CASE REPORT

A case of TSHoma mimicking Graves 'disease and makes GH cosecrete

Emine Sener Aydin, Bahri Evren, Ibrahim Sahin

Inönü University, Medicine Faculty, Department of Endocrinology And Metabolis, Malatya, Türkiye

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Abstract

Thyrotropinomas (TSHoma) are rare pituitary adenomas. TSHomas can synthesize other hormones simultaneously. Co-secretion of TSH and GH is rarely reported in the literature. In these patients, signs of hyperthyroidism and acromegaly can be observed together. Its clinic is heterogeneous and in some cases, symptoms of thyrotoxicosis may mask the acromegaly symptoms. Some TSHoma patients may also be mistakenly diagnosed with Graves and experience a delay in diagnosis. We aimed to present a unique case with a diagnosis of TSHoma, who was referred to our center when Euthyroidism was not achieved and was followed up with a pre-diagnosis of Graves and also had GH co-secretion.

Keywords: TSHoma, acromegaly, graves

Introduction

Thyrotropinoma (TSHoma) is one of the rare causes of functional pituitary adenomas. They are seen in 0.5-3% of all pituitary adenomas [1,2]. Most of them are macroadenomas at the time of diagnosis [3]. TSHoma releases thyrotropin-releasing hormone [TSH]. It can synthesize other hormones simultaneously. Growth hormone (GH), prolactin, and gonadotropin secretion may also may be co-secreted [4]. TSHomas are more common in the fifth and sixth decades. Studies have found that it does not differ in terms of ethnic origin and gender [5,6]. In this case, we aimed to show that macroadenomas and TSHomas with simultaneous TSH and GH secretion can progress with minimally suppressed TSH level and thyrotoxicosis symptoms may mask clinical signs of acromegaly.

Case Report

Sixty-one year old male patient. He applied to our clinic with complaints of tremor in the hands, feet, sweating in the first place, growth in the hands and feet, palpitations and headache for a year. While the patient was being followed with the diagnosis of Graves for a year at an other center, he was referred to us because euthyroidism could not be achieved. When he applied, he was receiving 40mg methimazole and 40mg propranolol daily. In the physical examination of the patient, the pulse rate was 80 beats / min rhythmic, the skin was moist, and the hands had a square hand appearance. (Figure 1,2) Thyroid was palpable with nodules, and was stage 2. In the examinations of the patient; TSH: 0.24mIU / ML (0.35-5.5), free triiodothyronine (fT3): 11.36pg/ml (2.3-4.2), ((fT4): 7.34ng/ml (0.89-1.76), thyroid receptor specific antibody was negative. Due to the minimally suppressed TSH value of the patient, anterior pituitary hormones and control thyroid function tests were requested in terms of secondary hyperthyroidism. Control values TSH: 1.77mIU /ml, fT4: 3.82ng/ml, fT3: 4.92pg/ml, growth hormone (GH ): 2.02ng/ml, IGF-1: 586ng/ml (44.7-210) Other anterior pituitary hormones of the patient were found to be normal. Dynamic tests were applied to the patient with pre-diagnosis of TSHoma and acromegaly. TRH TSH stimulation test was applied for the differential diagnosis of TSHoma. In our patients, it was observed that there was no TSH response in the TRH stimulation test. In the growth hormone suppression test, the growth hormone level was 2,6ng/ml, there was no supression. The patient's pituitary MR (Magnetic resonance imaging):was reported as “There is a macroadenoma structure that is approximately 28.5x7x17mm in size that invades the right cavernous sinus grade 2 in the adenohypophysis gland region and is observed heterogeneously hypointense in dynamic contrast series (Figure 3).

The computerized visual field test of the patient was normal. In the thyroid USG performans on the patient, the thyroid was bilaterally ondular and a nodül with the largest 22x17mm in the right lobi and 20x15mm in the left lobe was observerd. Fine needle aspiration biopsy was performed from the nodules...
observed in the patient's thyroid gland. Biopsy result was reported as "benign cytology". With these findings, the patient was diagnosed with TSHoma and Acromegaly. The operation decision was made by talking to the neurosurgery department and it was planned to give the patient a somatostatin analogue until surgery.

**Figure 1.** Acromegalic facial image

**Figure 2.** Growth in hands

**Figure 3.** MR image of pituitary adenoma

**Discussion**

Sixty-one year old male patient. The patient, who had symptoms of thyrotoxicosis and acral growth for one year, was treated with the diagnosis of Graves disease in an external center, but was referred to our clinic when euthyroidism was not achieved.

TSHomas are rarely seen among pituitary adenomas. They are seen in 0.5-3% of all pituitary adenomas [1,2]. They may be microadenoma or macroadenoma, but most of them are macroadenomas at the time of diagnosis [3]. TSHomas are more common in the fifth and sixth decades. Studies have found that it does not differ in terms of ethnic origin and gender [5,6]. Our patient was also a patient who was diagnosed in the sixth decade in accordance with the literature.

Although the molecular mechanisms in the development of TSH are not known exactly, PIT 1 overexpression [7,8] and Trotropin Hormone receptor Beta mutation are molecular changes observed in TSH oma. TSH levels that are not suppressed in TSHomas are probably related to thyroid hormone receptor beta mutation [9,10]. Rarely, it may progress with cavernous sinus invasion. PIT-1 overexpression and high Ki-67 increase the risk of invasive course and recurrence of TSHoma [6,11]. TSH can synthesize 25% of hormones other than TSH simultaneously. Growth hormone (GH), prolactin, and gonadotropin can be synthesized [4]. This situation is associated with the expression of PROP-1, PIT-1 of adenoma [12].

TSH/GH Co-secretion adenomas are rare tumors. Therefore the information about these tumors is limited. According to a case series of 12 patients retrospectively examined in China adenomas that secrete TSH/GH together are generally in the form of macroadenomas. Hyperthyroidism due to clinical TSH and GH effects and with symptoms of acromegaly. The clinical findings of the secreted hormones may not always occur or they mask the effects of each other TSHomas are in the group of aggressive
pituitary adenomas according to the WHO (World Health Organization) classification TSH/GH secreting tumors are more aggressive than tumors that secrete only TSH. In particular, tumors containing transcription factors such as PIT and PROP have a more aggressive course and a high recurrence rate. The treatment of TSH/GH secreting tumors is surgical excision. Recurrences commonly occur after surgery [13]. Our patient also had a hyperthyroidism clinic led him to be followed up in an external center with the diagnosis of Graves and the diagnosis of acromegaly was delayed.

Since TSHomas are often diagnosed late, they are symptomatic at the time of diagnosis. Thyrotoxic symptoms are the most common [3,14]. Our patient had symptoms of thyrotoxicosis. Headache and vision loss can be observed in 20-25% of patients due to the effect of the mass [15]. The gonadal axis can be suppressed, amenorrhea in women and a decrease in libido in men can be observed [16]. Our patient also had a complaint of headache. TSH-omas are typically benign [11]. Rarely, it may progress with cavernous sinus invasion [6,11]. Our case also had cavernous sinus invasion radiologically. TSH can synthesize 25% of hormones other than TSH simultaneously. Prolactin and gonadotropin, being the most growth hormone, can be synthesized [4]. Acromegaly symptoms can be masked in adenomas synthesized together with TSH and GH [17,18]. Since the symptoms of sweating and palpitations were prominent in our patient and they were mainly associated with hyperthyroidism, he was not questioned for acromegaly and was not investigated. The size of the adenoma and the thyroid size may be larger in patients with a combination of TSH and acromegaly. Acral growth, thyroid nodule and sweating can also be observed in patients depending on the height of growth hormone [19,20]. Our patient also had acral enlargement, thyroid nodule, and sweating symptoms.

In a patient with clinical symptoms of thyrotoxicosis, TSH levels that are not suppressed despite increased fT3 and fT4 levels are consistent with laboratory findings of central hyperthyroidism [3]. Our patient had increased free thyroid hormones and minimally suppressed TSH levels. In this respect, he had different laboratory data from the cases in the literature. The concomitant diagnosis of acromegaly is made by increased insulin like growth-factor-1 (IGF-1), GH levels, clinical and GH suppression test [21]. In addition to acromegaly symptoms, our patient also had increased GH and IGF1 levels. In the Thyrotropin releasing hormone (TRH) stimulation test, which is one of the dynamic tests performed on patients, a decreased response in TSH-oma is obtained. TSH response is increased in thyroid hormone resistance. Another dynamic test is the T3 suppression test. In this test, the TRH stimulation test and TSH-oma are applied when the differential diagnosis of thyroid hormone resistance is not made. In this test, the absence of suppression in TSH is interpreted in favor of TSH-oma, and the presence of TSH suppression in favor of thyroid hormone resistance [22]. In addition, TSH suppression can be measured using somatostatin analogues. If there is suppression at TSH level, TSH is interpreted in favor of thyroid hormone resistance if suppression does not develop [23]. In our case, the TRH stimulation test was performed. No stimulation response occurred in TSH. For the diagnosis of acromegaly, GH suppression test was performed on the patient. There was no suppression response in GH. Pituitary magnetic resonance (MR) is used in the diagnosis of TSHoma in radiological imaging. They are generally observed as macroadroma [3]. In our patient, it was the size of a macroadenoma.

Surgery is the gold standard treatment for TSHoma. Post-surgical remission rate is between 35-58% [1,22,24]. Preoperative medical treatment can be initiated in patients to increase remission after surgery. Since TSHomas contain somatostatin and dopamine receptors, somatostatin analogs (SSA) and dopamine agonists can be used in treatment. The response to somatostatin analogues is very good when GH and TSH are released together giving preoperative somatostatin treatment reduces tumor size, improves visual functions, facilitates postoperative euthyroidism, decreases thyroid volume, and decreases growth hormone and IGF1 levels [4,15,25]. Resistance to SSA is rarely observed. Gastrointestinal side effects can be monitored temporarily [16]. We also started a preoperative somatostatin analogue for our patient.

After surgical treatment, cure evaluation is made with TSH, IGF1, alpha glycoprotein sub unit (aGSU). TSH levels that cannot be detected in the serum one week after surgery are an indicator of good prognosis [15]. Stereotactic radiotherapy can be applied in cases where medical and surgical treatment is contraindicated or unsuccessful [4]. Gamma knife is a frequently used radiosurgery method. It should not be applied to masses with a diameter greater than 4 centimeters, as it will increase pituitary tissue damage [2]. Long-term follow-up of patients is performed by pituitary MR imaging in patients with symptoms, laboratory findings, and especially residual tissue [27].

Conclusion

In conclusion, secondary hyperthyroidism should be considered in differential diagnosis in patients with hyperthyroidism resistant to treatment at advanced ages. Findings of second hormone elevation that may accompany with a careful history and detailed physical examination should not be missed.

Conflict of interests

The authors declare that there is no conflict of interest in the study.

Financial Disclosure

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Ethical approval

Ethical approval was not received because it is a case report.

References


