ABSTRACT

Bipolar disorder (BD) is a psychiatric disorder that presents with manic and depressive episodes. The mood episodes appear as random and unpredictable episodes. The frequency and course of manic and depressive episodes may vary in each case and be determined by environmental factors as well as patient susceptibility. A 25-year-old man, looks age appropriate, lacks self-care. He was taken to the emergency room because he was making noise about recommendations since 1 week before he was admitted to the hospital. 3 days before came to hospital was confused, easily emotional and had difficulty sleeping, talking to herself, having difficulty communicating, including being in a trance and starting to borrow and owe money to other people. Patients also see and hear sounds that other people do not hear. Further studies are needed for the evaluation of patients with bipolar disorder with psychosis and to acknowledge the treatment options with psychosocial educations as the support the treatment of bipolar disorder.

Keywords: Bipolar disorder, Delusion, Hallucination, Manic, Psychosis
INTRODUCTION

Bipolar disorder (BD) is one of the 10 diseases leading causes of disability in worldwide. Bipolar disorder characterized with episodes of mania or hypomania alternating with depression that occurred chronically and often misdiagnosed initially. 

There is a predominance of depression, from the onset of the illness and throughout its course including the inter-episodic periods. Therefore, distinguishing BD from unipolar depression is difficult. The full spectrum of BD commonly includes milder and subthreshold disorders that overlap with normal variations of mood, personality, and other non-mood disorders. In contrast, the more severe forms such as psychotic BD are often indistinguishable from schizophrenia. These complexities mean that the accurate diagnosis and initiation of treatment are often delayed by several years.  

Psychosis in BD characterized with the presence of delusions or hallucinations or both of the manifestations. It is well known that over half of the patients with BD develop psychotic symptoms during their lifetimes. Psychotic symptoms are more frequent in bipolar than in unipolar depression. Psychotic symptoms are much more frequent during manic than depressive episodes. Their rates are so high in mania that it is often indistinguishable from primary psychotic disorders. All kinds of psychotic symptoms may occur among patients with BD, though grandiose, persecutory, and referential delusions, auditory verbal hallucinations or hearing voices, and visual hallucinations are particularly common.

Given their ubiquity, psychotic symptoms in BD have the potential to adversely affect its course, outcome, and response to treatment. Somewhat surprisingly, the impact of psychosis on the course and outcome of BD remains unclear despite extensive research on the subject. While some reviews regarding the impact of psychosis on BD have indicated that psychotic BD represents a more severe form of the illness with an adverse course and outcome, the majority of the others have not been able to find an association between psychotic symptoms and outcome in BD. Nevertheless, the presence of psychotic symptoms in BD may be of some significance in determining its current nosology. Moreover, the similarity of psychotic BD with schizophrenia on genetic, neurobiological, and cognitive aspects indicates common etiological underpinnings of these disorders. In both aspects, BD seems to lie in an intermediate position between psychotic and non-psychotic disorders, leading to the hypothesis of a continuum of psychosis stretching from major depressive disorders with psychosis to psychotic BD and schizophrenia. Finally, from the clinical perspective, psychotic symptoms have a considerable influence on the way BD is diagnosed and treated. The high prevalence of psychotic symptoms in BD often results in a mistaken diagnosis of schizophrenia. This can lead to inappropriate treatment and can have negative social and economic consequences for those with BD. Moreover, the best way to manage psychotic BD is not clear. Though guidelines emphasize the role of antipsychotics or electroconvulsive therapy, research on adjunctive psychosocial interventions for psychotic symptoms is limited.

CASE REPORT

A 25 year old man was taken by his father and friends to Dr. Arif Zainuddin Mental Hospital because of the manifestations of noisiness, restless, insomnia, talked incoherently and disturbing their neighbors about 3 days before entering the hospital.

According to information from family and friends, the patient was taken to dr. Arif Zainudin Surakarta Mental Hospital because the patient had run away from home. According to family information, several days after being hospitalized at the Mental health, the patient recovered but did not take medication and then started running away from home using a motorbike.

The patient's general condition is good, the conjunctiva is not anemic, the sclera is not icteric. Blood pressure 112/80 mmHg, pulse 98 x/m, respiratory rate 20 x/min, with cardiovascular, respiratory and musculoskeletal systems within normal limits. The patient's neurological status was within normal limits.

On the patient's examination carried out on 7th October 2023 at 12.00, the patient was a man who appeared to be age appropriate with poor self-care. The patient's mood appears irritable, affect increases, and empathy can be felt. The patient's thought process is realistic, there are persecutory delusions and a flight of ideas. There were no hallucinations or illusions during the examination. The patient's social values and assessment of reality are disturbed, with grade 1 insight. The patient cannot control his impulses, and the level is unreliable.

The patient's general condition is good, the conjunctiva is not anemic, the sclera is not icteric. Blood pressure 112/80 mmHg, pulse 98 x/m, respiratory rate 20 x/min, with cardiovascular, respiratory and musculoskeletal systems within normal limits. The patient's neurological status was within normal limits.

On 7th October 2023, a blood laboratory examination was carried out with results of Hb 14.1 gr/dl, RBC 4.21x10^6/uL, WBC 5.330/uL, Platelet count 227,000/uL, Hematocrit 39.7%, MCV 94.3 fl, MCH 33.4 pg, SGOT 15 U /L, SGPT 20 U/L, Current Glucose 99 mg/dL.

Axis I with Bipolar Affective Disorder, Current Episode Manic with Psychotic Symptoms. Axis II with Histrionic
DISCUSSION

Bipolar disorder (BD) is a psychiatric disorder that presents with manic and depressive episodes. The mood episodes appear as random and unpredictable episodes. The frequency and course of manic and depressive episodes may vary in each case and be determined by environmental factors as well as patient susceptibility.9

Bipolar and related disorders include bipolar I disorder (BD-I), bipolar II disorder (BD-II), cyclothymic disorder, other specified bipolar and related disorders, and bipolar or related disorders, unspecified. The diagnostic label of "bipolar affective disorders" in the International Classification of Diseases 10th Revision (ICD-10) was changed to "bipolar disorders" in the ICD-11. The section on bipolar disorders in the ICD-11 is labeled "bipolar and related disorders," which is consistent with the Diagnostic and Statistical Manual of Mental Disorders, 5th edition.8

Currently, the etiology of BD is unknown but appears to be due to an interaction of genetic, epigenetic, neurochemical, and environmental factors. Heritability is well established. Numerous genetic loci have been implicated as increasing the risk of BD; the first was noted in 1987 with "DNA markers" on the short arm of chromosome 11. Since then, an association has been made between at least 30 genes and an increased risk of the condition.10

Although it is difficult to establish causation between life events and the development of BD, childhood maltreatment, particularly emotional abuse or neglect, has been linked to the later development of the condition. Other stressful life events associated with developing BD include childbirth, divorce, unemployment, disability, and early parental loss. In adulthood, more than 60% of patients with BD report at least one "stressful life event" before a manic or depressive episode in the preceding 6 months.10,11 The etiology of BD is thought to involve imbalances in systems associated with monoaminergic neurotransmitters, particularly dopamine and serotonin, and intracellular signaling systems that regulate mood. However, no singular dysfunction of these neurotransmitter systems has been identified.11

As with the etiology, the pathophysiology of BD is unknown and is thought to involve interactions between multiple genetic, neurochemical, and environmental factors. A recent neurobiology review article discusses in detail the "genetic components, signaling pathways, biochemical changes, and neuroimaging findings" in BD.12 Evidence supports a strong genetic component and an epigenetic contribution. Human studies have shown changes in brain-derived neurotrophic factor (BDNF), nerve growth factor (NGF), neurotrophin-3 (NT-3), and neurotrophin-4 (NT-4) in patients with BD, indicating neurotrophic signaling is a molecular mechanism associated with decreased neuroplasticity. Other proposed mechanisms include mitochondrial dysfunction, oxidative stress, immune-inflammatory imbalance, and compromised hypothalamic-pituitary-adrenal axis. Additionally, neuroimaging studies have shown "evidence of change in regional activity, functional connectivity, neuronal activity, and bioenergetics associated with BD," and anatomic studies have revealed dendritic spine loss in the dorsolateral prefrontal cortex in the post-mortem brain tissue of patients with BD.13

Because BD is a clinical diagnosis, making a correct diagnosis requires a comprehensive clinical assessment, including direct interviews with patients, preferably supplemented by interviews of their relatives and the longitudinal course of the disease. On this patient, a thorough history was taken regarding the patient's illness and explored the stressors that triggered the patient's illness.

In terms of diagnostic criteria, hypomania is defined as a version whereby mania symptoms affect social and professional functionality less.3 Moreover, another difference between a manic episode and a hypomanic one according to the DSM-5 diagnostic criteria is their duration. Duration of 1 week for mania and 4 days for hypomania are required (in both diagnoses, if there is treatment, duration criteria are annulled). However, in cases where hypomania lasts long or relapses occur frequently, functionality might also be adversely affected even in hypomania. There is a change in the definition of hypomania between DSM-IV and DSM 5 whereby increase in activity and energy has become one of the two main symptoms. The note that hypomanic episodes triggered by medication and treatment are adequate for a bipolar disorder diagnosis was also added. Both hypomanic and manic episodes can be seen in BD-1. However, in BD-2 patients, no manic episodes are observed, only depressive and hypomanic episodes are present. It was reported that only manic episodes (unipolar mania) were observed in a small group of BD-1 patients. Manic episodes with mild cognitive and mood symptoms, as well as those with serious behavioural organizational disturbances may be seen in the clinical context. In case of mild symptoms, such as the hypomanic episodes, an increase in productivity is possible. In the case that the disorder becomes uncontrollable during the episode of mania, it may lead to situations that pose danger to the patient or the public. Cases that have the potential to engender serious situations in particular, such as self-harming behaviour, sexual behaviour that is outside the person’s usual life experience, random and unnecessary spending of money, over activity and risky behaviour tend to worry the people in the patient’s life and the clinicians. In order to be prepared for such risky situations, patients, their relatives and physicians tend to take precautions against manic
episodes. Therefore, it could be said that the choice of treatment during the symptom-free periods of BD is aimed more towards being preventative against manic episodes. However, in such relatively heavy treatment regimens, treatment compliance tends to be proportionally low. Therefore, defining treatment targets from the very beginning gains precedence. Treatment targets include the treatment of acute manic and depressive episodes, prevention of switches to the opposite pole during acute treatment, prevention of relapses during periods of remission, and prevention of suicidal behaviours and behaviours that have the potential to effect social adaptation. Since such features as lability in mood, mixed symptoms like those in dysphoric mania, rapid cycling course, history of swings to the other pole, number of past episodes, presence or absence of psychotic symptoms, history of alcohol or drug use, and psychiatric or physical dual diagnoses can also be influential in treatment.9,14

Psychosis is an especially prevalent phenotype in bipolar disorder (BP), with greater than half of all individuals diagnosed with BP experiencing psychotic mood episodes in their lifetime. Consequently, there is a common clinical assumption that BP with psychosis represents a more ‘severe’ form of illness than BP without psychosis, and may resemble the clinical and functional deterioration commonly seen in primary psychotic disorders.15 Although numerous clinical practice guidelines exist for the treatment and management of bipolar disorder, there is not enough consistency to generate a ‘meta-consensus’ model.

Most patients with bipolar disorder will require maintenance treatment for many years, possibly lifelong, to prevent recurrent episodes and restore their pre-illness functioning. The current recommendation is for continuous rather than intermittent treatment, with treatments that were effective during the acute phase often continued initially to prevent early relapse. Mood stabilizers and atypical antipsychotics alone or in combination are the mainstays of maintenance pharmacotherapy. There is substantial evidence showing lithium monotherapy’s effectiveness against manic, depressive, and mixed relapse. Additionally, lithium is associated with a decreased risk of suicide in patients with BD. Monitoring during treatment, including serum lithium concentrations, is a standard of care.1

The mainstay of management of BPAD is mood stabilizers. The available mood stabilizers include lithium, valproate, lamotrigine, carbamazepine/oxcarbazepine and topiramate.

Lithium is the oldest mood stabilizer used in the management of BPAD. It has been found to be efficacious in management of acute episode of either polarity and has been found to be efficacious in prevention or relapse of episodes of either polarity. Additionally, it has been shown to have a role in prevention of suicide in patients with BPAD. The serum levels of lithium, which are usually required for management of acute episode, are in the range of 0.6 to 1.0 meq/litre and for prophylaxis range from 0.6 to 0.8 meq/litre; however, few studies suggest that serum levels as low as 0.4 to 0.8 meq/litre may be sufficient for prophylaxis, albeit are associated with higher risk of relapse. Once the dose is stabilized, patient may be shifted to once a day dose to reduce the side effects and improve the medication compliance. Serum lithium levels may be monitored every 3-4 months. Renal function tests need to be monitored once in every 2-3 months during the initial 6 months of therapy and thyroid function tests need to be monitored once or twice during the first 6 months of treatment. Later, renal and thyroid function tests may be monitored once in 6 months to 1 year in clinically stable patients and more frequently if so indicated.16

Divalproex and its formulations (sodium valproate and valproic acid) have been found to be useful in the management of BPAD. It has been found to be efficacious in management of acute mania and mixed episodes. Usually valproate is started in low doses, i.e., 250 mg BD or 250 mg TID and titrated upwards with monitoring of side effects and serum levels. However, some of the studies have also evaluated rapid titration of valproate dose with initial dose of 20-30 mg/day and have shown that it is well tolerated. Maximum daily dose which is recommended is 60 mg/day but most patients do not require such high doses. The usual therapeutic serum levels which are considered to be efficacious vary from 50 to 100µg/ml. Once the dose of valproate is stabilized, the dosing schedule need to be changed to OD or BD dosing to reduce the side effects and improve compliance. In case OD dosing is given, extended release formulation may be used.16

The role of lamotrigine in management of BPAD has been well studied now and it has been shown to be efficacious in management of bipolar depression and prevention of relapse of depression. However, the most dreaded side effect of lamotrigine includes skin rash, including Stevens - Johnson syndrome and toxic epidermal necrolysis. When the rash is more widespread, diffuse and associated with systemic symptoms like fever or sore throat, lamotrigine may be stopped. When initiated, lamotrigine may be started at the dose of 25 mg/day for initial 2 weeks, then it may be given at the dose of 50 mg/day during the 3rd and 4th week. After that 50 mg/day can be increased per week depending on the therapeutic response.16

Over the last decade or so, many large multicentric double blind placebo controlled and active comparator randomised controlled studies have evaluated the role of various atypical antipsychotics like olanzapine, quetiapine, aripiprazole, risperidone, paliperidone, amisulpride, asenapine, ziprasidone and haloperidol etc. in the management of bipolar depression, bipolar mania and for maintenance phase treatment. There is evidence to suggest that when lithium or valproate is combined with antipsychotics in the management of acute mania, the efficacy is higher and the onset of action is faster than that reported for single agent. Accordingly, depending on the severity of mania, combinations may be used.16
CONCLUSION

Several studies show that psychotic symptoms are often found in manic episodes of bipolar disorder. The differential diagnosis of bipolar disorder includes other conditions characterized by depression, impulsivity, mood lability, anxiety, cognitive dysfunction, and psychosis. The most common differential diagnoses are MDD, schizophrenia, anxiety disorders, substance use disorders, borderline personality disorder, and in the pediatric age group, attention-deficit/hyperactivity disorder and oppositional defiant disorder.

Bipolar affective disorder is a mood disorder characterized by repeated episodes (at least two episodes) in which the patient's affect and activity level are clearly disturbed, at certain times consisting of increased affect accompanied by increased energy and activity (mania or hypomania), and at certain times others include decreased affect accompanied by reduced energy and activity (depression). Psychotic symptoms are often found in manic episodes of bipolar disorder. Several studies show that psychotic symptoms that often appear are thought process disorders, delusions, hallucinations,
mood incongruent psychosis, catatonia, and delirious mania. This is why bipolar disorder is often misdiagnosed with schizophrenia and schizoaffective. In carrying out therapy for bipolar disorder, especially manic episodes, a clinician must confirm the diagnosis by carrying out an initial assessment. In the early stages, the algorithm uses simple therapy (monotherapy) because it considers safety, tolerability, ease of use, and side effect profile, while in the late stages it uses several drugs. However, bipolar disorder therapy is effective if carried out comprehensively. Comprehensive therapy includes pharmacotherapy and psychosocial interventions. Several psychosocial interventions that have been proven effective for people with bipolar disorder are cognitive-behavioral therapy, psychoeducation, family-focused therapy, and social and interpersonal rhythm therapy. The prognosis for bipolar disorder varies greatly depending on many influencing factors.

REFERENCES