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PROLONGED AND UNTREATED HYPOTHYROIDISM AS ONE OF POSSIBLE CAUSES OF ACUTE PSYCHOTIC EPISODE

Abstract: Psychosis is a set of symptoms that lead to contact disorders or even cessation of contact with reality. It can be in the form of disorders of perception, emotions, thoughts, and behavior. Psychosis has many causes, and one of them is hypothyroidism. Thyroxin is important for the global function of brain activity, cholinergic activity in the frontal cortex and hippocampus increases significantly in its presence. The diagnosis of psychotic episodes is made on the basis of autoanamnesis and heteroanamnesis, as well as psychiatric examination. The presence of: positive syndrome, disorganization and negative syndrome. After the diagnosis of a psychotic disorder, antipsychotics are included in the therapy, and upon arrival, the findings that verify hypothyroidism, include thyroxin in the therapy. The therapeutic response is achieved after a few days or a week. In patients with an acute psychosis, and especially in those with a positive personal and family history of hypothyroidism, one should think in the direction of an unrecognized endocrine disease.

Key words: psychosis, psychotic episode, hypothyroidism

Introduction

Psychosis is a set of symptoms that lead to the patient's alienation from reality (1). It is reflected in disturbed contact or even cessation of contact with reality, which is manifested through a deep disturbance of perception, emotions, thoughts or behavior (2). Psychosis has many causes. The rough division could be into inorganic (or primary), organic (or secondary) and psychoses caused by the use of psychoactive substances (1). Inorganic would include schizophrenia and bipolar disorder, and or-

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ganic all conditions that lead to homeostatic disorders in the brain, including endocrine disorders. Hypothyroidism is a decreased secretion of thyroid hormones. Causes of hypothyroidism can be congenital (atherosis, thyroid hemiagenesis) or acquired. The most common cause of hypothyroidism is Hashimoto's thyroiditis with a prevalence of 3% in the general population (3). Psychotic symptoms including paranoid ideas, visual and auditory hallucinations were previously considered common symptoms of hypothyroidism, while today it is known that these symptoms occur in about 5% of patients with hypothyroidism (4). These symptoms usually appear after the appearance of physical symptoms, i.e. a few months to several years from the beginning of hypothyroidism.

Diagnosis

The diagnosis of a psychotic episode is made on the basis of autoanamnesis and heteroanamnesis, as well as a psychiatric examination. Mental disorders most commonly present in patients with suspected psychotic episode are presence of:

I positive syndrome

- a) hallucinations – most often auditory, visual, tactile and olfactory.
- b) lunatic ideas – persecution (the impression that someone is following, observing the patient), influence (that the patient's behavior is under someone's control) and relationships (messages from the environment sent only to the patient).

II disorganization

- a) speech disorder as the most conspicuous symptom, impoverished speech, thought flow disorders, neologisms, echolalitis.
- b) disorganization of behavior in the domain of motor skills and social interaction where symptoms can be present from catatonic stiffness, through agitation all the way to social distancing and neglect of hygiene.
- c) affective mismatch in terms of inadequate reaction, ideo-affective dissociation.

III negative syndrome

- a) alogia – difficulties in communication as a consequence of thinking disorders.
- b) anhedonia – a feeling of emotional emptiness, difficulty finding pleasure.
- c) abulia / hypobulia – complete or partial loss of will which is manifested by lack of initiative, passivity, decreased general functioning.
- d) attention deficit disorder (2).

After the suspicion of a currently present psychotic episode, and during the hospitalization of the patient, laboratory diagnostics is performed: determination of

complete blood count, biochemistry, urinalysis with toxicological findings (which exclude the abuse of psychoactive substances). In patients with a positive personal history of hypothyroidism (thyroiditis, radioiodine therapy), in those in whom inspection and palpation show changes in the neck (presence of goiter, scar from surgery) or inspection of medical records (endocrinologist reports on the treatment of hypothyroidism) it is necessary to determine the level of TSH, FT4, T4, T3. If the results indicate a high level of TSH with reduced thyroid hormones in consultation with an endocrinologist, it is necessary to include / correct thyroxine therapy and monitor the potential maintenance / withdrawal of psychotic symptoms.

It is especially important to be careful and think about this diagnosis in the elderly population because certain somatic symptoms of hypothyroidism can be presented as a normal aging process and be unrecognized. In such persons, it has been described in the literature that the symptoms of psychosis appear first, not because it is really so, but because the development of hypothyroidism and numerous previous symptoms are not recognized or interpreted as an aging process and the expected consequence (5,6).

Treatment

Patients with an acute psychotic episode are hospitalized for a period of 4 to 6 weeks, after which, in case of need, treatment can be continued in the conditions of a daily hospital with the aim of maintaining the stability of remission. During hospitalization, in parallel with the examination, the patients are initially treated with thyroxin or a combination of psychopharmaceutical (antipsychotics + thyroxin) and psycho/sociotherapy.

Internal medicine therapy used to correct endocrine imbalance represents the basis of treatment, and very soon after starting to take thyroxin, relief occurs psychotic symptoms.

Upon arrival of laboratory results in case of verified hypothyroidism (decreased FT4 with elevated TSH) in addition to psychopharmaceutical, patients are also prescribed thyroxin. Daily dose of thyroxin is optimized according to body weight 1.6 mcg /kg/day, with TSH measurement after 4-8 weeks (7). Preferably, the TSH level is up to 2.5 mIU /L (8).

As soon as the symptoms of psychosis are noticed, it is necessary to start treatment with antipsychotics even before proving endocrine disbalance. Additionally antipsychotics can be used as an adjunct therapy thyroxin, with the aim of achieving remission faster. However, the last review of the literature calls into question whether there is a scientific reason for such an approach (although it does not exclude the possibility given the small number of papers with topic) (9). So far, treatment with low initial doses is recommended second-generation antipsychotics (except clozapin, which has severe side effects that cause is recommended as the last line).

National guide for good clinical practice for the diagnosis and treatment of schizophrenia in its work "Acute phase therapy" provides guidance and analysis of antipsychotics based on different international guides, and in accordance with registered antipsychotics in Serbia, so it can serve as a guide for clinicians in choosing a drug for acute psychosis due to hypothyroidism. Antipsychotics of the second generation (atypical antipsychotics) is given priority over those of the first generation (classical antipsychotics) because they do not lead to extrapyramidal side effects (10). On the other hand, their use should be cautious, because their use is accompanied by the appearance of side effects, primarily in terms of the development of metabolic syndrome. Currently registered antipsychotics of the second-generation in the Republic of Serbia are: clozapine, risperidone, olanzapine, sertindole, quetiapine, ziprasidone, amylsupride and paliperidone.

Of the classic antipsychotics, which can be used as alternatives, registered in the Republic of Serbia are as follows: chlorpromazine, fluphenazine, haloperidol, levopromazine, sulphiride and cyclopentixol (11). Regardless of the choice of antipsychotics, it is always necessary to find balance in terms of the application of the minimum effective doses that reduce the risk of side effects and monitor potential occurrence of the same.

Literature data of the frequency of psychotic episodes resulting from prolonged and untreated hypothyroidism

Thyroxin is important for the global function of brain activity, and cholinergic activity in frontal cortex and hippocampus significantly increases in its presence. Thyroid dysfunction most likely leads to changes in cholinergic activity, global perfusion and global glucose metabolism in the CNS (12). Recent results of PET scanner of people with hypothyroidism have shown that there is a reduction in untreated hypothyroidism cerebral blood flow as well as decreased glucose metabolism (13).

The most common cause of hypothyroidism in the general population is Hashimoto's thyroiditis with prevalence of 3% in the general population. The peak incidence is in the fifth decade of life, and occurs 10-20 times more often in women than in males (3). The clinical presentation of hypothyroidism encompasses a wide range of mild symptoms such as: dry skin, constipation, hair loss, weight gain or depression; if the disease progresses and it is not treated for a very long time, it can cause myxedema, acute psychosis, acute mania and myxedema coma.

A causal link between thyroid disease and dysfunction of central nervous system was described in the late nineteenth century ("Report on Myxoedema", Clinical Society of London, 1888). After this description, clinicians began to publish case reports of patients with psychosis which was caused by prolonged unrecognized-untreated hypothyroidism. In 1949, Asher et al. published a paper describing 14 patients with

myxedema psychosis and hypothyroidism, of which 9 recovered only from application thyroxin replacement therapy (14). The hallucinations that occur in myxedema psychosis usually withdraw within a week after starting with thyroxin therapy. Psychosis has been described in the literature in persons with hyperthyroidism, but also it was described that hyperthyroidism was the cause of an acute psychotic episode, so clinicians should be careful when administering high doses of thyroxin because that sudden peak in thyroxin level in patients who had psychotic episodes may be trigger psychotic recurrence (15, 16).

In addition to psychotic symptoms, prolonged and untreated hypothyroidism can also be manifested other psychiatric disorders. Giunio-Zorkin and co-workers described a patient with mania as the first symptom of severe hypothyroidism (17). Hypothyroidism is a common comorbidity in patients with bipolar disorder, and patients with therapeutically resistant bipolar disorders have a higher incidence of hypothyroidism than the general population (18). In prospective cohort study conducted in Denmark in which patients with hypothyroidism were monitored, the results showed that patients with hypothyroidism are more likely to get sick and hospitalized at psychiatric clinics due to depression and bipolar disorder (19). Ueno and al. confirmed that psychotic disorders may occur before the physical manifestation of hypothyroidism or symptoms of hypothyroidism may not be pronounced in psychotic patients especially in the elderly population where the symptoms of hypothyroidism are attributed to the aging process (6).

Sancez et al. analyzed 27 cases from literature and they showed that period of reduction of psychosis can vary: from 4,4 days in patients who were on single thyroxin therapy; 6,25 days in patients who were treated with initially thyroxin and few days after with antipsychotic if there was need for it; 17.27 days was recovery in patients who was treated initially with antipsychotic and thyroxin (9). In all three groups of patients faster recovery was seen in mail than in female patients. This data suggests that antipsychotic drugs are not necessary in patients with acute psychosis that was caused by prolonged untreated hypothyroidism (9). This presumption would be wrong because of several reasons: 1) comparison between length of therapy and years of patient wasn't made; 2) response to therapy can vary and usually it is prolonged in elderly population than in younger people; 3) in all case reports there might be confounding factors that may impact on response to therapy; 4) authors pointed that one of limitation of their study is that they have analyzed 27 case reports in which decision on therapy could be under confounding factors that were not recognized and noticed (9). At this moment literature on this topic does not give clearly answer to question is antipsychotic necessary along with thyroxin. From analyzed case reports we can not find consensus about length of antipsychotic therapy. In every patient with this pathology who are initially treated with antipsychotic drugs those drugs should be gradually exclude.

Conclusion

Since changes in behavior and mental status can occur as a sign of untreated and prolonged hypothyroidism, regardless of the presence of its other clinical signs, it is very important that in patients with psychiatric diseases and manifestations, especially with acute ones, we must seek for its endocrine background. Therapeutic choice in patients with acute psychosis that occur as result from hypothyroidism or in combination with it, requires thyroxin treatment, and combination with antipsychotic is often needed, although the justification for such therapy is still not recommendation. After administration of thyroxin, and after reaching the reference values of FT4 and TSh, patients are transferred to a lower dose-maintenance therapy which is enough to control thyroid status in reference levels, by an endocrinologist. Initially administrated antipsychotics into the therapy are gradually reduced when we see withdrawal of the psychosis symptoms, and their final exclusion may be made with the continuous supervision of a psychiatrist.

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