Psychosis Related with Hashimoto Thyroiditis: a Case Report

ABSTRACT
Psychosis related with Hashimoto thyroiditis: a case report
Hashimoto’s thyroiditis is an autoimmune disease characterized with inflammation of the thyroid gland. Psychiatric symptoms frequently accompany Hashimoto’s thyroiditis. Major depression is the most common affective disorder with the prevalence of 33-43%. Psychotic disorders may accompany at 5% rate. In this case report; a patient, recently diagnosed with hypothyroidism and involved into a psychotic process due to his hypothyroidism, is discussed. The patient’s refusal of oral intake and lack of parenteral preparation of thyroxine in our country were the factors that made the treatment more complicated. The aim of this case report is to emphasize the importance of the routine laboratory examinations especially during the first admission to the hospital, and to underline difficulty of thyroid replacement therapy due to lack of preparation of parenteral thyroxine in our country in patients who do not or can not get medications orally.

Keywords: Anxiety disorders, psychiatric comorbidity, thyroid diseases

INTRODUCTION
Hashimoto thyroiditis is an endocrine disease with autoimmune origin, and it is characterized by inflammation of the thyroid gland (1).

Hashimoto thyroiditis is the most common cause in regions where there is no iodine deficiency. The most commonly encountered symptoms in hypothyroidism are fatigue, cold intolerance, dry skin, falling out of hair, menstrual disorders, and constipation. The most common signs may be listed as coarseness of the voice, bradycardia, edema without leaving impression, and decreased deep tendon reflexes (2).

Psychiatric complaints are not rare in hypothyroidism. Frequently, cognitive, affection and behavioral changes accompany this disease. The most commonly encountered psychiatric signs are mental slowness, difficulty in concentration, and mental disorders which may progress to dementia (3). Major depression is the most commonly encountered mood disorder with the rate of 33-43%, and it is followed by anxiety disorder with the rate of 20-33%. Psychotic disorders may be observed at 5%
in these patients (4). In the literature, cases with manic episodes related to primary hypothyroidism have been reported rarely (5,6).

Action mechanism of thyroid hormone diseases leading to psychiatric diseases is not clearly defined, yet. The brain has a special sensitivity to thyroid hormones, and it uses thyroid differently from other organs (7). Hormone receptors are located within nerve network along the nerves, and these receptors affect sequentially the neural activity. High concentrations of triiodothyronine (T3) receptors in amygdala and hippocampus, and effects of these receptors on neural activity emphasize importance of thyroid hormone in cognitive functions (8). Thyroid hormones and related functional deficits affect the brain differently at different time periods of life. Thyroid hormones play a role in both development of central nervous system and persistence of its homeostasis (9). In one of a few number of studies performed in effects of thyroxine (T4) on brain activities, it was shown that effects of T4 hormone on neurobehavioral effects might be related to hormonal effects on neurotransmitters. It was noted that increase in cerebral dopamine activity was directly correlated to increase in tyrosine hydroxylase activity in rats with hypothyroidism (10). On the other hand, decrease in brain tyrosine hydroxylase activity was shown in rats with hyperthyroidism (11). In hypothyroidism, as serum T4 level is decreased, intracerebral conversion of T4 to T3 is increased due to the decrease in type 2 deiodinase activity. Animal and human studies indicated that T3 decreased serotonin 1A (5-HT1A) receptor sensitivity presynaptically in the brainstem, whereas synthesis and release of 5HT were increased in the hippocampus. Increase in tyrosine hydrokinase activity in the brain leads to increase in dopamine level (12).

The background causes of manic episode development in hyperthyroidism are elevation of thyroid hormones, increased beta adrenergic sensitivity, and thus leading to elevation in catecholamine levels (13). High levels of serum free T4 (fT4) levels are observed concomitantly with anxiety disorders. It is accepted that thyrotropin releasing hormone has a prominent antidepressant efficacy (14). On the other hand, no proportional correlation has been defined between free T3 (fT3), thyroid stimulating hormone (TSH) levels, and anxiety disorders (15).

Psychosis related to hypothyroidism was first defined in the study of Asher (in 1949) (16). In that study, Asher defined the relationship between a subacute encephalopathy picture of “Myxedema Delusion” and hypothyroidism, and then reporting of other cases in the literature, this relationship has been frequently emphasized (17).

In this case presentation, we aimed to report a noisy psychotic process in a patient diagnosed with hypothyroidism but discontinued his treatment. Informed consent was obtained for the case.

CASE

A 31 years old male patient, who was married, had one child and was graduated from high school, applied to emergency unit of our hospital with complaints of insomnia, irritability, seeing light, and being frightened from light which started one month ago and intensified gradually over time. This was the first psychiatric application of the patient. According to information obtained from his wife, he got a permission leave from his work 45 days before his hospitalization for an orthopedic operation which would be performed electively. Thinking that he could not work again, he became very anxious during his permission leave. His anxiety was increased by time, he started to talk nonsense, and he told that he was seeing a light. He told during hospitalization for the operation that he was anxious that he and his daughter would be killed, he was continuously irritated and had fears, so his orthopedic operation was cancelled for his psychiatric assessment and treatment, and he was transferred to the emergency unit of psychiatry clinic. He had no psychiatric disease history, and he did not smoke or consume alcohol or any psychoactive substances. His premorbid characteristics were intelligent, devoted to his family, popular among people, socially active, and he had no problem with people in his daily life. No psychiatric disease was present in his family history.
When his general medical condition and medical treatments he received until then were inquired, his wife told that he had no physical disorder other than the orthopedic problem he had lately, no drug use lately, and no previous trauma history.

The patient was evaluated at the emergency unit, and he was internalized to our clinic for treatment. His self-care was moderate, and he appeared at his chronological age. He refused to interview because of his negative attitudes. He had nonsense stereotypic movements in both hands as if he were counting money. He was closing his eyes tightly, and refused to open them with any external interventions. His mood was irritable, and his expression of feelings were increased. As the patient refused to communicate, the though content could not be evaluated. He refused to eat and medications given orally.

On the day of his hospitalization, samples, such as hemogram, biochemistry tests, thyroid function tests (TFTs), hepatitis and human immunodeficiency virus markers, serum ferritin, folate and vitamin B12 levels, urine for psychoactive substance and alcohol metabolite examinations, were obtained to exclude any causes for his general health condition.

One day later, tests were reported as fT3=2.57pg/mL (2.3-4.2), fT4=0.66ng/dL (0.88-1.72) and TSH=105.952µIU/mL (0.63-4.82). No other pathology was determined. Internal Medicine consultation was requested in the same day, and it was planned to perform thyroid ultrasonography (USG), and measure thyroid peroxidase antibody (anti-TPO), and thyroglobulin (Tg) levels for hypothyroidism. In the USG, marked heterogeneity in thyroid parenchyma, and signs consistent with chronic thyroiditis were observed. Hashimoto thyroiditis was diagnosed definitely as anti-TPO level was 138.1IU/mL (0-35) and Tg level was within normal limits.

Magnetic resonance imaging and electroencephalography (EEG) were also performed to rule out any intracranial pathology. Both examinations were reported as normal. Family interview about Hashimoto thyroiditis was repeated, and his wife told that the patient was diagnosed with hypothyroidism 3 months ago, but he did not take drugs prescribed for him. During detailed inquiry, it was learned that the patient was inactive, continuously tired, and forgetful in the last 3-4 months.

On Day 2 of his hospitalization, treatment was planned as thyroxin 150microgram/day and olanzapine 20mg/day. As the patient refused oral intake, fluid replacement was performed through intravenous line. The patient refused to communicate for 4 days. Tablet form of thyroxin was dissolved in water and was tried to be injected at the corner of his mouth. The patient was convinced to talk on Day 4. He was conscious, and his place, person and time orientations were intact. It was determined that he refused to communicate because of persecution delusions and auditory hallucinations. He told that he believed we would kill him by drugs, and the God told him “Do not take the drugs. Love your government and your nation”. The associations were regular and aimed to the target. Test reasoning and abstracting were sufficient.

Thyroid function tests were repeated on Day 4; the results were fT4=1.02ng/dL, and TSH=113.326µIU/mL. Despite high TSH level, fT4 level returned normal. He received 23 points out of 30 in the Mini Mental Test (MMT). It was determined that he lost points especially in attention and memory subjects. MMT, which was developed in 1975 by Folstein et al. (18), is a valuable and rapid test used routinely to evaluate primary assessment of cognitive functions in neurological diseases. Many previous studies indicated that the most appropriate cut-off point was 23/24 in patients with cognitive deficiency (19).

Daily olanzapine dose was decreased to 5mg on the 6th day of his hospitalization. The psychotic signs were completely recovered on the 10th day. He received 28/30 points in MMT which was performed one day before his discharge. Patient was discharged with improvement on the 11th day of his hospitalization with treatment of olanzapine 5mg/day, and thyroxin 150microgram/day. He was recommended to have a re-examination of TFTs and control physical examination 10 days later. When he attended the control visit, there was no psychotic sign in his psychiatric examination. His affect was normal, and mood was euthymic. The score of repeated MMT was 30/30.
The latest TFT results were completely normal as TSH=2.79µIU/mL, fT3=4.69pg/mL, fT4=1.7ng/dL. As it was definitely diagnosed that psychiatric complaints were related to hypothyroidism of the patient, antipsychotic treatment was discontinued, and he was directed to internal medicine outpatient clinic for further controls. He was interviewed 3 months later, and there was no psychopathology, and TFT results were within normal limits.

**DISCUSSION**

The most common symptoms and signs of Hashimoto thyroiditis are weakness, tiredness, lethargy, preorbital edema, cold intolerance, dry skin, and constipation (2). Depression, forgetfulness, slowing in thinking, and deterioration of concentration are the most commonly encountered psychiatric symptoms (20). The first starting symptoms in our case were psychomotor slowing symptoms such as forgetfulness, concentration disorder, and tiredness, and these symptoms and signs lasted until TFT results returned normal. As mentioned above, MMT scores and TFT results showed parallel recovery temporally.

Another important diagnosis which should be differentiated in concomitance of Hashimoto thyroiditis and psychiatric symptoms is Hashimoto Encephalitis (HE), which is commonly come across in the literature (6,21,22). Myoclonus, epileptic seizures, fluctuations in consciousness, ataxia, dementia, and psychotic symptoms are also frequently encountered in HE (23). The most important laboratory finding of HE is EEG abnormalities which reach up to 98%, and especially presence of diffuse slow waves (24). Another characteristic of HE, as it would be observe in other case reports in the literature, is that it responds treatment rapidly and dramatically (6,22). In our case, no abnormality in EEG, no signs such as epileptic seizures, myoclonus, and ataxia, and dramatic responsiveness of our case to thyroid replacement treatment helped us to rule out HE easily.

Concomitance of Hashimoto thyroiditis and mania is a rare condition in the literature (25). In our case, symptoms such as increased self-esteem, grandiosity thoughts, increased amount and speed of speech, increased targeted activities, and flying thoughts which we expected during a manic episode were absent, presence of persecution delusions and behavioral disorders related to delusions primarily helped us to rule out mania.

Our case was diagnosed with hypothyroidism 3 months before he admitted to our hospital with acute psychosis attack during a preoperative evaluation. Thinking that he had no serious diseases, but only nonspecific symptoms such as fatigue and tiredness; our patient discontinued the replacement treatment 1 month after the initiation. In his physical examination, he did not have any specific sign indicating thyroid pathology. When he was inquired for general medical conditions of himself and his family, he did not mention about this diagnosis, and hypothyroidism was re-diagnosed by performing routine laboratory tests. Sudden onset of clinical picture, absence of psychopathology history, and markers of hypothyroidism in general condition examination directed us to diagnosis of “psychosis due to Hashimoto thyroiditis”. As the patient recovered rapidly after thyroid hormone replacement therapy and low dose antipsychotic drug treatment, and persistence of his well-being without antipsychotic treatment during control examinations supported our diagnosis also.

Diagnosis and follow-up processes of the present case indicate that laboratory tests have a very significant place in diagnosing psychiatric diseases. Moreover, it should also be considered in each patient with psychiatric signs that there may be an underlying predisposing or accompanying medical disease. If we only focus to diagnose a psychiatric disease, medical diseases may be missed and as accurate treatment is not planned, disease may progress and even mortality may be observed. In such cases, the most appropriate approach is correction of the underlying diseases primarily, and follow-up of these patients by consultation-liaison psychiatry. Although medical history taken from the patient and his/her relatives is very important, obtained information may not be enough and reliable, so these laboratory tests gain more importance.
Another point, which would like to be emphasized about the case is that parental form of levothyroxine is absent in our country. This caused difficulties in treatment, and affected treatment negatively. Parenteral form of levothyroxine, levothyroxine sodium, is being used in hypothyroidism treatment in many countries, and it is accepted as a good option in treatment of patients who refuse oral intake (26). As parenteral form of the drug was absent in our market, we tried to dissolve the tablet in saline and tried to inject it at the corner of his mouth, but majority of these attempts were ended up with failure. This situation had negative effects on the relationship between the patient who was in a paranoid picture, and treatment team, and this difficulty caused problems in calculations of drug doses given. If there were the parenteral form of the drug in the market, it would have been accelerate the recovery. We believe that presence of parenteral form of this drug will help both patients and healthcare personnel in the treatment, if enteral route is not eligible for use.

In conclusion, in the present case presentation it has been emphasized once more that thyroid function tests should be routinely screened, and parenteral levothyroxine form should be available in our country.

### Contribution Categories

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<td>Follow up of the case</td>
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### Conflict of Interest

Authors declared no conflict of interest.

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### REFERENCES


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