Toxic Thyroid Adenoma and Acromegaly: An Unusual Association

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Abstract

Hyperthyroidism is seen in 3.5-26% of acromegalic subjects, and can occur through TSH-dependent or independent mechanisms. Thyrotoxicosis as the first presenting illness in acromegaly is particularly uncommon, as described in this patient who had both acromegaly and a toxic thyroid adenoma.

INTRODUCTION

Hyperthyroidism can occur in about 3.5-26% of acromegalic subjects, and may be due to a concurrent TSH-secreting adenoma, or because of the effects of growth hormone (GH) excess on thyroid follicles. We report a patient with acromegaly who initially presented with thyrotoxicosis.

CASE REPORT

A 28 year lady was referred to us for management of thyrotoxicosis. Six months ago, she had presented to her family physician with palpitations, heat intolerance and weight loss. At that time the thyroid function tests showed: T4: 27 µg/dl (normal 5-12.6) and TSH 0.03 µIU/ml (0.6-4.5). She had been started on propyl-thiouracil tablets initially, and later changed over to carbimazole tablets, the dose increased to 80 mg/day, with which dramatic improvements occurred. A repeat TSH obtained after 6 weeks of therapy was 0.2 µIU/ml. Currently, she did not have thyrotoxic or hypothyroid symptoms involving temperature intolerance, altered bowel habits or fatigue. She admitted to having noticed mild body swelling, especially of the hands and feet, and a ring that had become tight around a finger. She was married for eight years, with no children, and had undergone unsuccessful evaluation for infertility. Menstrual cycles were irregular, usually delayed by 2-4 weeks on most occasions. There was no history of headache or visual disturbances. Family history was unremarkable. On examination, her pulse was 90/minute and the blood pressure 130/90 mm Hg; there was no postural fall of blood pressure. There was a mild prominence of the supra-orbital ridges and malocclusion of the teeth. Hands and feet appeared muscular. A thyroid nodule measuring 3 cm in size could be palpated over the isthmus, and the rest of the gland was no palpable. Secondary sex characters were normally present. Nervous system examination was normal, including visual field assessment by confrontation and fundus examination. Systemic examination was otherwise unremarkable. Investigations: Total hemogram, electrolytes and renal function parameters were normal. Serum calcium was 9.0 mg/dl, phosphorus 4.1 mg/dl and alkaline phosphatase 120 units/l. Hormone assays showed: T3 100 ng/dl (70-240), T4 7 µg/dl, TSH 13 µIU/ml, Prolactin 18 ng/ml, 8.00 AM cortisol 13 µg/dl (5 to 20). LH and FSH levels were 1.2 and 2.8 IU/L (2 to 6 and 1.8 to 7.2 respectively). After glucose suppression; the growth hormone level was 6.8 ng/ml (normal <1). MRI pituitary revealed a 13 x 18 x
18 mm pituitary macroadenoma just adjacent to the optic chiasma (Fig. 1). Anti TPO antibodies were negative. Fine needle aspiration cytology showed sheets of follicular cells with large follicles and hyperplastic epithelium. Ultrasound revealed a single 3 x 4 cm nodule in the thyroid without regional lymphadenopathy. Automated perimetry revealed field defect in superior temporal quadrant. A chest X-ray, echocardiogram and electrocardiogram were normal. Carbimazole has been stopped and she awaits transsphenoidal pituitary surgery.

DISCUSSION

Acromegaly is associated with a spectrum of thyroid abnormalities, the most common being goiter (70%). Most of these goiters are diffuse. The prevalence of goiter in acromegalics from iodine deficient areas is reported to be 30%. Only about 5% of these goiters are associated with hyperthyroidism. Thyrotoxicosis as the presenting symptom of acromegaly (as in our patient) is distinctly rare, there being only one anecdotal report of a patient presenting concomitantly with both diseases.

The possibility that toxic thyroid adenoma preceded acromegaly is unlikely, considering that acromegaly becomes clinically apparent only after several years. It is plausible to conclude that toxic thyroid adenoma followed the onset of acromegaly.

The growth promoting effects of GH on thyroid follicular cells or a concurrent TSH excess are the conventional hypotheses liking acromegaly to thyrotoxicosis. Current evidence favours a TSH independent mechanism in most cases. In addition, G protein abnormalities can constitutively activate GH releasing hormone (GHRH) receptors leading to acromegaly, as well as cause a constitutive TSH receptor activation leading to thyrotoxicosis. The most characteristic abnormality is a mutation in the gene encoding the alpha subunit of the Gs protein, which mediates the actions of TSH and GNRH. These abnormalities have been associated with the Mc Cune Albright Syndrome, which consists of café au lait spots, endocrine hyperfunction and polyostotic fibrous dysplasia. In a report similar to ours, a variant of Mc Cune Albright Syndrome has been described in a 36-year old woman, who had acromegaly and toxic nodular goiter. Skin pigmentation was absent, and fibrous dysplasia was a chance finding on pituitary imaging. It is difficult to precisely pin point the molecular defects underlying the linkage between thyrotoxicosis and acromegaly in most cases. However, such cases highlighting unusual associations often yield fascinating insights into the genesis of multiple endocrine hyperfunction as a result of the Gs alpha protein abnormality.

It has been reported that the coexistence of thyrotoxicosis increases cardiovascular risk in acromegalic subjects, especially in subjects with high GH and IGF-1 levels. Therefore treatment should aim at normalizing both thyroid hormone and GH levels in such cases. The documentation of such cases is important as they help in a better understanding of the association between thyrotoxicosis and acromegaly.

REFERENCES