BIPOLAR DISORDER, NOT SO RARE DIAGNOSIS: SUBTYPES OF DIFFERENT DEGREES OF SEVERITY, DIAGNOSIS, THERAPY

Ioana Cristina Amihăesei
University of Medicine and Pharmacy “Grigore T. Popa” – Iaşi
Faculty of Medicine
Discipline of Histology

BIPOLAR DISORDER, NOT SO RARE DIAGNOSIS: SUBTYPES OF DIFFERENT DEGREES OF SEVERITY, DIAGNOSIS, THERAPY (Abstract): Bipolar disorder is manifesting as a mood disorder, typically showing episodes of mania, alternating with depressive episodes. The subtypes are including bipolar I disorder (one or several manic episodes) and bipolar II disorder (hypomanic episodes and one or several major depressive episodes). Nevertheless, sub-threshold diagnosis criteria may include another 5.1, up to 6.4 % of the population as having a bipolar spectrum disorder diagnosis. Anyone who received the diagnosis is not considered cured afterwards (just in remission). Diagnosis is considering the symptoms of mania, hypomania and depression. Therapy is based on lithium, anticonvulsants, for the manic symptoms, lamotrigine for the depressive episodes and antipsychotics. Under medication, most of the affected subjects are living a normal life; to a certain degree, medication may also prevent the relapses. Keywords: BIPOLAR DISORDER, MANIA, HYPOMANIA, MAJOR DEPRESSIVE EPISODES.

Bipolar disorder is considered a mental illness manifested as a mood disorder, also known as bipolar affective disorder, manic-depressive disorder, or manic depression. Typically, subjects with bipolar disorder show episodes of mania alternating with periods of depression. Approximately 4 % of the general population is affected by bipolar disorder. Prevalence is the same in men and in women and in different cultures and ethnic groups.

Variations in moods and energetic level were observed as part of the human personality, since ancient times. Terms like melancholia and mania have origins in Ancient Greek language. At the beginning of the 19th century, a French psychiatrist Jean-Etienne Dominique Esquirol described lypemania, an affective monomania and became the first to contour the modern depression (1).

In 1854 Jules Baillarger detailed to the French Imperial Academy of Medicine a biphasic mental illness, manifested with periodic mood changes between mania and depression; he used the term of “dual-form insanity”, named afterwards by Jean-Pierre Fairet “circular insanity”(2). The concept was further developed by the German psychiatrist Emil Kraepelin, who used the concept of cyclothymia and he studied the evolution of the untreated bipolar cases. Adolf Meyer introduced the concept of bipolar disorder, as a result of genetic factors influenced by social and psychological factors.
In 1957, the German Psychiatrist Karl Leonhard was the first to define the subtypes of bipolar disorder, he also introduced the concept of bipolar and unipolar, to characterize the forms with exclusively depressive episodes.

**EPIDEMIOLOGY**

Approximately 4 % of the population has one of the bipolar disorder types at a certain period in their life. Further analysis of data from the USA is showing that 0.8 % of the population experience at least an unique manic episode (the diagnosis criterion for bipolar I) and 0.5 % have a hypomanic episode (the diagnosis criterion for bipolar II or cyclothymia).

When sub-threshold diagnostic criteria were included (such as one or two symptoms over a short time-period), another 5.1 % up to 6.4 % were considered as having a bipolar spectrum disorder (3). A recent analysis of data from US National Comorbidity Survey showed that 1 % of the population had lifetime prevalence criteria for bipolar I, 1.1 % for bipolar II and 2.4 % for sub-threshold symptoms. Data are similar in both sexes and in different cultures and ethnic groups. However, the severity of the disease may vary widely across the globe. Late adolescence and early adulthood are peak years for the onset of bipolar disorder (4).

Bipolar disorder can cause suicidal ideation that leads to suicidal attempts. One out of three patients with bipolar disorder reports past attempts of suicide, or succeeds it. The annual average suicide rate is 0.4 %, 10 to 20 times higher than in the general population. The standardized mortality ratio from suicide in bipolar disorder is reported to be between 18 and 25 (5).

**SUBTYPES**

There is no clear consensus in what concerns how many types of bipolar disorder do exist. The concept of bipolar disorder is referring to a spectrum of disorders; the newest classification includes three specific subtypes and a non-specified form.

Bipolar I disorder is characterized by one or several manic episodes. Further is registered if there were several episodes and the type of the most recent episode. A depressive or hypomanic episode is not required for diagnosis, but it often occurs.

Bipolar II disorder is characterized by the missing of the manic episodes; instead are appearing one or several hypomanic episodes and one or more major depressive episodes. Hypomanic episodes do not show as severe manifestations as mania does, and usually do not impair drastically social and/or professional life and do not manifest psychotic symptoms. This can make bipolar II disorder harder to diagnose; hypomanic episodes may look like periods of successful achievements, being less reported, unlike distressful depressive episodes.

Cyclothymia is described like a history of hypomanic episodes, alternating with episodes of depression, which do not meet diagnosis criteria for major depressive episodes. A low degree of mood cycling does exist, which is observed as a personality trait and is interfering with functioning of the individual.

Bipolar disorder NOS (not otherwise specified) is the diagnosis established when the disorder is not meeting the criteria for a specific subtype (6).

**DIAGNOSIS**

Signs and symptoms of bipolar disorder include abnormally elevated (manic or hypomanic) mood estates which impair
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normal functions of daily life. Numerous cases experience also depressive episodes, although not all. A test suitable for the diagnosis does not exist, and the diagnosis may be difficult to establish, even for the psychiatric specialists. It is also hard to differentiate the depression found in the bipolar disorder, from the pure unipolar depression. An earlier age of onset is often predicting depression as the first few episodes. Since bipolar diagnosis needs a manic or hypomanic episode, many bipolar patients are first diagnosed and treated as having major depression (7).

Mania is the characteristic feature of the bipolar disorder, being a period of elevated or irritable mood, which can take the form of euphoria and is lasting at least one week. Patients usually have an increase in energy and a decreased need for sleep (most of them need just three or four hours of sleep per night). Some can go days without sleeping. Usual symptoms are pressured speech with the feeling of racing thoughts. Attention is affected, and the individual is easily distracted. Rational capacities may be impaired and the subjects may be engaged in risky behaviors, which otherwise are not characteristic for them. They may experience alcohol, cocaine or other stimulants, or sleeping pills abuse. The behavior may be aggressive, intolerant or intrusive. They may feel unstoppable, or “chosen” and “in a special mission”, or may have another delusional ideas. Hyper sexuality may appear. At extreme, a manic estate can manifest psychosis, a break with reality, the process of thinking being affected together with the mood; sometimes this may lead to violent behaviors. Manic states may induce severe anxiety and irritability, or euphoria and grandiose ideas. Specific rating scales can measure the severity of the manic symptoms. Sleep disturbances, psychomotor and appetite changes may announce the onset of a manic episode, two or three weeks before (8).

Hypomania is a mild to moderate state of elevated mood, manifested by optimism, pressure of speech and activity and a reduced need for sleep. Unlike mania, most of the times hypomania does not interfere with normal functioning of the subject. People with hypomania are usually more productive, while manic subjects show attention troubles, which are impairing daily activities. Hypomanic subjects do not have delusions or hallucinations. Because it generally generates a state of well-being, hypomania is rarely reported as a pathologic condition. Only when depression is accompanying it, or if the mood changes are uncontrollable, hypomania may lead to search for specialized assistance. Untreated, a hypomanic episode may last from a few days to several weeks. Usually, symptoms may last a few weeks, up to a few months (9).

The depressive phase of bipolar disorder appears as persistent feeling of sadness, anxiety, guilt, anger, isolation or hopelessness. Disturbances of sleep and appetite are common, as well as: fatigue and lack of interest for enjoyable activities, decrease of concentration capacity, apathy, depersonalization, loss of interest in sexual activity, social anxiety, irritability, lack of motivation and morbid, suicidal thoughts. In severe cases psychosis may appear, known as severe bipolar depression with psychotic features. Psychotic symptoms are represented by usually unpleasant delusions or more rare, hallucinations. A severe depressive episode may last from two weeks, up to more than six months, if untreated (10).

Mixed affective episode is a condition in which symptoms of mania and depression occur simultaneously. Classical examples are weeping during mania and racing
thoughts during a depression phase. Mixed episodes are the most dangerous of the bipolar phases, since during this; the risk of suicide attempts greatly increases (5).

The later diagnosis of bipolar disorder may be preceded by different pathologic conditions developed during childhood, such as mood abnormalities, major depressive condition and ADHD (attention deficit hyperactivity disorder) (11).

Bipolar disorder should be differentiated from other mental disorders which do manifest similar symptoms, like schizophrenia, attention deficit hyperactivity disorder (ADHD) and borderline personality (12).

Bipolar disorder diagnosis is officially defined such that anyone who has a history of hypomania and depression receives this diagnosis, whatever their functioning and vulnerability are. This is considered „an ethical and methodological issue”, as long as no one is considered as being recovered from bipolar disorder, only in remission, according to official criteria. This situation is delicate, since brief hypomanic episodes are widespread in population and not associated with any dysfunction (13).

THERAPY

Several medications are used in the treatment of bipolar disorder. Lithium is effective in the therapy of acute manic episodes and in preventing manic relapses; it is also decreasing the risk of suicide and self-harm in bipolar disorder (14). Sodium valproate, which was initially used as anticonvulsant, is now an usually prescribed drug, effective in treating manic episodes (15).

Lamotrigine is to a certain degree, effective in the treatment of the bipolar depression (16). According to the severity of the disease, anticonvulsants can be used in combination with lithium, or alone.

Antipsychotics are used in the therapy of mania, although the long term effects are not clear. Olanzapine is used for prevention of relapses, even if it is not as effective as lithium.

Antidepressants showed no higher efficacy than that of the mood stabilizers. Benzodiazepines are used as adjuvants to medications.

Psychotherapy is targeting the alleviation of main symptoms, recognition of relapse risk and maintenance of remission. Psychoeducation and cognitive behavioral therapy are efficient in preventing relapses (17).

RECOVERY AND RECURRENCE

Studies showed that 50 % of hospitalized (which means most severe cases) had full recovery in six weeks, and 98 % in two years. In two years, 72 % had symptomatic recovery (lack of all symptoms) and 43 % functional recovery (prior occupational and living status). Nevertheless, 40 % experienced a new episode within two years of syndrome recovery and 19 % evolved without recovery (18).

REFERENCES

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ORAL APIXABAN FOR THE TREATMENT OF ACUTE VENOUS THROMBOEMBOLISM

Apixaban, an orally administered factor Xa inhibitor, may be, according to a recent study, an alternative to the standard treatment of venous thromboembolism. In this study, double-blind, randomized, was compared apixaban (at a dose of 10 mg x 2/day 7 days followed by 5 mg x 2/day 6 months) with conventional therapy (subcutaneous enoxaparin followed by warfarin) in 5395 patients diagnosed with acute venous thromboembolism. Apixaban proved noninferior to conventional therapy (p < 0.001). Major bleeding occurred in 0.6% of patients receiving apixaban and 1.8% of those who received conventional treatment. Rates of other adverse effects were similar in the 2 groups. The results of next studies will provide data on the safety and efficiency of administration to selected groups of underweight patients with cancer or with a creatinine clearance below 50ml/min. (Agnelli G, Buller HR, Cohen A, et al., Oral Apixaban for the treatment of acute venous thromboembolism, N Engl J Med 2013; 369: 799-808)