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Venlafaxine-induced Thyroiditis: A Case Report

Ideh Ghafour (MD)[1], Forouzan Elyasi (MD)[2]*

[1]*Student Research Committee, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.*
[2]*Department of Psychiatry, Psychiatry and Behavioral Sciences Research Center, Addiction Institute, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.*

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ABSTRACT

Thyroiditis is the most common inflammatory disorder that affects thyroid gland. The diagnosis is mainly based on clinical findings, in particular the degree of pain and tenderness of thyroid. Confirmatory laboratory test includes presence of thyroid specific autoantibodies. Treatment is based on the severity of symptoms (pain and redness) and aims to restore the normal function of thyroid. Drug-induced thyroiditis has been described previously in the literature. Venlafaxine is an antidepressant agent with an efficacy similar to that of selective serotonin reuptake inhibitors. The dose of this medicine can be adjusted up to 150 mg/day one year after initiation. However, usage of venlafaxine may be limited due to the dose-dependent side effects. Here we describe a patient diagnosed with generalized anxiety disorder and migraine headache who developed venlafaxine-induced thyroiditis following dose adjustment to the maximum of 150 mg/day. The diagnosis was made based on the clinical symptoms and confirmatory laboratory tests according to the Naranjo Adverse Drug Reaction Probability Scale. Thyroiditis symptoms subsided after reducing venlafaxine dose and initiating prednisolone therapy. It should be noted that thyroid function was fully restored to normal only after cessation of venlafaxine administration..

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Introduction

The term thyroiditis generally refers to an inflammatory condition of thyroid comprising the most common disorder of thyroid gland (1,2). Thyroiditis may develop in the context of autoimmune disorders or might not be related to the immune system (3). Clinically, thyroiditis is a heterogeneous disorder mimicking symptoms of other diseases (1). Thyroiditis induced by infection, trauma, or exposure to radiation presents with pain. On the other hand, pain may be absent in thyroiditis related to the autoimmune conditions, pharmaceuticals, or idiopathic fibrosis.

During the course of thyroiditis, functional status of thyroid falls into either normal, hypofunctional (hypothyroidism), hyperfunctional (hyperthyroidism), or intermediate states.

The diagnosis of thyroiditis is based on both clinical and laboratory findings. The presence or absence of pain and tenderness is an important clinical feature.Moreover, detection of accompanied autoantibodies is considered as the most significant laboratory evidence. Absorption of radioactive iodine diminishes in patients affected by thyroiditis induced by viral infections, radiation, trauma, autoimmune disorders, or medications. The treatment of thyroiditis aims to ameliorate the pain and redness, in addition to restoring thyroid function.

Drug-induced thyroiditis accounts for10-15% of all the thyroiditis cases and has been described in association with a number of medicines, such as amiodarone, interferon-α, and interleukin-2.

***Corresponding author:** Forouzan Elyasi.
Psychiatry and Behavioral Sciences Research Center, Addiction Institute,School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.
E-mail: forouzan.el@gmail.com
Tel:+ 989111551097

The psychotropic agents (including lithium) have also been reported to induce thyroiditis. In one report, thyroiditis was reported in 13 per 100,000 individuals treated with lithium (4). Furthermore, a relationship has been noted between the abnormalities of thyroid axis and psychiatric disorders(5).

Many studies have described a range of alternations in hypothalamic-pituitary-thyroid axis in patients with major depressive disorders. These changes entailed reduction in serum levels of thyrotropin (TSH), blunted TSH response to thyrotropin-releasing hormone (TRH), and elevated serum thyroxine (T4) levels (6). Moreover, efficacy of thyroid hormone therapy in improving depression has been described (7).

The impacts of tricyclic antidepressants administration on thyroid function have been studied so far. Nevertheless, new therapeutics, namely selective serotonin reuptake inhibitors (SSRIs), serotonin and noradrenaline reuptake inhibitors (SNRIs), and selective noradrenaline reuptake inhibitors (NARI) are increasingly used as alternatives of tricyclic antidepressants in current practice. Few information is available regarding the influence of these new agents on thyroid function (8). Changes in the levels of thyroid hormones have been reported in patients treated with fluoxetine (9), paroxetine (10), and combination of fluvoxamine and maprotiline (11).

Venlafaxine, an SNRI, is an antidepressant with an efficacy similar to that of SSRIs. Venlafaxine is associated with dose-dependent side effects limiting its application (12). Common complications of the medicine encompass dizziness, headache, sweating, nausea, constipation, and hypertension (13). Goiter, thyroiditis, hypothyroidism, and hyperthyroidism are the other rare complications of SNRIs with an incidence rate of less than 0.1% (14). In this case report, we describe a patient with generalized anxiety disorder and migraine under treatment with venlafaxine who presened with thyroiditis after boosting the venlafaxine dose to the maximum of 150 mg/day.

Case report

A 28-year-old married woman referred to the Psychiatric Clinic of Imam Khomeini Hospital, Sari, Iran. The patient complained of anxiety, fear, and restlessness. She had concerns about the possibilities of mishaps and challenges in her future to the extent that she could not allow another person to watch her daughter and brought her to the clinic in the first visit. The woman was depressed during the first interview. However, the joy absence, thoughts of death, and suicidal ideations that marked the first interview were not observed in the follow-up interviews.

Her self-reported health history included migraine headaches and thalassemia minor. In addition, she reported using Novafen for her headaches and had no previous history of psychotropic or any other medications. Major depression, generalized anxiety, and separation anxiety disorders were observed in the family history of her mother. Following the clinical interview and physical examination, the patient was diagnosed as generalized anxiety disorder, as well as migraine based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5).

Venlafaxine (18.75 mg/day) along with propranolol (10 mg twice a day) were administrated. On the second visit after two months, the anxiety and restlessness were decreased. The venlafaxine dose was gradually increased to 75 mg/day and this dose was continued for one year. During the future visits, symptoms of generalized anxiety were effectively managed and the patient could gradually trust a family member for child attendance during the visits.

In order to resolve the anxiety symptoms completely after one year, the venlafaxine dose was increased to 75 mg twice a day (150 mg/day). In addition, the propranolol dose was augmented to 20 mg/day for controlling her migraine symptoms. One month after administrating 150 mg/day venlafaxine, the patient developed thyroiditis symptoms with a painless swelling in the anterior cervical region of thyroid. The patient had no previous history of similar symptoms. She also had no family history of thyroid problems.

Laboratory evaluations rendered the following values: erythrocyte sedimentation rate 4 mm/hr, C-reactive protein 3 mg/L, TSH0.02 MIU/L, T4 18.5 pg/dl, T3 ELISA 3.1ng/ml, anti-thyroperoxidase antibodies> 1000 IU/ml, whiteblood-cell count 7800 (1000/cumr), redbloodcell count 6.21 million/uL, mean corpuscular volume 65.4 (fl), mean corpuscular hemoglobin 20.6 (pg), and platelet count 383,000 (1000/cumr).

Consecutive ultrasonography images showed progressive enlargement of thyroid lobes, as well as heterogeneous parenchymal echogenicity in thyroid and cervical lymph nodes. Scattered hypoechoic micro-nodules were noted in both thyroid lobes. Moreover, hypoechoic and non-hypoechoic nodules with sharp edges, some with echogenic foci were observed. Overall, the findings favored the diagnosis of goiter colloid cyst.

At this point, the patient underwent nuclear scanning of thyroid. Impaired removal of radioactive material from both thyroid lobes was observed along with increased uptake of radioactivity in the background and salivary glands. Graves'

disease and automatic thyroid nodule function were excluded based on the radioistopic scan findings (Figure 1). Regarding the history of patient, specially the venlafaxine regimen and thyroiditis after increase in the dose, the pattern observed on nuclear scans was suggestive of thyroiditis.

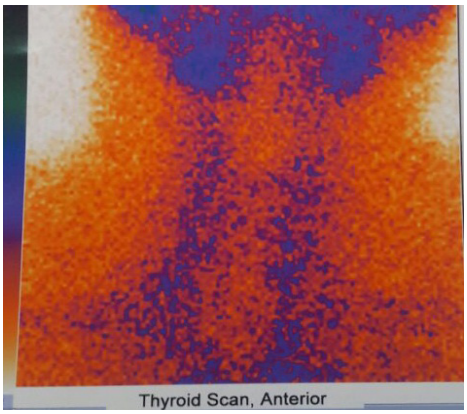

Figure 1. Thyroid nuclear scan

After consultation with an endocrinologist, Prednisolone (50 mg/day) was started and the venlafaxine dose was initially reduced to 75 mg/day and then to 37.5 mg/day. As an alternative to venlafaxine, sertraline (25 mg/day) was administrated and gradually elevated to the dose of 100 mg/day. After one month, thyroid was painless but the warmth and redness continued with less intensity (Figure 2). Venlafaxine administration was completely ceased, while continuing the treatments with sertraline (100 mg/day), propranolol (10 mg/day) and prednisolone (50 mg/day). After discontinuation of venlafaxine, the thyroiditis symptoms completely resolved and the blood tests demonstrated hypothyroidism.

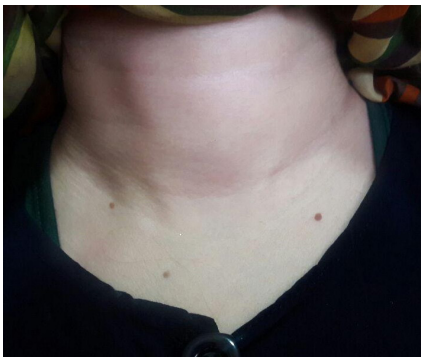

Figure 2. After one month, thyroid was painless but the warmth and redness continued with less intensity

Discussion

In this case report, we described a patient with generalized anxiety disorder and migraine who developed venlafaxine-induced thyroiditis while venlafaxine dose was increased to 150 mg/day after one year of treatment initiation.The patient experienced painless warmth and redness in the anterior cervical region of thyroid. The laboratory tests and nuclear imaging of thyroid confirmed thyroiditis.

Based on the Naranjo adverse drug reaction probability scale (15), the patient obtained a score of 6 out of 10, which is indicative of a probable adverse drug reaction. When the venlafaxine dose was reduced and prednisolone was administered, the thyroiditis symptoms partially resolved. However, the thyroid status only fully recovered after complete withdrawal of venlafaxine. Autoimmune thyroiditis was another differential diagnosis.

Thyroid disorders should be taken into consideration in patients under treatment for emotional disorders. Thyroid function affects biology of nervous system as thyroid hormones can regulate the expansion and differentiation of glial cells and neurons. Moreover, these hormones modulate homeostasis and function of brain, neuronal plasticity, and synaptic transmission function. Coincidence of thyroid problems with mental disorders is not an uncommon phenomenon. In fact, iatrogenic disorders are among the factors that can alter the course and treatment strategies forthyroid diseases (9).

In addition, the effect of antidepressants on thyroid is important. Several studies investigated the plasma levels of thyroid hormones, especially T4, during antidepressant therapy (7,8,16). some of these reports described reduction in the serum levels of free T4 or T4 (16,17) and T3 (8,16) during antidepressant therapy. Thyroid dysfunction following SSRIs therapy is a rare incident with only few reported cases of hypothyroidism in patients receiving escitalopram (18), paroxetine (19), fluoxetine (20), and sertraline (21).

A case report by Lai et al. (2016) demonstrated that short-term fluoxetine therapy can lead to hyperthyroidism in some patients. In this report, a 38-year-old woman with major depressive disorder who received fluoxetine (40 mg/day) represented with symptoms of hyperthyroidism (reflected by increased heart rate and appetite) after 10 weeks. Hyperthyroidism was confirmed based on the laboratory findings, including elevatedT4, free T4, and free T3, in addition to decreased TSH serum levels.

The mechanisms for thyroiditis development following fluoxetine therapy are not fully understood. However, due to the accumulation of serotonin in the cerebrospinal fluid following fluoxetine therapy, serotonin can act as a 5HT-2 receptor on the surface of thyroid follicular cells and raise the production and release of thyroid hormones. Therefore, it is necessary to monitor thyroid hormone fluctuations during treatment

with SSRIs, especially when the clinical response is inadequate, unusual, or vague (9).

Conclusion

Most of the previous studies on the impacts of antidepressants on thyroid gland function investigated the effects of SSRIs. However, few studies exist concerning the influence of SNRIs. According to the present case report, it is recommended to examine thyroid in terms of size, warmth, redness, and pain to rule out thyroiditis following prolonged usages of antidepressants.

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None.

Conflict of Interest

The authors declare no conflict of interest.

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