic panel; thyroid-stimulating hormone, vitamin B₁₂, and folate measurement; and a negative rapid plasma reagin test). A magnetic resonance imaging scan of the brain revealed a few punctate foci of increased T2 signal within the periventricular white matter, and findings of an electroencephalogram were normal.

Further history from Ms. A's daughter revealed that over the previous year Ms. A had become increasingly forgetful and functioned less well; she was no longer able to cook or manage her finances. Psychiatric consultation was requested to assist with making a diagnosis and to provide input regarding behavioral management and Ms. A's living situation upon discharge from the hospital.

Ms. A was diagnosed with dementia of the Alzheimer's type, and she was started on treatment with an atypical antipsychotic and a cholinesterase inhibitor. She was referred for an occupational therapy evaluation for an assessment of home safety and for recommendations regarding her living situation.

What Is the Differential Diagnosis of Late-Onset Psychotic Symptoms?

The most common causes of new-onset psychosis in later life are dementia-related syndromes with psychosis, delirium or drug-induced

psychosis, and primary psychiatric disorders, most commonly depression.¹ Dementia is the greatest risk factor for development of psychotic symptoms in the geriatric population both as a result of dementia itself and through an increased vulnerability to delirium.^{1,2}

Dementia. A diagnosis of dementia is based on the presence of persistent memory loss and 1 other feature of impaired function: aphasia, apraxia, visuospatial, or executive function.³ The presence of memory lapses alone does not warrant a diagnosis of dementia; they may be the result of normal age-related changes in frontal lobe function rather than a neurodegenerative process. *Mild cognitive impairment*, which may represent a pre-dementia state, refers to memory loss greater than that expected from normal aging in the absence of functional impairment. While most causes of dementia are progressive and irreversible, some types of dementia are reversible. Specifically, a workup for the reversible causes of dementia is a first priority in the evaluation of an elderly psychotic individual. These causes include normal pressure hydrocephalus (see below) and vitamin deficiencies (including B₁₂ and thiamine).

Delirium. Delirium is a syndrome with an alteration in consciousness, change in cognition, attentional deficits, an acute onset, and a fluctuating course. *Delirium* refers to a constellation of clinical phenomena and not to an underlying cause. The most common causes of delirium in the elderly are the use of prescription medications (up to 40% of cases) and infection.^{1,2,4-6} Other medical causes, as well as alcohol and sedative-hypnotic intoxication and withdrawal, can also result in delirium. Delirium may be multifactorial; in some cases, the source remains undiscovered even after thorough workup.

Psychiatric disorders. Late-onset psychotic symptoms may also result from a psychiatric cause (e.g., schizophrenia, delusional disorder, depression, bipolar disorder). Patients with a history of thought or mood disorders may have a reemergence of symptoms later in life as part of a remitting and relapsing course. In addition, the first onset of psychosis may occur in the setting of late-onset schizophrenia or a primary mood disorder, such as depression with psychotic features. A careful evaluation to rule out delirium and dementia is required prior to making a diagnosis of a thought or affective disorder.

What Is Involved in the Workup of Late-Onset Psychosis?

The first step in determining the etiology of late-onset psychosis is to search for underlying causes of delirium. This workup generally includes identification of potentially offending prescription medications, especially anticholinergic and sedative-hypnotic medications; exclusion of an infectious etiology (most often urinary tract infection or pneumonia); and exclusion of other metabolic causes.^{1,4-6} Exacerbation of chronic illnesses, such as con-

gestive heart failure, chronic obstructive pulmonary disease, renal insufficiency, and anemia, may also cause metabolic changes responsible for delirium.

Once delirium is excluded as an etiology, the next step is to determine whether the psychotic symptoms stem from a dementia or from another psychiatric disorder. At times, due to comorbidity and overlapping features, it may be difficult to differentiate between dementia and other psychiatric etiologies. For example, an individual with dementia may report depressed mood and/or meet the criteria for depression, and an individual with depression and schizophrenia may perform poorly on cognitive testing. Notwithstanding these difficulties in establishing a diagnosis, careful history-taking with the use of collateral information from family members and others, as well as functional and cognitive assessments, can be helpful in establishing a working diagnosis and a treatment plan.

What Are the Most Common Types of Progressive Dementia and Their Characteristics?

Dementing illnesses can be placed into multiple diagnostic categories. However, there is emerging evidence that these subtypes overlap.

Dementia of the Alzheimer's type (DAT) is the most common dementing disorder, comprising at least two thirds of dementia cases. It affects 1% to 2% of people older than 60 years.^{7,8} The prevalence doubles every 5 years after the age of 60, which translates into a prevalence of approximately 50% of individuals older than 85.^{7,8} The main risk factors for DAT are age and family history, although other risk factors include a history of head trauma and Down syndrome.² The early stages of DAT are characterized by a subtle loss of short-term memory, which progresses into word-finding and naming difficulties, often manifesting as vague speech and circumlocution. As DAT progresses, so does cognitive impairment; motor apraxias may develop. In the late stages, judgment becomes impaired, personality changes, and social withdrawal may occur.

Vascular dementia (previously referred to as multi-infarct dementia) is one of the most common causes of dementia, comprising 15% to 20% of cases.^{2,7,8} Typically, it is characterized by a stepwise decline in cognitive function and is accompanied by focal neurologic deficits. Risk factors are the same as for other vascular and embolic diseases. Stroke is an important contributor to dementia, yielding a 9-fold increase in risk of dementia.^{2,7,8} Vascular defects from a single infarct, multiple infarcts, or white matter ischemia may cause dementia.

A dementia with Lewy bodies (DLB) diagnosis requires a finding of dementia and 1 or more of the following 3 symptoms: visual hallucinations, parkinsonism, and fluctuation in alertness or attention. Postmortem studies show that up to one quarter of those who had dementia

have Lewy bodies, but this pathologic finding may overlap with DAT and Parkinson's disease.^{2,7,8}

Less common types of dementia include frontotemporal dementias and normal pressure hydrocephalus. Frontotemporal dementias include Pick's disease, which generally presents insidiously with disinhibition, a decline in hygiene, and impulsivity that precede cognitive changes. Depression, anxiety, and delusions, as well as language impairment, may also occur.

Normal pressure hydrocephalus is characterized by a triad of gait disturbance, urinary incontinence, and cognitive impairment associated with ventriculomegaly, with or without diffuse cortical atrophy. Improvement with serial lumbar punctures and removal of cerebrospinal fluid is both diagnostic and therapeutic.

Other dementias include those secondary to Parkinson's disease (in which dementia is a late finding in approximately 70% of cases), Huntington's disease, progressive supranuclear palsy, and corticobasal degeneration.^{2,7,8} Alcohol dependence may also cause dementia.

Are There Characteristic Dementia-Related Psychotic Symptoms?

More than half of patients with DAT experience psychotic symptoms during the course of their illness.^{9,10} Delusions are the most common psychotic symptom in patients with DAT, and it is estimated that up to 70% of patients with DAT develop delusions over the course of the illness.^{9,10} The most common delusions involve simple paranoid beliefs, most commonly of theft. Other delusions include the beliefs that a person's house is not their home, a caregiver is an imposter (Capgras syndrome), a caregiver will abandon the patient, or a mate is unfaithful. These delusions may be "misidentifications" due to cognitive impairment rather than true psychotic symptoms.¹¹

Hallucinations are another common psychotic symptom in dementia, occurring in up to half of patients with dementia. Visual hallucinations are the most common type, especially in DLB, in which the frequency is estimated to be up to 80%.¹¹ These hallucinations often do not upset patients, and they may be pleasant. However, they may be upsetting to caretakers. Auditory hallucinations may also occur.

What Treatment Is Available for Psychotic Symptoms in Dementia?

Antipsychotic medications are the first-line treatments for function-impairing delusions and hallucinations. Typical antipsychotics such as haloperidol and chlorpromazine are effective in treating these symptoms, but they have significant side effects including extrapyramidal symptoms (e.g., parkinsonism, tardive dyskinesia) and anticholinergic effects (e.g., sedation, worsening cognitive deficits).¹²⁻¹⁵

Although less studied, there is an emerging literature on the role of atypical antipsychotics in demented individuals with psychosis.^{12,14} Due to the lower incidence of side effects than with typical antipsychotics, atypical agents have emerged as the first-line treatments for these symptoms. Placebo-controlled trials of risperidone and olanzapine have shown a decrease in psychosis (with 1 and 2 mg/day of risperidone and 5 and 10 mg/day of olanzapine).¹² In a nonblinded trial, quetiapine at a mean dosage of 100 mg per day decreased psychotic symptoms at 12 months.¹²

Although atypical antipsychotics have fewer side effects than traditional agents, attention must still be given to adverse effects, including orthostatic hypotension, anticholinergic symptoms, sedation, weight gain, and prolongation of the QT interval. Clozapine is the most anticholinergic of the atypical antipsychotics (followed in descending order by quetiapine, risperidone, and olanzapine) and the most prone to causing orthostatic hypotension. All agents may cause sedation and QT prolongation. Clozapine and olanzapine are most strongly associated with weight gain in nondemented patients, but there has been little study regarding their effects on weight in patients with dementia.

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- Kindermann SS, Dolder CR, Bailey A, et al. Pharmacological treatment of psychosis and agitation in elderly patients with dementia: four decades of experience. *Drugs Aging* 2002;19:257–276
 –This review provides an analysis of 48 studies (from 1960 to 2000) of medication efficacy in the treatment of psychosis, agitation, and aggression in demented patients. It provides a synopsis of each study in a tabular format, as well as a summary discussion of the data. It covers use of antipsychotic agents, both typical and atypical, and other agents (including benzodiazepines, mood stabilizers, and cholinesterase inhibitors).
- Targum SD, Abbott JL. Psychoses in the elderly: a spectrum of disorders. *J Clin Psychiatry* 1999;60(suppl 8):4–10
 –This overview considers the differential diagnosis of psychosis in the elderly and includes a discussion of multiple etiologies. It provides an examination of delirium, drug-induced psychosis, and medical and neurologic conditions associated with psychosis, in addition to a discussion of dementia and primary psychiatric disorders (such as schizophrenia, mood disorders, and delusional disorder). The article also provides a brief introduction to the pharmacologic management of symptoms.