ABSTRACT
Schizophrenia is a complex, heterogeneous, and disabling psychiatric disorder that impairs cognitive, perceptual, emotional, and behavioral functioning. It has a worldwide prevalence rate of about 1%. There are a number of physical and mental illnesses which are co-morbid with schizophrenia and this article will include a brief description and management of some of the commoner ones. Similarly, it can be mimicked by several mental and physical illnesses and accurate diagnosis is important to reduce the disability associated with the illness. Morbidity and mortality is elevated in patients in Schizophrenia as compared to the general population. More than 50% of patients with schizophrenia have co-morbid psychiatric or medical conditions including impairment of cognitive function, depression, obsessive-compulsive behavior, substance abuse, and aggressive behavior, and these reflect on prognosis of both acute as well chronic schizophrenia.

Keywords: Differential diagnosis, co morbidity, schizophrenia, schizoaffective disorder

INTRODUCTION
In an ideal world, each disorder will be in its own neat slot and it will be easy to diagnose a patient and treat an illness according to what is written in the text books. The clinical reality is that patients often do not present with “pure” diagnoses but rather with multiple coexisting psychiatric and medical conditions. Differential diagnoses need to be considered and these can include a number of medical and neuropsychiatric illnesses. Substance use, schizoaffective and bipolar affective disorders, delusional and certain personality disorders, metabolic, endocrine and infectious illness can mimic and complicate a diagnosis of schizophrenia.

DIFFERENTIAL DIAGNOSES
Differential diagnoses that need to be considered are as follows:

- Bipolar I Disorder with psychotic features
- Delusional Disorders
- Schizoaffective Disorder
- Brief Psychotic Disorder
- Psychosis NOS
- Certain personality disorders
- Drug and medication induced psychosis

1) Bipolar disorder with psychotic features
Bipolar disorder with psychotic features are often misdiagnosed as schizophrenia. The two disorders have certain features in common.

a) The positive symptoms of schizophrenia can resemble the symptoms in manic episodes, especially those with psychotic features. (These can include delusions of grandeur, hallucinations, disorganised speech, paranoia, etc).

b) They share medications as some of the current atypical antipsychotics originally approved to treat schizophrenia are now also approved as treatment for acute mania.

c) The negative symptoms of schizophrenia can closely resemble the symptoms of a depressive episode (these include apathy, extreme emotional withdrawal, lack of affect, low energy, social isolation, etc).

d) The two disorders share abnormalities in some of the same neurotransmitter systems. For example, both depressive episode symptoms and the negative symptoms of schizophrenia are at least partially mediated by serotonin. Likewise, the positive symptoms of schizophrenia and the symptoms of mania are mediated in some way by excesses of dopamine. The atypical antipsychotics approved for both these disorders work on both the serotonin and the dopamine systems.

Some key differences are visible at the initial onset of symptoms. According to a Depression and Bipolar Support Alliance survey (formally the National Manic-Depression Association), 33% of people diagnosed with bipolar disorder remember depression as being their initial symptom experiences, and 32% recall mania at their first onset. Only 9% of survey respondents experienced psychotic symptoms first. This shows that even though these symptoms can appear in people with either disorder, certain types of symptoms may be more likely to appear at the onset of one disease than the other. Similarly, the classic onset of schizophrenia symptoms will be more likely to include delusions that are odd or bizarre, not so much delusions of religious grandiosity, which are more often seen in bipolar disorder. Rapid onset and family history of affective disorder is common in bipolar disorder and a more insidious onset and positive family history of schizophrenia will also help to differentiate the two.

2) Delusional disorder
In delusional disorder the person has a variety of paranoid beliefs, but these beliefs are usually not bizarre and are not accompanied by any other symptoms of schizophrenia. For example, a person who is functioning well at work but becomes...
unreasonably convinced that his or her spouse is having an affair has a delusional disorder rather than schizophrenia.

3) Schizoaffective disorders
Schizoaffective disorders are characterised by recurring episodes of mood/affective symptoms and psychotic symptoms.

Mood symptoms maybe manic, depressive or both manic and depressive.

Psychotic symptoms may occur before, during or after their depressive, mixed or manic episodes. The illness tends to be difficult to diagnose since the symptoms are similar to other disorders with prominent mood and psychotic symptoms like bipolar disorder with psychotic features, depression with psychotic features and schizophrenia.

The main similarity between schizoaffective disorder, bipolar disorder with psychotic features, and major depressive disorder with psychotic features, is that in all three disorders psychosis occurs during the mood episodes.

By contrast, in schizoaffective disorder psychosis must also occur during periods without mood symptoms.

4) Brief Psychotic Disorders
In brief psychotic disorders, there is presence of one or more of the following symptoms: Delusions, Hallucinations, Disorganised speech (e.g., frequent derailment or incoherence), grossly disorganised or catatonic behavior similar to schizophrenia. However, the duration of an episode is at least 1 day but less than 1 month and with eventual full return to premorbid level of functioning.

5) Psychoses NOS (Not Otherwise Specified)
Here the patient has psychotic symptoms but does not qualify for any of the other categories.

6) Personality disorders
There are three personality disorder s that need to be considered in the differential diagnosis.

(a) Schizotypal personality disorder is characterised by a pervasive pattern of discomfort in close relationships with others, along with the presence of odd thoughts and behaviors. The oddness in this disorder is not as extreme as that observed in schizophrenia.

(b) Schizoid personality disorder, the person has difficulty and lack of interest in forming close relationships with others and prefers solitary activities. No other symptoms of schizophrenia are present.

(c) Paranoid personality disorder, the person is distrustful and suspicious of others. No actual delusions or other symptoms of schizophrenia are present.

7) Substance abuse
Substance abuse (eg, abuse of alcohol, cocaine, opiates, psycho stimulants, or hallucinogens) often leads to disturbed perceptions, thought, mood, and behavior. The anabolic steroids used by body builders and athletes can lead to psychotic symptoms. Anticholinergic medications can lead to delirium, especially if abused.

Many prescribed medications have been associated with mental status changes, especially the following:
Corticosteroids (psychosis or mania)
Levodopa (hallucinations or insomnia)
Antidepressants (mania)
Beta blockers (depression)
Sibutramine, an anti obesity medication, (contained in many slimming products) is often used by patients to lose weight.
A history of use of slimming pills should always be enquired into, to rule out psychoses secondary to it.

8) Psychoses secondary to organic causes
There are several psychoses that may are secondary to organic causes.

(a) Metabolic illnesses
(i) Wilson disease, (hepatolenticular degeneration), an autosomal recessive illness is a disorder of the metabolism of copper. The first symptoms are often vague changes in behavior during adolescence, which are followed by the appearance of odd movements.

(ii) Porphyria is a disorder of heme biosynthesis that can present as psychiatric symptoms. The psychiatric symptoms may be associated with electrolyte changes, peripheral neuropathy, and episodic severe abdominal pain. Abnormally high levels of porphyrins in a 24-hour urine collection confirm the diagnosis.

(iii) Hypoxemia or electrolyte disturbances may present with confusion and psychotic symptoms.

(iv) Hypoglycemia can produce confusion and irritability and may be mistaken for psychosis.

(b) Delirium from whatever cause (eg, metabolic or endocrine disorders) is an important condition to consider, especially in the elderly or hospitalised patient. Although patients with delirium may have a wide range of neuropsychiatric abnormalities, the clinical hallmarks are decreased attention span and a waxing-and-waning type of confusion.

(c) Endocrine disorders
Infrequently, thyroid illness may be confused with schizophrenia. Severe hypothyroidism or hyperthyroidism can be associated with psychotic symptoms. Hyperthyroidism is usually associated with depression, which if severe may be accompanied by psychotic symptoms. A hyperthyroid person is typically anxious, and irritable.

Both adrenocortical insufficiency (Addison disease) and hypercortisolism (Cushing syndrome) may result in mental status changes. However, both disorders also produce physical signs and symptoms that can suggest the diagnosis. In addition, most patients with Cushing syndrome will have a history of long-term steroid therapy for a medical illness.
Hyponorathyroidism or hyperparathyroidism can on occasion be associated with vague mental status changes. These are related to abnormalities in serum calcium concentrations.

(d) Infectious illnesses
Many infectious illnesses, such as influenza, Lyme disease, hepatitis C, and any of the encephalitides including the Anti-NMDA (N-methyl-D-aspartate) receptor encephalitis can cause mental status changes such as depression, anxiety, irritability, or psychosis. Elderly people with pneumonias or urinary tract infections may become confused or frankly psychotic.

The infectious illnesses of particular interest are the following: Neurosyphilis, HIV infection, Cerebral abscess, Creutzfeldt-Jakob disease (CJD).

The Venereal Disease Research Laboratory (VDRL) and rapid plasma reagin (RPR) tests are nontreponemal tests that use antigens to detect antibodies to Treponema pallidum.

Patients with systemic lupus erythematosus, typically young women, may present with psychiatric symptoms, such as psychosis or cognitive deficit, in association with of malar flush and the laboratory findings of anemia, renal dysfunction, and others (including suicide), psychotic relapse, substance-related problems, and psychiatric hospitalization. In conclusion, concurrent depressive symptoms in schizophrenia are common and are associated with significantly poorer long-term functional outcome. Active treatment of depression targeting specific symptoms should be a standard of care.

OCD in Schizophrenia
The common themes are of contamination, sexual, somatic, religious, aggressive, and somatic, with or without accompanying compulsions. These manifestations overlap with the underlying psychosis, demonstrating overvalued ideations and delusional manifestations. Recent evidence suggests a poorer clinical course and long-term outcome, as well as greater neuropsychological dysfunction.

The syndrome may manifest during the prodromal phase or during active psychotic illness, as obsessive ruminations during recovery or the remission phase, as a de novo OC syndrome associated with treatment with Atypical Antipsychotics, or as a concurrent independent OC disorder. Treatment is use of adjunctive anti-OC pharmacotherapy with antipsychotics like haloperidol. Cognitive Behaviour Therapy could also be used.

Eating Disorder in Schizophrenia
An eating disorder is often difficult to distinguish from psychotic phenomena, as the patient may not eat due to delusions. Case reports and open-label trials have investigated informal use of second-generation antipsychotics with potent metabolic side effect profiles in the treatment of anorexia, both by itself and as a co-morbidity with schizophrenia.

Schizophrenia and Persistent Aggressive Behavior
It is important to manage aggressive behavior in schizophrenia. Epidemiology revealed that co-occurring substance abuse and intoxication increase the risk of violence in patients with schizophrenia. Some studies have reported that ten percent of patients attack others within 24 hours after their admission in hospitals. Transient violence is associated with environmental factors and positive symptoms of psychosis.

Several medication strategies are considered for treatment of persistently aggressive psychotic patients, including conventional neuroleptics, atypical neuroleptics, and mood stabilisers like sodium Valproate and occasionally lithium carbonate. A recent study revealed the effectiveness of clozapine on violence in patients with schizophrenia.
REFERENCES

1. Medscape Education Psychiatry & Mental Health. Management of Schizophrenia With Comorbid Neuropsychiatric Disorders. Henry A. Nasrallah, MD; Michael Y. Hwang, MD.

2. Schizophrenia.com


LEARNING POINTS

- Schizophrenia is a complex, heterogeneous, and disabling psychiatric disorder that impairs cognitive, perceptual, emotional, and behavioral functioning.

- The differential diagnoses are: Bipolar I Disorder with psychotic features; Delusional Disorders; Schizoaffective Disorder; Brief Psychotic Disorder; Psychosis NOS; Certain personality disorders; Drug and medication induced psychosis; and Psychosis secondary to organic causes; Psychotic Depression.

- Schizophrenia can be mimicked by several mental and physical illnesses and accurate diagnosis is important to reduce the disability associated with the illness.

- More than 50% of patients with schizophrenia have co-morbid psychiatric or medical conditions including impairment of cognitive function, depression, obsessive-compulsive behavior, substance abuse, and aggressive behavior, and these reflect on prognosis of both acute as well chronic schizophrenia.