UNIT NO. 3

DIFFERENTIAL DIAGNOSIS OF SCHIZOPHRENIA & CO-MORBID PSYCHIATRIC CONDITIONS IN SCHIZOPHRENIA AND THEIR MANAGEMENT

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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

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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
- Psychosis secondary to organic causes
- Psychotic Depression

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[2].

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

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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 disorder, 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[3]. 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.

The diagnosis can be indicated by increased urinary levels of copper, low serum levels of copper and ceruloplasmin or by the detection of Kayser-Fleischer rings (copper deposits around the cornea) with or without a slit-lamp examination. The diagnosis is usually confirmed by finding increased hepatic copper at biopsy. As adolescence is often the period when psychotic symptoms may appear in a patient with schizophrenia, diagnosis could be confused.

(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. Hypothyroidism 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.

Hypoparathyroidism 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, elevated erythrocyte sedimentation rate (ESR), and, most specifically, elevated antinuclear antibody.

(e) Heavy metal toxicity may cause changes in personality, thinking, or mood. Occupational exposure is the usual source of heavy metal toxicity, but cases have also resulted from ingestion of herbal medications contaminated with heavy metals. So, a detailed occupational history and history of consumption of over the counter herbal medications should be obtained.

9) Psychotic Depression

People with psychotic depression have symptoms of depression and psychosis. The symptoms of low mood are prominent and it may be associated with mood congruent depression delusions and hallucinations. For example, some patients may hear voices criticising them, or telling them that they don't deserve to live. The person may develop false beliefs about their body, for example that they have cancer.

CO MORBIDITIES AND THEIR MANAGEMENT IN SCHIZOPHRENIA

The commoner co morbidities and their management are as follows:

Schizophrenia with Substance Use Disorders

The most commonly abused drugs include alcohol, cannabis, and cocaine, and the use of these substances markedly worsens the course of illness. In addition, between 50% and 90% of schizophrenic patients smoke cigarettes, contributing to increased mortality from medical illness. Smoking also decreases the effectiveness of some antipsychotics. Co morbid substance use disorder in schizophrenia is associated with greater deterioration of function, higher rates of psychotic relapse, and increased social dysfunction. Furthermore, the dual diagnosis is associated with increased suicidal ideation and victimisation[4-6]. The use of longer-acting oral medications and depot injections have also been shown to help, owing to poor treatment adherence in patients with dual diagnoses[7]. Clozapine treatment seems to be most effective in reducing alcohol and substance abuse in schizophrenia[8,9]. The increased potential for adverse effects from mixing prescribed medications with abused substances should also be considered in dual-diagnosis patients. Sibutramine, an anti obesity medication is often used by patients to lose weight.

Depression in Schizophrenia

The prevalence of depression in schizophrenia is 25% - 81%[10]. The presence of depressive symptoms in schizophrenic patients worsens quality of life[11] and increases the risk for danger to self and others (including suicide), psychotic relapse, substance-related problems, and psychiatric hospitalization[12-15]. 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[16,17]. These manifestations overlap with the underlying psychosis, demonstrating overvalued ideations and delusional manifestations[18]. Recent evidence suggests a poorer clinical course and long-term outcome, as well as greater neuropsychological dysfunction[19-22].

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[23,24]. 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[25-27].

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[28] revealed the effectiveness of clozapine on violence in patients with schizophrenia.

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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.**