

## METABOLIC SYNDROME - THE CONSEQUENCE OF LIFELONG TREATMENT OF BIPOLAR AFFECTIVE DISORDER

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### SUMMARY

Mood disturbances are characteristic and dominant feature of Mood disorders. Bipolar Affective Disorder (BAD) is a mood disorder which occurs equally in both sexes. BAD may occur in co morbidity with other mental diseases and disorders such as: Anorexia Nervosa, Bulimia Nervosa, Attention Deficit, Panic Disorder and Social Phobia. However, medical disorders (one or more) can also coexist with BAD. Metabolic syndrome is a combination of metabolic disorders that increase the risk of developing cardiovascular disease.

A 61-year old female patient has been receiving continuous and systematic psychiatric treatment for Bipolar Affective Disorder for the last 39 years. The first episode was a depressive one and it occurred after a child delivery. Seventeen years ago the patient developed diabetes (diabetes type II), and twelve years ago arterial hypertension was diagnosed. High cholesterol and triglyceride levels as well as weight gain were objective findings. During the last nine years she has been treated for lower leg ulcer. Since metabolic syndrome includes abdominal obesity, hypertension, diabetes mellitus, increased cholesterol and serum triglyceride levels, the aforesaid patient can be diagnosed with Metabolic Syndrome.

When treating Bipolar Affective Disorder, the antipsychotic drug choice should be careful and aware of its side-effects in order to avoid the development or aggravation of metabolic syndrome.

**Key words:** bipolar affective disorder - metabolic syndrome

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### INTRODUCTION

Bipolar Affective Disorder is one of the most frequent and severe mental illnesses (among 10 most prevalent mental illnesses in the world) which leads to disability of the affected person thus causing his/her life-long dysfunction (Miklowitz et al. 1997).

The results of some researches show that people affected by Bipolar Affective Disorder have impaired life-quality, that their health life period is 12 years, and working life 9 years shorter. Moreover, they lose, on average, 9 years in life expectancy while divorce rates and employment problems of such patients are two times higher (Coryell et al. 1993, Scott 1995, Babić et al. 2010).

The female patient affected by Bipolar Affective Disorder described in this article is married and despite the illness, was regularly employed and retired on pension.

Metabolic syndrome includes symptoms such as dysfunction in fat regulation, insulin resistance, hypertension and obesity, therefore patients with developed Metabolic Syndrome are more likely to develop cardiovascular diseases and diabetes type II.

World Health Organisation (WHO, 1999) defines Metabolic Syndrome with the presence of the following:

diabetes mellitus, impaired glucose tolerance, insulin resistance or elevated fasting blood glucose level (5.6-6.0 mmol/L) accompanied by two or more of the following criteria: Blood pressure  $\geq 140/90$  mmHg, Dyslipidemia: serum triglyceride (TG):  $\geq 1.695$  mmol/L and serum HDL cholesterol (HDL-C)  $\leq 0.9$  mmol/L (men),  $\leq 1.0$  mmol/L (women), Abdominal Obesity: waist to hip ratio  $>0.90$  (men);  $>0.85$  (women), and/or BMI  $>30$  kg/m<sup>2</sup>, and Microalbuminuria (WHO 1999, Konzumplik et al. 2010).

As to the described patient, Metabolic Syndrome had existed long time before it was diagnosed as a separate entity, and at that time the patient had been treated for diabetes and hypertension.

### CASE REPORT

A 61-year old female patient, married, retired, has received psychiatric treatment for Bipolar Affective Disorder for the last 39 years and has been hospitalised seven times. Despite such a severe mental illness, she has retired on pension and during the remission periods her social functioning and working ability were regulated. Unlimited family support as well as the patient's compliance with treatment had great influence on good treatment outcome.

During her life-long treatment the patient has had only three different psychiatrists, and was assisted by the same psychiatrist for 25 years until his retirement five years ago. Since then, i.e. for the last five years the patient has been seeing a new doctor.

### **From anamnesis**

The patient was among the youngest and the only female child and grew up in a traditional numerous patriarchal family. As a young girl, and after a short relationship, she gave birth to a female child. However, her family was not a supportive one so she soon left parental home and moved to another town where she did not have any accommodation and was therefore placed in a welfare institution. Soon afterwards mental disorders began to appear.

### **First treatment**

At the age of 22 the first depressive episode developed (F 32.2) and the patient was admitted to a psychiatric hospital for the first time. Family heredity was positive (mother's sister – depression; mother's first grade cousin – BAD). Further information and medical records are not available on this stage of illness and treatment.

Soon after the hospital discharge, the patient found employment and temporary accommodation. She regularly attended psychiatric check-ups and took medications, her occupational functioning was adequate and she took good care of herself and her daughter.

Twenty-two months after the first hospitalisation the patient experienced an increase in energy and diminished need for sleep. She offered to do extended work shifts and took loans and made money transactions which she could not afford. Hospitalisation was advised and the manic episode supported the diagnosis of BAD. A mood stabilizer was introduced (lithium carbonate, stable dose- 900 mg/day) as well as haloperidol (5 mg/day).

After the second hospitalisation she met her present husband, got married and had another child. Her husband provided persistent support and showed understanding for her health problems. She took good care of both children.

Depressive symptoms and impaired social functioning caused the third hospitalisation.

The fourth hospitalisation revealed a significant loss in weight due to a manic episode which lasted for over a month. Since laboratory workup revealed an elevated glucose concentration (13 mmol/L), a diabetologist recommended a diet regime and prescribed suitable medication. The patient complied with treatment by following the appropriate diet and taking antidiabetics and succeeded in regulating diabetes problems successfully so sugar blood levels returned within referential values (7-11 mmol/L).

The patient was again hospitalised nine months after the fourth hospitalisation due to a depressive episode and attempted suicide by overdosing with medication. She spent four days in the intensive care unit and was then transferred to the department of psychiatry where she received inpatient care. During the hospitalisation remission was established and it was maintained for the next four years during which the patient regularly continued the treatment on an outpatient basis.

She visited a cardiologist with complaints of subjective physical symptoms (breathing difficulties, occasional headaches, chest pain) and essential hypertension was diagnosed. Antihypertensive drugs were introduced and blood pressure values returned within referential values (160/95 – 180/110). The patient has been under treatment for hypertension for the last 12 years. The patient's cholesterol and triglyceride levels were elevated (7.2 mmol/L; 3.1 mmol/L) and she was overweight (ca. 90 kg).

Considering her long-life disease and treatment, the patient recognized and managed hypomanic and manic episodes more easily. Such episodes were always accompanied by characteristic symptoms such as: diminished need for sleep, excessive house cleaning, wish to help others (she placed advertisements offering free house cleaning services), excessive need for walking and constant agitation. During one of the aforesaid episodes, occurred nine years ago, calf ulcer appeared and still has not been completely healed. Possible risk factors for development of skin ulcer in this patient were diabetes, hypertension and overweight. Dermatologic interventions (gangrenous tissue removal and attempts of tissue reepithelisation) were the reason of two short hospitalisations.

### **Current treatment**

The patient was treated by the same psychiatrist for 25 years but after his retirement she did not attend psychiatrist consultations for few months. She has been seeing her present psychiatrist for the last five years. At the very first visit the new psychiatrist suggested to review and modify her life-long therapy and the patient readily accepted although the introduction of new psycho pharmacotherapy required frequent laboratory blood testing (due to possible side-effects). Laboratory workup revealed the following: fasting glucose level: 8.3 mmol/L, serum triglyceride: 2.8 mmol/L, serum HDL: 1.48 mmol, blood pressure was 175/100 mm Hg. Moreover, waist circumference was measured (96 cm) due to the specific presence of excessive fat tissue in and around the abdomen. The aforesaid values as well as excessive weight (103 kg, BMI=32.5) indicated the presence of the metabolic syndrome.

Carbamazepine (titrated to a stable dose of 600 mg/day), alprazolam (1.5 mg/day) and risperidone (2 mg/day) were introduced and the patient responded well to such therapy. Laboratory values remained unchanged

and metabolic syndrome symptoms persisted. The patient followed recommendations regarding diabetes diet and regular physical exercise. Further laboratory analyses showed lower values compared to the previous ones, but they were still not within the reference range (fasting glucose level: 7.4 mmol/L, serum triglyceride: 2.1 mmol/L, serum HDL: 1.33 mmol). Although blood pressure value was lowered to 165/95 mm Hg, waist circumference reduced to 92 cm, and the patient lost 6 kg, the metabolic syndrome still persisted.

After a year of outpatient treatment and stable remission the patient experienced a stressful family situation which caused another depressive episode. Laboratory analyses revealed low serum values of carbamazepine and it was agreed to replace the mood stabilizer.

A combination of medications (lamotrigine 150 mg/day, risperidone 2 mg/day) has ensured a stable remission for the last three years. The patient has been compliant with treatment and has regularly attended the sessions with the psychiatrist. She has also introduced significant changes in her lifestyle (more physical exercise and reduction of carbohydrate and fat) thus reducing her body mass (96 kg, BMI 30.3). Fasting glucose level is now: 7.2 mmol/L, serum triglyceride: 21.9 mmol/L and serum HDL: 1.31 mmol. Blood pressure value is around 165/95 mm Hg and waist circumference has also been reduced to 89 cm. Although metabolic syndrome parameters to be monitored have showed certain improvement, metabolic syndrome criteria are still present.

During the five-year long collaboration with the patient's "new" psychiatrist, not only has her medication been reviewed and partially changed, but metabolic syndrome has also been diagnosed.

## DISCUSSION

Bipolar Affective Disorder is a chronic mental disorder. According to current diagnosis criteria (DSM IV and MKB 10 classification) Bipolar Affective Disorder is not a unique entity, but it can be subdivided into Bipolar I Disorder (occurrence of one or more manic or mixed episodes); Bipolar II Disorder (hypomania and recurrent major depressive episode), cyclothymia and spectrum of bipolar subtypes which continues to widen. BAD is a severe heritable disorder with a 75-90% recidivism rate which requires lifelong treatment.

Women are more likely to develop co morbidity with other psychiatric or somatic diseases (anxiety, obesity, migraine, thyroid disease), male co morbidity includes psychoactive substance abuse and personality disorder, while co morbidity among geriatric population results in development of organic brain dysfunctions.

Medical disorders that coexist with Bipolar Affective Disorder are cardiovascular diseases, diabetes,

obesity, thyroid disease, high blood pressure, high blood fat levels (Krishnan 2005). The aforesaid co morbidity is also present in the patient discussed herein.

The lifetime prevalence of BAD has been estimated at 0.4 to 1.6%. First-degree biological relatives of individuals with Bipolar Disorder have elevated rate of developing BD (our patient's heredity was positive). The most frequent onset period is adolescence or early adulthood although it may occur at any age. All forms of the aforesaid disorder are chronic diseases with a considerable morbidity and mortality (Angst et al. 2002).

The first episode developed by the patient discussed herein was a depressive episode which occurred after traumatic experience (extramarital pregnancy without any family support) and which caused hospitalisation. At further stage of illness course, during a depressive episode, the patient attempted suicide (Schneider 2007, Arslan 2009).

During her lifelong treatment the patient was compliant with treatment and was fully supported by her family. She was regularly employed and rarely used sick-leave until the retirement.

Due to medical disorders which developed subsequently she was also cured by an endocrinologist, cardiologist and dermatologist. According to new scientific findings, the aforesaid medical disorders indicate the presence of metabolic syndrome. American Association NCEP/ATP III has provided criteria and recommendations on metabolic syndrome and the latter have been observed in diagnosing and treating the aforesaid syndrome. Metabolic syndrome is a combination of metabolic abnormalities that increase the risk of developing cardiovascular disease (Freiberg 2009). Literature on this topic reveals that early detection of metabolic syndrome or its single components may have great clinical importance for some patients affected by mental disorders, including BAD (Jakovljević 2007, Babić et al. 2007, Vuksan et al. 2007).

In addition to the clinical recognition of metabolic syndrome, some of the literature displays critical views which debate the reality of metabolic syndrome as a specific clinical entity (Bakker et al. 2007).

The treatment of mentally ill patients, including those affected by BAP with a developed metabolic syndrome, requires a critical choice of antipsychotics, as well as the application of adequate preventive measures and continuous patient education. The choice of a single antipsychotic medication diminishes the risk of metabolic syndrome. Patients treated with antipsychotic monotherapy seem to have lower rate metabolic syndrome and markers of insulin resistance (triglyceride / HDL cholesterol ratio > 3.5) (Correll et al. 2007) than those treated with a combination of antipsychotics.

## CONCLUSION

Mental illness in co morbidity with additional medical disorders requires greater psychiatrist involvement in the management of patient, but also a firm patient's commitment. Compliance with treatment, patient's family support and appropriate medication are factors which increase favourable remission rate of basic disease. The case described herein showed that each aggravation of psychological state caused the aggravation of certain medical condition, which proves that mental and physical are actually a single system not to be separated from each other. The balance of mind and body is a prerequisite for healthy condition.

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