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Case Report

Nausea and vomiting as major presenting symptoms of thyrotoxicosis after bilateral adrenalectomy for Cushing's disease

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ABSTRACT

Thyrotoxicosis has a variety of presentations which depend on its severity and duration, as well as the age of the patient. In elderly patients, thyrotoxicosis may present with a variety of nonspecific symptoms. Nausea and vomiting as major presenting symptoms of thyrotoxicosis have rarely been reported. Thyrotoxicosis after adrenalectomy in patients with Cushing's syndrome and normal thyroid function, or with autoimmune thyroid dysfunction has rarely been reported previously. We describe a very rare case of an elderly patient with hypothyroidism due to Hashimoto's thyroiditis who presented with persistent nausea and vomiting as major presenting symptoms of thyrotoxicosis, which developed after bilateral adrenalectomy for Cushing's disease. Similar case has not been reported previously. In reporting this patient we aim at drawing attention to these forgotten symptoms of thyrotoxicosis, nausea and vomiting, and to emphasize that, at times, these symptoms may be the only presenting features of thyrotoxicosis, leading to considerable difficulty in diagnosis. Furthermore, cessation of glucocorticoid excess may sometimes be accompanied with thyrotoxicosis.

Keywords: Cushing's syndrome adrenalectomy, Nausea, Thyrotoxicosis, Vomiting

INTRODUCTION

Patients with thyrotoxicosis may present with a wide range of gastrointestinal symptoms such as diarrhea, frequent defecation, and increased appetite, often coexist with other typical thyrotoxic symptoms. Sometimes hyperthyroidism may present in various guises with typical thyrotoxic symptoms lacking in prominence, and sometimes almost totally absent, particularly in the elderly.[1,2] An increased appetite is accepted as being one of the cardinal symptoms of thyrotoxicosis. On the other hand, nausea and vomiting are poorly recognized and often are forgotten manifestations of hyperthyroidism. As major presenting symptoms of thyrotoxicosis, these manifestations have been rarely reported and have not been included as presenting symptoms for thyrotoxicosis in standard textbooks of medicine and endocrinology.[3-11] Thyrotoxicosis after adrenalectomy in patients with Cushing's syndrome and normal thyroid function, or with autoimmune thyroid dysfunction has rarely been reported previously. We describe a patient with hypothyroidism due to Hashimoto's thyroiditis who presented with persistent nausea and vomiting as major presenting symptoms of thyrotoxicosis which developed after bilateral adrenalectomy for Cushing's disease, leading to considerable difficulty in diagnosis, and un-necessary investigations.

CASE REPORT

A 56-year-old woman with primary hypothyroidism due to Hashimoto's thyroiditis which was diagnosed ten years

before and treated with L-thyroxine 0.15mg daily, was admitted to our hospital for Cushing's syndrome complicated with obesity, hypertension, diabetes mellitus, and hirsutism. The diagnosis of Cushing's disease due to pituitary adenoma was made. Medical treatment of the Cushing's disease did not succeed, and later, the patient underwent trans-sphenoidal surgery procedure which also did not succeed. She underwent bilateral adrenalectomy and was placed on hormonal replacement therapy with cortisone acetate, 25 mg in the morning and 12.5 mg in the evening.

The surgery was successful and was not accompanied by immediate complications. Before the bilateral adrenalectomy, serum level of FT4 was 15.76pmol/L (normal range: 12.0-22.0pmol/L), FT3 4.2 pmol/L (normal range: 3.1-6.8 pmol/L), and TSH 2.4μIU/mL (normal range: 0.27-4.2μIU/mL). The patient was discharged with cortisone acetate 37.5mg daily in addition to L-thyroxine 0.15mg daily as before the bilateral adrenalectomy. On discharge thyroid function tests revealed serum level of FT4 of 19.45pmol/L, FT3 of 5.1pmol/L, and TSH of 1.9μIU/mL.

Two weeks later, persistent nausea and vomiting after almost every meal developed without fever, headache, abdominal pain or other symptoms. She was readmitted to the hospital, and physical examination revealed fully conscious obese woman with blood pressure of 142/70mmHg, regular heart rate of 100beats/minute, and normal body temperature. Neck, chest, and abdominal examination was normal except of mildly rapid heart sounds. Neurological examination was also normal. Routine hematological and biochemical blood tests were within normal range except of a blood glucose level of 152mg/dL, and blood urea level of 67mg/dL. Venous blood gases and pH revealed mild metabolic alkalosis. The chest radiograph was normal, and the electrocardiogram demonstrated sinus tachycardia of 104beats/minute.

The patient was treated with anti-emetic agents and infusion of normal saline, but with no significant improvement of her symptoms. She underwent an extensive investigation, including abdominal ultrasonography, upper gastrointestinal endoscopy, and abdominal and cerebral CT-scan, however no apparent cause of the patient vomiting could be found. Later, thyroid function tests were performed, and revealed levels of FT4 of 26.2pmol/L, FT3 of 6.7pmol/L, and TSH of 0.01μIU/mL, which were normal on discharge. The L-thyroxine dose was decreased to 0.1mg a day, and within a few days the patient's symptoms completely resolved, the pulse decreased to normal range and her feeling improved significantly. Thyroid function tests, one and two months later, revealed FT4 of 16.3pmol/L, FT3 of 4.6pmol/L, TSH of 2.23μIU/mL, and FT4 of 16.9pmol/L, FT3 of 4.7pmol/L, TSH of 2.34μIU/mL respectively, while the patient remaining asymptomatic.

DISCUSSION

Hyperthyroidism has a variety of clinical presentations which depend on the severity of thyrotoxicosis, the duration of disease, individual susceptibility to excess thyroid hormones, and the patient's age.[1] Sometimes the typical thyrotoxic symptoms are lacking in prominence, and sometimes almost totally absent, particularly in the elderly.[1,2]

Patients with thyrotoxicosis may present with a wide range of gastrointestinal symptoms such as diarrhea, frequent defecation, and increased appetite, often coexist with other typical thyrotoxic symptoms. An increased appetite is accepted as being one of the cardinal symptoms of thyrotoxicosis. On the other hand, nausea and vomiting are poorly recognized and often are forgotten manifestations of hyperthyroidism. As major presenting symptoms of thyrotoxicosis, these manifestations have rarely been reported in the medical literature and have not been included as presenting symptoms of thyrotoxicosis in standard textbooks of medicine and endocrinology.[3-11] They are well recognized and usually seen as a presentation of thyrotoxic storm.[12-14] Thyrotoxic vomiting, however, was certainly known to earlier physicians, and Osler's principles and practice of medicine, vividly described such a case.[15] Cameron in 1945 knew it too, although he felt it a symptom of crisis or near crisis, as have others.[16-18]

Recent literature has suggested that vomiting may be more important as a cardinal symptom of thyrotoxicosis, and that it is not only seen in thyrotoxic storm but is part of a more prolonged chronic presentation.[4-9] In most of these cases the diagnosis was delayed because of the atypical presentation of thyrotoxicosis. During pregnancy, diseases that are initially observed with vomiting as the primary symptom may be difficult to distinguish from hyperemesis gravidarum due to thyrotoxicosis.[19-21] In one case because the diagnosis was delayed, severe malnutrition and thyroid storm developed, and the patient's symptoms resolved when thyroid functions returned to normal range.[19]

The primary hypothyroidism in our patient was due to Hashimoto's thyroiditis. Before the bilateral adrenalectomy there was an excess of glucocorticoids which may lowered further serum levels of thyroid hormones, as serum concentration of T3 and T4 are frequently decreased in patients with Cushing's syndrome.[22,23] This decrease in serum levels of T3 and T4 is due to glucocorticoid mediated suppression of both, serum thyroxine-binding globulin and TSH.[22-26] After bilateral adrenalectomy the glucocorticoid excess resolved drastically and with it also thyroid gland suppression. Transient thyrotoxicosis after unilateral adrenalectomy in patients with Cushing's syndrome and normal thyroid function has been reported previously.[27,28] Furthermore, exacerbation of autoimmune thyroid dysfunction and hyperthyroidism after unilateral

adrenalectomy for Cushing's syndrome due to adrenal adenoma, and after removal of ACTH-producing pituitary adenoma for Cushing's disease, have been also reported.[29,30] Glucocorticoids are known to suppress autoimmune reactions, and they have been used to treat patients with autoimmune thyroiditis.[29] So in Cushing's syndrome after unilateral or bilateral adrenalectomy, the autoimmune process may exacerbate and overt thyroid dysfunction may develop.

Our patient was in euthyroidism before bilateral adrenalectomy with treatment of 0.1 mg L-thyroxine a day, and excess of glucocorticoids. After adrenalectomy the excess of glucocorticoids resolved drastically and she continued to get the same dose of L-thyroxine. The above discussion explains why she developed thyrotoxicosis after the surgery procedure. A strong evidence that the patient was thyrotoxic after adrenalectomy is that; serum level of FT4, FT3, and TSH were within normal range before adrenalectomy, and after adrenalectomy FT4 level increased to 26.2pmol/L, FT3 increased to 6.7pmol/L, and TSH level decreased to 0.01µIU/mL. After lowering the dose of L-thyroxine the signs and symptoms of thyrotoxicosis resolved rapidly, with concomitant normalization of FT4, FT3 and TSH. The pathophysiology of nausea, vomiting in the setting of thyrotoxicosis is not fully understood. Increased thyroid hormone is known to cause a generalized increase in gut motility.[31] Thyrotoxicosis may cause hyperperistalsis resulting in a relative outlet dysfunction. Decreased gastric motility could also cause these symptoms and has been demonstrated in two thyrotoxic patients.[10,32]

Another, although unsubstantiated, possibility is that increased thyroid hormone levels have an effect on the central emetic center of the brain. Hypercalcemia has been shown to occur in some patients with hyperthyroidism and could be implicated as a possible cause of these symptoms.[33] However, Gordon et al, found no such correlation between calcium levels and presence of vomiting or abdominal pain.[34] In our three cases no patient had hypercalcemia. Hyperemesis associated with hyperthyroidism occurs predominantly in females; a likely emetic factor estrogen.[3,23,31] Hyperthyroidism may potentiate this effect, as levels of estrogen are raised in thyrotoxicosis.[35] Atypical forms of thyrotoxicosis tend to be more common in the elderly, and the main features may be cardiovascular, metabolic, neuropsychiatric and others.[1,2] Important symptoms, such as nausea and vomiting, have gone largely unrecognized. As a result, the correct diagnosis has been delayed in some patients, leading to such unnecessary investigations with unnecessary morbidity, suffering, and perhaps, preventable death.

CONCLUSION

In reporting this patient, we aim at drawing attention to these forgotten symptoms of thyrotoxicosis, nausea and vomiting, and to emphasize that, at times, these symptoms may be the only presenting features of thyrotoxicosis, leading to considerable difficulty in diagnosis, unnecessary investigations with unnecessary morbidity, suffering, and perhaps, preventable death. Furthermore, cessation of glucocorticoid excess may sometimes be accompanied with thyrotoxicosis.

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