



Psychiatric Manifestations of Medical Disease

Urgent message: Mistaking medical symptoms for psychiatric disease can delay care and lead to adverse outcomes.

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Case Presentation

A 23-year-old man presented with a strange complaint: visual hallucinations. He had no psychiatric history and was otherwise healthy, but felt for the last few weeks “someone” was following him around. He reported seeing shadows of others when he was home alone. He also had begun to have headaches. The urgent care provider performed a thorough history and an exam including a neurological exam which failed to show any focal deficit. The patient was referred for psychiatric evaluation. However, within a few hours of returning home, he began to seize unremittingly. A companion called 911 and he was transported to the emergency department where a CT scan of the brain showed previously undiagnosed neurocysticercosis.

Introduction

Medical etiologies of illness, such as infection, cancer, and polypharmacy can present with symptoms that mimic psychiatric illness, making diagnosis and treatment difficult. Errors leading to misdiagnosis and inappropriate referrals to Psychiatry can be more pronounced in early stages of care, when objective data are often ambiguous or incomplete.

A retrospective study of patients 18 to 65 years of age found 2.8% of patients admitted to psychiatric units had psychiatric symptoms attributable to a medical disorder.¹ More concerning, a comparable study of patients aged



65 and over indicated that 2.3% of patients admitted to psychiatric units had a disorder that required a medical intervention within 12 hours.² Jointly, the studies revealed that patients inappropriately admitted to psychiatric units had lower rates of adequate medical histories, physical examinations, cognitive assessments, laboratory studies, and treatment of abnormal vital signs when compared with patients admitted to medical units.¹

At the bedside in urgent care, we need to balance the risk of missing serious disease with the risk of overtesting, over-referring, and subsequent patient harm which can result from false positives.

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Coupling a sound decision-making strategy with a broad differential that includes the numerous (and often serious) medical causes of apparently psychiatric presentations can help protect against a critical miss.

Common Pitfalls

The intersection of biologic and psychologic manifestations of disease can present a diagnostic dilemma. Being aware of the types of bias that can confound each step of patient evaluation and treatment is important in avoiding catastrophic errors.

This patient population is at risk for falling prey to several types of errors or bias.

- *Premature closure* describes arriving at conclusions regarding the patient’s diagnosis prior to obtaining sufficient information. This can occur when a psychiatric diagnosis is revealed, leading to symptoms being categorized before thorough evaluation. This can lead to missing an underlying medical diagnosis.³
- *Diagnosis momentum* occurs when a patient has previously been diagnosed with a medical condition. New data are then interpreted through the lens of the prior diagnosis. Even if the diagnosis is accurate, it is not always the cause of the presenting complaint. For example, if a patient attributes their own chest pain to previously diagnosed anxiety, it is tempting to assume that’s the case. However, an appropriate history and physical should be completed to assess the chest pain.³
- *Countertransference* occurs when a patient triggers an emotional response in the physician. Being aware of this possibility can mitigate the risk of this form of bias.³

Medical Diseases Which Can Present With Psychiatric Symptoms

Parkinson’s Disease

Parkinson’s disease (PD) is one of the most common neurodegenerative diseases. It is a progressive, chronic disease with both motor and nonmotor features. Motor symptoms are related to the loss of striatal dopaminergic neurons which can cause resting tremor, bradykinesia,

and muscular rigidity.⁴ Less commonly considered are the nonmotor features which also may present prior to onset of the motor symptoms; these can include depression, poor impulse control, anxiety and panic disorder, psychosis, cognitive changes, and sleep disorders. It is also important to be aware that treatment of motor symptoms with dopaminergic agents can produce increased symptoms of anxiety and panic.⁵

Coronary Artery Disease and Myocardial Infarction

There is a well-established correlation between heart disease and psychiatric symptoms. Acute coronary syndrome (ACS) commonly presents with anxiety among the chief complaints. Additionally, after the diagnosis of heart disease, 15% to 20% of patients develop a major depressive disorder (MDD). Approximately 50% have anxiety following ACS.⁶

Pulmonary Embolism

Pulmonary embolism (PE) is a common, life-threatening diagnosis with symptoms that overlap with psychiatric conditions (principally, anxiety disorders). Patients may present with a sense of impending doom with or without chest pain and shortness of breath. In recent decades, there has been an increase in survivorship of acute PE, but with patients subsequently developing prolonged psychiatric symptoms including depression and anxiety.⁷

Seizure Disorders

Complex partial seizures (CPS) result in impairment of consciousness during the episode with a focal onset localized to one area of the cerebral hemisphere. CPS that arise in the temporal region of the brain are often misdiagnosed as a primary psychiatric disorder secondary to the affective, behavioral, and cognitive symptoms that are commonly present. If left untreated, this can result in worsening seizure disorder, status epilepticus, and death.⁸

Hypoglycemia

Hypoglycemia can produce symptoms which overlap with many psychiatric disorders. Patients with hypoglycemia may present with anxiety, somnolence, confusion, irritability, or altered mental status. Often, patients presenting with symptoms concerning for stroke are revealed to have hypoglycemia by virtue of a finger-stick blood glucose test. Hypoglycemia is usually iatrogenic in nature and occurs in patients due to oral and/or injectable agents (eg, insulin) for diabetes. Fear of hypoglycemia is a potential long-term sequela for patients who experience hypoglycemia and can cause severe anxiety that can significantly affect function and quality of life.⁹

Adrenal Disorders

Pheochromocytoma

An adrenal tumor that releases catecholamines into the blood stream, pheochromocytomas mimic the stress response. Catecholamines released intermittently produce symptoms such as high blood pressure, heart palpitations, sweating, and anxiety which can last from seconds to hours, strongly mimicking panic attacks. New onset of anxiety symptoms that are treatment-resistant, associated with abnormal vital signs such as tachycardia and hypertension and that are intermittent and unpredictable, warrants consideration for pheochromocytoma. Definitive treatment involves surgical removal of the adrenal tumor and usually leads to significant reduction in symptoms.¹⁰

Cushing's syndrome

Characterized by elevated levels of cortisol, Cushing's syndrome can occur from tumor production or from exogenous steroid administration and is associated with a variety of psychiatric diagnoses including MDD, generalized anxiety disorder, and panic disorder.

Other symptoms which may be present in at least 50% of cases include cognitive and emotional changes such as decreased attention, memory disturbances, irritability, emotional lability, insomnia, and reduced libido. These symptoms are related to neuronal damage and brain atrophy from excess glucocorticoids.¹⁰ Anxiety and irritability may also be related to the hyperactivity of the hypothalamic-pituitary-adrenal axis and activation of the sympathetic nervous system.¹¹

Risk factors for more severe symptoms include female gender, older age, severity of clinical condition, and urine cortisol levels.¹⁰ Symptoms often resolve when cortisol returns to normal.

Encephalitis

Encephalitis, an inflammation of the brain parenchyma, may be due to infection, vascular disorders, metabolic disorders, toxins, or rheumatoid disease. Although the incidence of infectious encephalitis has remained relatively unchanged in recent years, diagnosis of autoimmune encephalitis has increased significantly with advances in detection and represents a growing proportion of encephalitis cases.¹²

Symptoms of encephalitis which may falsely be attributed to a psychiatric disease include disorientation, cognitive and memory dysfunction, catatonia, mood changes, anxiety, obsessive-compulsive behaviors, and sleep abnormalities.¹³ Of particular concern are rapidly progressive psychotic or mood symptoms that are not

mitigated with the use of psychotropic agents.

Despite advances in detection and treatment, encephalitis continues to represent a significant cause of neuropsychiatric morbidity and mortality.

Therapies for confirmed autoimmune encephalitis include corticosteroids, immunoglobulins, and plasmapheresis.¹⁴

Neurosyphilis

Neurosyphilis is a central nervous system infection that commonly results in psychiatric symptoms. Prior to the widespread availability of penicillin, neurosyphilis accounted for a large proportion of institutionalized psychiatric patients in the United States.

Unfortunately, syphilis has had a resurgence in recent years; the rate of syphilis in the United States increased over 70% during the most recent reporting period, rising from 23.2 cases per 100,000 population in 2015 to 39.7 cases per 100,000 in 2019.¹⁵

Frequently, the illness begins with symptoms that can occur within weeks after infection, including confusion, amnesia, and nonspecific personality changes.¹⁶ An estimated 2% of all late syphilis cases manifest psychiatric symptoms,¹⁷ including psychosis, mania, delusions, and personality changes.¹⁸ Standard treatment continues to be penicillin G. Psychiatric symptoms resolve unpredictably with treatment.

Huntington's Chorea

Huntington disease (HD) is an incurable autosomal dominant central nervous system disease characterized by purposeless choreatic movements, behavior changes, and dementia. Psychiatric symptoms are very frequently present in the early stage of the disease, with onset commonly occurring prior to the onset of motor symptoms.¹⁹ The Neurobiological Predictors of Huntington's Disease observation study (PREDICT-HD) evaluated 10 years of psychiatric symptoms demonstrating significant baseline and longitudinal differences between healthy controls and prodromal HD in depression, anxiety, hostility, and psychosis.²⁰ The most frequently occurring psychiatric symptom of HD is depression.¹⁹

Carcinoid Tumor

Carcinoid tumors are the most commonly occurring neuroendocrine tumors in the gastrointestinal tract.²¹ These tumors often produce high levels of serotonin.

Carcinoid syndrome commonly presents with recurrent diarrhea, flushing, and abdominal cramping. A retrospective cohort study of 1,269 patients with GI neuroendocrine tumors found that 40% of patients had at

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least a moderate anxiety score on a standardized measure for anxiety disorders.²² A National Institutes of Health survey of 663 neuroendocrine tumor patients (536 with carcinoid tumors) revealed that patients with recurrent carcinoid syndrome had much higher levels of anxiety compared with the general public.²³

While new therapies continue to emerge, surgery and somatostatin analogs remain the mainstays of treatment.

B12 Deficiency

Cobalamin, or vitamin B12, is a key element in the metabolism of homocysteine to methionine; elevated levels of homocysteine can directly affect levels of neurotransmitters and cause psychologic symptoms.²⁴ Vitamin B12 deficiency has been shown to be associated with increased likelihood of depression, irritability, delirium, psychosis, attention deficit-hyperactivity disorder, and obsessive-compulsive disorder. Adequate B12 usually will result in dramatic improvement in symptoms if related to B12 deficiency.²⁴

Thyroid Disorders

Largely due to the number of T3 receptors in the hippocampus, and the serotonergic activity of T3, both hypo- and hyperthyroid states generate significant psychiatric symptoms.

Hyperthyroidism

Excess thyroid activity stimulates a fight-or-flight response through the activation of the sympathetic axis, leading to aggression, anxiety, hypomania, psychosis, insomnia, restlessness, and attention deficits. As many as 60% of patients with hyperthyroidism have demonstrated anxiety.¹⁰ There is mixed evidence as to whether these symptoms resolve upon correction to euthyroid levels.¹⁰

Hypothyroidism

Historically, low thyroid activity has been one of the most often overlooked causes of organic psychosis.¹⁰ Severe cases are strongly associated with delusions and hallucinations and are cited in multiple sources as “myxedema madness.”¹¹ Even mild hypothyroidism is associated with slowing of cognitive functions and depressive symptoms. It is a leading cause of treatment-resistant depression.¹⁰

Correction of thyroid levels, including supplementation of T3, has mixed evidence in its efficacy for resolving all psychiatric symptoms. Dementia and memory impairment typically do not resolve with treatment, but depressive symptoms respond well.¹¹

Hypercalcemia

Hypercalcemia most commonly arises from either primary hyperparathyroidism or malignancy. The other 10% of cases come from a variety of other diagnoses often involving the renal and endocrine systems.²⁵ The range of psychiatric symptoms resulting from hypercalcemia is dependent on the cause, severity, and duration of the elevated calcium. Mild cases present with impaired concentration, fatigue, and confusion, whereas more severe cases can result in more profound obtundation and alterations in mental status.²⁶

Treatment is related to severity and underlying cause of hypercalcemia. Psychiatric symptoms typically resolve with restoration of normal serum calcium levels.

Substances

When looking for organic etiologies of psychiatric illnesses, it is important to consider recreational drugs patients may be using or withdrawing from as possible causes. Drugs of abuse can be prescription, over-the-counter, or illicit. Some of the most commonly used substances that can produce symptoms mimicking mental health disorders include:

- Alcohol
- Cocaine
- Methamphetamines
- Ecstasy (MDMA)
- Benzodiazepines
- Antihistamines
- Phencyclidine (PCP)
- Bath salts

Physical Exam Findings Suggestive of Organic Disease

It is important to consider additional symptoms when evaluating for possible psychiatric illness. Certain additional signs or symptoms warrant further investigation

and consideration for organic disease. Cognitive impairment, agitation, focal neurologic deficits, syncope, new or changed headache, shortness of breath, chest pain, and jaundice are unusual findings with a purely psychiatric diagnoses and require further investigation. Suspicion should be higher in elderly patients and patients with significant comorbidities, particularly diabetes and thyroid disorders.

In many cases, vital sign abnormalities can provide the earliest and most valuable clues that an underlying organic etiology is creating or contributing to apparently psychiatric symptoms. However, vital signs are unfortunately frequently neglected in “psych patients.” One chart review study showed only 50% of patients with schizophrenia had had a full set of vital signs collected in the emergency department.²⁷ This is why vital signs are included on the SMART Medical Clearance Form used by many EDs to determine whether further medical evaluation is needed prior to psychiatric admissions.

The Psychiatric Evaluation

The topic of what constitutes an adequate medical evaluation prior to psychiatric admission is one of some debate. In some cases, such as young patients with previous psychiatric admissions, there may be little diagnostic uncertainty. But for first-time psychiatric symptoms, especially in older patients, there is a higher risk of misdiagnosis.

Whereas it is important to rule out medical causes of psychiatric symptoms, it is also important to ensure that chronic medical conditions such as diabetes or hypertension are stable and that acute medical conditions, such as pulmonary embolism or significant infection, are absent prior to admission to a psychiatric unit, where diagnostic resources and expertise may be less accessible.²⁸

Regardless of demographics, all patients should have a thorough history and exam, with consideration of medical cause of psychiatric symptoms.

Summary

- Many different medical conditions and states of intoxication or withdrawal can mimic psychiatric disease.
- Patients presenting with apparent psychiatric complaints warrant consideration of organic causes prior to concluding psychiatric symptoms are related to primary psychiatric disorders. In many cases, a thorough history and physical will yield information to guide this consideration.
- Older age, abnormal vital signs, extensive medical

comorbidities, and absent history of prior psychiatric conditions should alert clinicians to the highest probability of organic disease masquerading as psychiatric illness. ■

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