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Case Report

Euthyroid Hyper Thyroxinemia in Acute Psychiatric Illness with Associated Primary Hyperparathyroidism

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Abstract

Acute psychiatric illness is associated with alterations of serum thyroid hormone levels including normal or high T3 levels and elevated T4 levels with normal or high TSH that have no clinical signs or symptoms and resolve within 2 weeks. This phenomenon is called euthyroid hyperthyroxinemia. We present a case of primary hyperparathyroidism contributing to a patient's depression with psychosis that developed euthyroid hyperthyroxinemia. We also review the literature to present current thoughts about pathophysiology and treatment.

Introduction

There are several disorders that can cause hyper thyroxinemia without thyrotoxicosis. These include abnormalities of serum thyroid hormone binding proteins, peripheral resistance to thyroid hormone, acute non-thyroidal illness, drug-induced conditions and acute psychiatric illness [1-2]. The association between thyrotoxicosis and an altered mental state was recognized as early as 1835 by Graves [3]. Further research has demonstrated that thyrotoxicosis can cause prominent psychiatric symptoms such as restlessness, nervousness, hyperactivity and emotional liability [4-5]. Nevertheless, overt psychosis is not a common occurrence [6]. Thyroid function studies are commonly obtained in patients hospitalized with psychiatric illnesses, in order to detect undiagnosed thyroid disorders. Patients admitted with acute psychiatric illnesses have been found to have normal or high T3 levels and elevated T4 levels with normal or high TSH. Generally, the thyroid function tests normalize within 2 weeks [7-8]. Potential etiologic mechanisms for these findings include increased T4 bound in the plasma due to an increased amount of binding proteins, a shift of T4 from the peripheral tissues to the extracellular compartment or hyper secretion of T4 from the thyroid. A prospective study from Roca et al., which found elevated T4 levels in 36% of cases, supported the hypothesis of a TSH induced increase in thyroidal secretion of T4 by taking serial measurements of TSH, T4, T3, thyroid binding globulin (TBG) and T3 resin uptake [9]. They postulated that this could occur from a disturbance in the pituitary feedback system resulting in a transient increase in the TSH secretion at the onset of acute psychiatric illness.

Case

81 year old Caucasian female with a history of Depression NOS and Anxiety disorder NOS who presented to the Emergency Department reporting suicidal ideation due to worsening symptoms of depression and guilt over her daughter's pregnancy (later determined to be a delusion). During work-up of possible organic causes she was discovered to have an elevated free T4 level of 2.03 ng/dL (normal 0.80-1.90), normal Thyroid Stimulating Hormone (TSH) of 1.63 mIU/L (0.55-4.78), and an elevated calcium of 11.4 mg/dL (normal 8.4-10.2) with an elevated Parathyroid Hormone (PTH) of 227.9 pg/mL (normal 14-72). TSH, Free T4, Free T3 and PTH all were performed using Chemi luminescent Micro particle Immunoassay (CMI) methodology. Calcium was Arsenazo III methodology.

On physical exam, vital signs revealed a Temperature of 97 °F (36.1°C), Blood Pressure of 136/63 mmHg, Pulse 86 and Respiratory Rate 18. In general she appeared well-developed and well-nourished. Her head was normocephalic and atraumatic. Eyes showed pupils being equal, round, and reactive to light without scleral icterus. Her neck demonstrated no tracheal deviation or thyromegaly. No nodules were palpable. Cardiovascular examination showed normal rate, regular rhythm and normal heart sounds with no gallop, friction rub or murmur. Pulmonary exam showed normal effort and breath sounds, without respiratory distress, wheezes, or rales. Her abdomen was soft without distension, masses, tenderness and normal bowel sounds. Extremities demonstrated no edema. Neurologically she had a delayed reflex with mild clonus, but otherwise the exam was normal. Upon psychiatric evaluation she had delayed speech and she appeared slowed and withdrawn. Her thought content was delusional and she exhibited a depressed mood. She did not have any suicidal or homicidal ideation.

Hospital Course

The patient was admitted to the inpatient psychiatric unit and she was started on treatment with a tetracyclic antidepressant, Mirtazapine, and a 2nd generation antipsychotic, Olanzapine. Repeat thyroid function tests revealed similar results with a normal TSH of 1.01 mIU/L, elevated Free T4 of 2.0803 ng/dL and normal Free T3 of 3.2pg/mL (2.3-4.2). Thyroid stimulating immunoglobulin, thyroid peroxidase antibody and thyroglobulin antibody were undetectable. Further work-up of the patient's hyperparathyroidism with a technetium sestamibi parathyroid scan with SPECT/CT revealed a 1 cm left inferior parathyroid adenoma. The patient was not on biotin. A previous bone density exam supported a diagnosis of osteoporosis, with a T-score of -2.6 of the left hip, -2.5 of the right hip, -2.3 of L1-L4, and -4.4 of the distal radius. The patient had no history of fractures or nephrolithiasis.

The patient was treated for refractory depression with psychosis with 7 sessions of electroconvulsive therapy. Because of the patient's depression, decreased bone mineral density and elevated calcium levels, she also underwent a left inferior parathyroidectomy with intraoperative PTH returning back to normal. She had return of euthymia at completion of her electroconvulsive therapy and normalization of her serum calcium and PTH levels. Thyroid function tests were repeated a week after the initial lab abnormalities were found, and showed the resolution of euthyroid hyper thyroxinemia with a Free T4 of 1.63 ng/dL. Upon follow-up, the patient continued to have euthymia several months after her initial presentation.

Discussion

Euthyroid hyper thyroxinemia has been associated with acute psychiatric illness, although the exact mechanism is not understood. The complex neuro chemical alterations of adrenergic, serotonergic and dopaminergic neurotransmission in major psychiatric illness may influence the feedback loop in the hypothalamic-pituitary-thyroid axis at the pituitary level through several mechanisms. One possible mechanism could be a decrease in intra pituitary conversion of T4 to T3, which blunts the negative pituitary feedback by the thyroid hormones and leads to a temporary surge in TSH production. Since TSH has a much shorter half-life of 50 minutes [10] than T4's 7 days [11], the thyroid function tests could reveal an increase in both TSH and T4 levels when obtained early at the onset of psychiatric illness, or only an increase in T4 levels when obtained later. TSH hyper secretion could lead to down-regulation of pituitary TRH receptors, and decrease in TSH responsiveness to exogenous administration of TRH, a finding frequently encountered in severely depressed patients [12].

Our final diagnosis was euthyroid hyper thyroxinemia accompanying acute psychiatric illness. The initial elevated Free T4 was confirmed, in order to exclude lab error. A Free T3 was checked to rule out subclinical hyperthyroidism, as well as thyroid stimulating immunoglobulin to assess for possible Graves' disease. The exam was not notable for signs or symptoms of thyrotoxicosis, with a normal heart rate, and no diaphoresis nor tremor. The patient had no clinical findings of Graves's disease, including orbitopathy, nail changes and dermopathy. The hyper thyroxinemia was resolved when repeat lab testing was performed one week later, which is consistent with previous observations of this phenomenon. It is also appears likely that the patient's primary hyperparathyroidism and hyper calcemia contributed to her depressive episode which was severe enough to cause associated psychosis.

Weber's study showed that preoperatively, patients with Primary Hyperparathyroidism (pHPT) suffered more from depression, suicidal ideation, and anxiety, and they had reduced Health-Related Quality of Life (HRQOL), compared with a control group with nontoxic thyroid diseases and the general population. After receiving a parathyroidectomy, symptoms of depression and anxiety declined, and HRQOL significantly improved in the first year. Para thyroid ectomies were also associated with a 51% reduced prevalence of suicidal ideation. These findings suggest that successful Para Thyroid ectomies not only cure pHPT physical symptoms but reduce patients' psychologic distress and improves their HRQOL [13].

In conclusion, while psychiatric illnesses can be associated or even triggered by various thyroid disorders, there also appears to be frequent instances of abnormal thyroid findings secondary to the onset of an acute psychiatric illness. The common thyroid function profile is that of normal or high T3 with high T4 and high or normal TSH. There is currently no data to suggest a clinical significance of this manifestation of euthyroid hyper thyroxinemia, and the thyroid function tests return to normal within a few weeks. No intervention is required to correct the abnormal findings, but repeat thyroid function tests should be obtained within a few weeks to confirm the return to normal levels.

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