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Case report / Prikaz slučaja

PSYCHIATRIC COMPLICATIONS DUE TO UNDERLYING CUSHING'S SYNDROME: A CASE REPORT

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Summary

Cushing's syndrome is a multisystem disorder, which can present with a spectrum of manifestations. It might be particularly hard to detect the disorder in early stages if psychiatric symptoms are also presenting features. Major depression, mania, anxiety, and neurocognitive impairment are the most important clinical abnormalities found in these patients. Cushing's syndrome should always be considered as a cause of organic psychiatric illness, especially if there are other features like adiposity, hirsutism, glucose intolerance and hypertension present. A prompt diagnosis and treatment is important to decrease morbidity and mortality. In this article, we discuss a case of a young female patient presenting with a variety of psychiatric symptoms - anxiety, panic attacks, accompanied by fear of suffocation, tightening in the throat, sweating, racing heart, dizziness, mood swings, psychotic symptoms with auditory hallucinations and neurocognitive dysfunction, associated with iatrogenic Cushing's syndrome.

Key words: iatrogenic Cushing's syndrome, psychiatric symptoms, anxiety, panic attacks, depression, euphoria, psychotic decompensation

INTRODUCTION

Cushing's syndrome affects nearly all systems of the human body. The typical developed clinical picture is characterised by progressive central adiposity, hirsutism, glucose intolerance, hypercholesterolemia, hypertension, atherosclerosis, immunosuppression, stress fractures, myopathy, and dermopathy. Although this classical presentation is easy to recognize in

clinical practice, more subtle manifestations are difficult to diagnose, particularly if psychiatric symptoms are present at the beginning.

Until recently, the link between neuropsychiatric symptoms and endocrine diseases was not investigated adequately. Over the latest decades, attention has been focused on the effect of hormonal factors on the development of psychiatric symptoms such as mood disorders (euphoria and anxiety disorders), cognitive disorders, psychotic decompensation, and suicidal behavior. The outcome of such complex association is reflected in manifesting the same behavioral disturbances in different endocrine disorders, most frequently in the form of depressive mood and cognitive impairments [1, 2, 3]. Psychiatric and neurocognitive disorders usually improve when patient reaches eucortisolaemia.

Long-term follow-up and careful periodical investigation of psychiatric and neurocognitive symptoms should always be performed in patients with Cushing's syndrome both in the active phase and after disease remission.

THE CASE REPORT

A 33- year-old female was admitted to the Psychiatric Clinic due to panic attacks and severe anxiety, fear of suffocation, throat tightness, insomnia, mood swings with occasional psychotic decompensation, leg swelling and secondary amenorrhoea.

Symptoms began 12 years ago, after her husband's death. Prior to his death, her husband suggested her to commit suicide. A year after, she started feeling tingling sensations in her head, tongue, shoulders, and, later, the sensation has developed into fear, panic, sweating, racing heartbeats, dizziness and occasional auditory hallucinations. Only then, she had visited a psychiatrist

who prescribed her sulpiride and alprazolam. She was taking higher than prescribed dosages of alprazolam, due to her mood swings. These sensations were taking place alternately in irregular intervals; however, there were times when she was feeling well. Panic attacks used to emerge unexpectedly, with varying frequency and intensity. A year prior to admission, panic attacks have become daily, accompanied by feeling of suffocation. Due to daily aggravation of suffocation feeling, she turned to the emergency department (ED) physician. She was diagnosed with bronchial asthma - without any further diagnostic tests – and was prescribed intravenous corticosteroids (methylprednisolone). The feeling of suffocation would stop after drug admission, but it would always get back, and the patient used to go to the ED every day. Over that year, she received 300 methylprednisolone ampoules along with diazepam ampoules. Several months prior to her admission to our Clinic, she started noticing body weight increase, leg swelling, absent periods, insomnia, and increasingly frequent panic attacks.

Upon the admission to our Clinic, she was diagnosed with panic disorder with elements of psychotic decompensation, personality disorder and psychoorganic syndrome according to the WHO's 10th Revision of International Classification of Diseases (ICD 10) [4].

Laboratory test have shown elevated levels of cholesterol (5.74 mmol/L, low risk <5.20mmol/L; medium risk 5.20-6.20mmol/L; high risk > 6.20mmol/L), triglycerides (2.90 mmol/L, normal range 1.70 – 2.26 mmol/L), white blood cells and immeasurably low cortisol levels (27.9 nmol/L). Other biochemical parameters were all within normal range. The cortisol profile also showed immeasurably low levels. ACTH level was within the reference ranges (1.81 pmol/L), as well as glycaemia and electrolyte levels respectively. Her pituitary gland MRI as well as osteodensitometry was normal.

Endocrinologist administered hydrocortisone (30 mg pro die). She had also received selective serotonin re-uptake inhibitors (SSRIs) (Escitalopram 20 mg pro die), anxiolytic (Alprazolam 3 mg pro die) and antipsychotic (olanzapine, 10mg a day). Three weeks upon drug administration, drastic reversal of psychiatric and somatic symptoms took place. Her panic attacks were substantially reduced, she became emotionally stable and psychotic symptoms ceased. Swelling of the legs receded, menstrual cycle normalized, and she started to lose weight.

Psychological exploration showed that the patient was emotionally unstable, sensitive about disrespect and rejection, without self-criticism, highly suggestible, with intelligence well below the average. She had also demonstrated attention and concentration deficit, visual - spatial agnosia and motor coordination deficit.

The Rorschach test revealed that, in provocative situations, the patient would retreat into herself, was unable to think, was undetermined, emotionally restricted, and out of control, with organic disinhibition, which would aggravate the intrapersonal and interpersonal communication.

In relation to the impulses, she experiences out of her control, there might be respective feelings of helplessness, hopelessness, and guilt, which would all indicate depression and suicidal thoughts.

DISCUSSION

The aforementioned case describes in brief a female patient whose disorder started one year after a stressful event. It manifested by severe anxiety, panic attacks, throat tightness, insomnia, mood swings and occasional psychotic symptoms. One year prior to her hospitalization, panic attacks were on daily basis concurring with the daily administration of high dosages of

corticosteroids. The latter led to hypothalamic-pituitary-adrenal axis (HPA axis) suppression, immeasurably low cortisol levels and consequent weight gain and missing periods. Corticosteroids and anxiolytics reversed the symptoms temporarily, but symptoms always resumed couple of days, weeks, months... thereafter.

Psychiatric symptoms are very frequent, and, in many cases, they are associated with endocrine disorders. Many studies with patients suffering from Cushing's diseases have reported psychiatric disorders in more than 50 percent of the cases, and the emergence of psychosis and/or suicidal actions, sleep disorders, anxiety and hypomania in variable percentages depending on the study [1, 2, 3, 5-10]. The study published in 2003 revealed that psychiatric patients showing subtle abnormalities of endocrine function belong to the same continuum of patients suffering from severe manifestations of the same endocrine disease [11]. As a result of these very complex associations between hormonal axis and behavioral symptoms – one must be cautious in concluding what comes first [11]. HPA axis hypoactivity advances during the conditions of chronic stress, stress-related health problems such as posttraumatic stress disorder (PTSD), chronic fatigue and burnout syndrome, where the original HPA axis hyperactivity gradually evolves into hypoactivity [12, 13].

HPA axis disorder is associated with affective disorders. Both acute and chronic stress have been recognized as etiological cause of depression. Further, depression can influence HPA axis function considering that this axis plays a key role in neuroendocrine response to stress. In recent years, the phenomenon of the HPA axis hypoactivity in stress-induced diseases has been more frequently named hypocortisolism – it has been present for the last 10 to 15 years [13, 14].

Clinical signs developing into euphoria and depression, according to some authors, indicate that mood disorders vary depending on the disease stage. Euphoria and increased motor activity are very frequent in the early stage of the Cushing's syndrome, which has been presented in this case, whereas depression, irritability, attention and memory deficit and anxiety emerge in a later stage. However, the relation between higher levels of depression and hypercortisolism is not clear [15]. According to one hypothesis, the changes in cortisol levels lead to reduced release of serotonin and increased release of dopamine [16].

Psychological evaluation of our patient revealed attention and concentration deficit, visual - spatial agnosia, visual perception as well as motor coordination deficit. Neuropsychological symptoms of Cushing's syndrome are associated with the elevated glucocorticoid signaling via glucocorticoid receptors. Memory deficits are explained by neocortical and hippocampal dysfunction e.g., the dysfunction of the brain sections with the abundance of glucocorticoid receptors [16].

Psychiatric symptoms in Cushing's syndrome are associated with elevated levels of glucocorticoid signaling via glucocorticoid receptors. Both glucocorticoid and mineralocorticoid receptors regulate cortisol levels in blood and, consequently, their effects in the body. For that reason, psychiatric symptoms can be refractory to psychotropic treatment if hyper/hypocortisolism is left untreated. Therefore, depression in these patients is successfully treated by medicines that normalize cortisol level [17, 18]. In the outpatient unit, one month upon cortisone substitution, cortisol level increased (85 nmol/l), the patient's mood improved, she became emotionally more stabile, whereas panic attacks declined in number.

CONCLUSION

It is not rare to find disorders of HPA axis in psychiatric patients. Hence, it is challenging to distinguish between “psychiatric” patients suffering from endocrine disorder from those with mild Cushing’s syndrome. Early diagnosing along with an appropriate pharmacological treatment, can considerably reduce the mortality of these patients.

Consent

Written informed consent was obtained from the patient for publication of this case report.

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Sažetak

PSIHIJATRIJSKE KOMPLIKACIJE U OSNOVI CUSHINGOVOG SINDROMA: PRIKAZ SLUČAJA

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Cushingov sindrom je multisistemska poremećaj, koji se može ispoljiti sa spektrom manifestacija. Može biti osobito teško otkriti poremećaj u ranom stadiju ako se bolest manifestuje psihijatrijskim simptomima. Major depresija, manija, anksioznost i neurokognitivni poremećaji predstavljaju najznačajnije kliničke poremećaje koji se mogu naći u tih bolesnika. Cushingov sindrom treba uvijek istražiti kao uzrok organske psihijatrijske bolesti, osobito ako postoje i drugi simptomi poput pretilosti, dlakavosti, intolerancije na glukozu i povišenog krvnog tlaka. Pravovremena dijagnoza i liječenje su važni za smanjenje morbiditeta i mortaliteta ovih bolesnika. U ovom članku ćemo prezentirati slučaj bolesnice kod koje je spektar psihijatrijskih simptoma- anksioznost, napadi panike praćeni strahom od gusenja, stezanje u grlu, znojenje, ubrzani rad srca, vrtoglavica, depresija i euforija, psihotična dekompenzacija s auditivnim halucinacijama i neurokognitivni poremećaji, bio povezan s jatrogenim Cushingovim sindromom.

Ključne riječi: jatrogeni Cushingov sindrom, psihijatrijski simptomi, anksioznost, napadi panike, depresija, euforija, psihotična dekompenzacija