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Case report

Escitalopram-induced subclinical hypothyroidism. A case report

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ABSTRACT

Several conditions and drugs induce subclinical hypothyroidism. We report a case of asymptomatic and reversible subclinical hypothyroidism in a 48-year old woman with minor depressive disorder receiving therapy with escitalopram 20 mg daily for six months.

Key words: Depression, Escitalopram, Hypothyroidism

BACKGROUND

Subclinical hypothyroidism (SCH) is characterized by normal serum levels of thyroid hormones, namely free T_3 (FT_3) and free T_4 (FT_4), with a slightly elevated (typically 5-10 mIU/L) serum level of thyroid-stimulating hormone (TSH, thyrotropin), with or without symptoms.[1] SCH is more frequently observed among older women mainly in cases of autoimmune thyroid disease or during under-replacement of thyroid hormones in overt hypothyroidism.[1] The relation between SCH and drugs is well established in the literature. Drugs that impair thyroid function, such as iodine and iodine-containing medications (amiodarone, radiographic contrast agents), lithium, cytokines (especially interferon-alpha), aminoglutethimide, ethionamide, sulfonamides, and sulfonylureas, or factors that contribute to inadequate replacement therapy in overt hypothyroidism (inadequate dosage, non-compliance, drug interactions, increased T_4 clearance), are some of the pharmacologic causes of SCH.[1-4]

We herein describe a case of asymptomatic and reversible SCH in a woman with minor depressive disorder receiving therapy with escitalopram (Entact).

CASE REPORT

A 48-year-old woman visited our hospital for scheduled hematological control. She had a previous history of hypercholesterolemia (no medical treatment despite recommendations) and minor depression [minor depressive disorder; code 311-depressive disorder not otherwise specified (DD-NOS) according to DSM-IV-TR classification] and had been receiving therapy with escitalopram for six months. Her depressive complaints were resolved within a month after escitalopram initiation. The patient was not taking other drugs and had no personal or family history of thyroid disease. She refused disclosure any recent history of cold, neck pain or discomfort. The present laboratory tests revealed elevated total cholesterol (TC), low density lipoprotein cholesterol

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(LDL-C) and triglyceride (TG) levels (280 mg/dl, 203 mg/dl and 160 mg/dl, respectively), normal high density lipoprotein cholesterol (HDL-C) levels (45 mg/dl), an elevated TSH serum level (9.2 mIU/L; normal range: 0.3-4 mIU/L) with normal serum FT_3 (3.4 pg/mL; normal range: 1.6-5 pg/mL) and FT_4 (1.3 ng/dL; normal range: 0.8-2 ng/dL) levels, on first measurement; similar findings were obtained when these thyroid function tests were conducted again subsequently. An ultrasound scan of the thyroid gland was normal. It should be noted here that a year before arrival, thyroid gland ultrasonography, thyroid function tests (TSH, free T_3, free T_4), and the antithyroid antibodies (anti-thyroid peroxidase, anti-thyroglobulin) were all normal. Although our patient had hypercholesterolemia, her cardiovascular risk profile was very low as she was a middle-aged non-smoking woman with negative family cardiovascular history, normal arterial pressure, body mass index (BMI; 23 kg/m^2), glucose metabolism and normal cardiac function (estimated ten-year risk of fatal cardiovascular disease according to HellenicSCORE $<1\%$).[5] Moreover, no change in her weight was observed during escitalopram treatment. Based on the possible diagnosis of asymptomatic escitalopram-induced SCH, escitalopram was withdrawn. Thyroid dysfunction was restored (serum TSH: 2.8 mIU/L) after four months and no recurrence of thyroid dysfunction occurred during the 1-year follow-up. The levels of TC, LDL-C and TG were decreased to 268 mg/dl, 193 mg/dl and 140 mg/dl, respectively; HDL levels were increased to 47 mg/dl. A statin therapy (atorvastatin 10 mg) was suggested. Our patient refused to receive some other treatment against her minor depressive disorder.

DISCUSSION

Our case demonstrates that selective serotonin reuptake inhibitors (SSRIs), as escitalopram, may have the potential to induce asymptomatic SCH. Despite the well documented complex interaction between the central serotoninergic (5-HT) system and the hypothalamic-pituitary-thyroid (HPT) axis, and the impact of SSRIs on several thyroid indices, hypothyroidism is a rare adverse effect of SSRI treatment.[6-8] In a prospective, controlled, intervention study, neither fluoxetine nor sertraline was associated with clinically significant change in thyroid function or thyroid autoimmunity in either primary hypothyroid or normal thyroid function patients, during 90 days of observation.[9] Moreover, in this study,[9] patients without hypothyroidism who were treated with fluoxetine were more susceptible to minor changes within the complex serotoninergic system than patients with hypothyroidism receiving the same SSRI therapy. Specifically, a transient reduction in T3 and a persistent reduction in T4 among depressed patients on fluoxetine treatment with normal basal thyroid function was demonstrated.[9] In a prospective study, the administration of sertraline for approximately six months in a group of 15 patients with normal thyroid function was associated with a significant increase in T3 levels.[10] Another prospective study with 19 subjects with major depression and normal thyroid function revealed a significant association between administration of either fluoxetine or sertraline and a decrease in the levels of T3 and T4 after approximately 2.5 months of therapy.[11] It has been hypothesized that reduction of serum T4 levels during antidepressant treatment is caused by a compensatory uptake of T4 that is converted into T3 in the brain, and thus an increased availability of T3 may be associated with an enhancement of serotoninergic neurotransmission.[9] Moreover, it is known that mental disorders, as depression, are frequently associated with primary thyroid disorders, but though the thyroid hormone T3 is believed to have an antidepressant effect due to its central role in potentiation of the neurotransmitter serotonin (possibly by reducing the sensitivity of 5-HT_{1A} autoreceptors in the raphe area, and by increasing 5-HT_2 receptor sensitivity) and due to stimulation of specific nuclear gene transcription.[9,12] Experimental and clinical data have also demonstrated disturbances in the functioning of the brain 5-HT system in hypothyroidism, such as losses of cortical 5-HT_{2A} receptors.[13] To the best of our knowledge, only one case of reversible and asymptomatic escitalopram-induced hypothyroidism is described in the medical literature.[6] This case concerns a 53-year-old woman with Hashimoto's thyroiditis on levothyroxine sodium therapy for eight years.[6] Other cases of SSRI (paroxetine or sertraline)-induced hypothyroidism (mainly in thyroxine-treated patients) have also been reported in the literature.[7,8,14] Possible mechanisms via which escitalopram is capable of increasing TSH could be a loss of serotonin receptors (5-HT_{1A} and

especially 5-HT_{1B}) in certain brain areas, an effect on transporters or a direct action of the drug, but the exact mechanism by which escitalopram raised serum TSH concentrations in our patient remain uncertain.

Our patient had no previous history of thyroid disease, radioactive iodine therapy or neck irradiation which might have accounted for this condition. Moreover, the negative antithyroid antibodies, the normal ultrasound of thyroid gland, the absence of thyroid pain and tenderness, the normal values of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) ruled out other known causes of SCH, as painful or painless types of thyroiditis.[15,16] An overweight/obesity related SCH was also excluded, considering the normal BMI of our patient and the fact that there were no changes in her weight during escitalopram treatment. Escitalopram is, in any case, not associated with weight changes and therefore is a suitable antidepressant drug for subjects at risk of weight gain.[17] Since the patient was not taking any other drugs except escitalopram, we believe that it was the most possible cause of SCH. In addition, no recurrence of thyroid dysfunction occurred during the 1-year follow-up after after escitalopram withdrawal.

Apart from the withdrawal of escitalopram, replacement therapy with levothyroxine sodium might have been indicated in our patient with serum TSH level < 10 mIU/L and elevated TC and LDL-C levels, despite the negative antithyroid antibodies and the absence of symptoms or neck ultrasound changes.[1,18] However, we did not recommend this therapy based on the possible diagnosis of drug-induced SCH and awaiting the results of thyroid function tests after escitalopram withdrawal. It was taken into account that only some cases of drug-induced hypothyroidism can be treated successfully by simply removing the pharmacologic agent.[1]

CONCLUSION

This case report highlights a potential side effect of escitalopram therapy that warrants thorough investigation with large series of patients.

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