

# Follicular Cell Thyroid Carcinoma in a Patient with Acromegaly

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Acromegaly is a disease resulting from excessive production of growth hormone in adults most commonly as a result of pituitary adenoma. The clinical features of acromegaly are bony and soft tissue overgrowth, metabolic abnormalities, visceromegaly, and symptoms related to tumoral mass itself. Patients with acromegaly have demonstrated an increased incidence of benign and malignant tumor occurrence. Thyroid and colon are the organs often involved in tumoral process. We report an acromegaly case with follicular cell thyroid carcinoma.

**Key words:** Acromegaly, thyroid carcinoma

## Introduction

Growth hormone (GH) excess results in acromegaly in adults. Acromegaly is an insidious disease associated with bony and soft tissue overgrowth and usually not diagnosed till the cosmetic changes developed. It's estimated prevalence is 1 case per 20 000 and incidence is 3 cases per million per year. The peak incidence is at 4<sup>th</sup> and 6<sup>th</sup> decades (1).

Almost all patients with acromegaly (>99%) have pituitary adenomas with somatotroph or somatomammotroph origin. Adenomas are usually sporadic but may be, associated with multiple endocrine neoplasia syndromes. Acromegaly rarely results from pituitary somatotroph hyperplasia. Clinical features results from both systemic effects of GH and insulin like growth factor-I (IGF-I), and tumoral mass itself (1).

The incidence of both benign and malignant tumors were reported to be increased and related to

the increased levels of GH and IGF-I in patients with acromegaly. The most common encountered benign tumoral condition associated with acromegaly is nodular goiter. Patients with acromegaly suffer from an increased incidence of malignancy, particularly thyroid, colon, breast, ovary, and lymphoma (2). We present and discuss a follicular thyroid carcinoma case with acromegaly in the light of the literature.

## Case Report

Fifty four year old male patient admitted to our clinic with a two months history of dispnea. Physical examination revealed enlargement of the thyroid gland (grade III), and normal oscultation findings of the chest. Posterior-anterior X-ray of the chest revealed a mass image in the upper part of the mediastinum. Thyroid ultrasonography showed enlargement of the thyroid gland containing nodules bilaterally and extending to retrosternal region. Scintigraphic examination of the thyroid gland revealed a suppressed right lobe, and a hyperactive nodule in the left lobe. The results of the laboratory examination were as follows: Free-T<sub>3</sub>: 5.35 (1.8-4.6) pg/ml, Free-T<sub>4</sub>: 1.81 (0.9-1.7) ng/ml, TSH: 0.134 (0.2-4.2) µIU/ml. The patient underwent surgical intervention and total thyroi-

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dectomy was performed. The histopathologic findings of the thyroid gland were minimally invasive follicular thyroid carcinoma with micro-follicular variant.

In the history of the patient, he had been diagnosed as acromegaly and had been performed transphenoidal hypophysectomy in 1990. In the follow-up period, magnetic resonance imaging (MRI) of the sella revealed a suspicion of mass image, but the laboratory examinations were within the normal limits in 1995. In 1990, he had been performed a fine needle aspiration biopsy of the thyroid gland because of multinodular goiter and finally was prescribed L-thyroxin, but he did not take the medication regularly. The physical examination revealed increased foot and hand size, and prognathism. Laboratory examination revealed after surgery: Free-T<sub>3</sub>: 1.33 (1.8-4.6) pg/ml, Free-T<sub>4</sub>: 0.089 (0.9-1.7) pg/ml, TSH: 31.1 (0.2-4.2)  $\mu$ IU/ml, GH: 24 (0.06-5.0) ng/ml, IGF-I: 373 (111-314) ng/ml, while prolactin, LH, FSH, cortisol, ACTH levels were within the normal limits. Electrocardiography and echocardiography examinations were normal. In the post-operative period, I<sup>131</sup> scintigraphy examination of the whole body only revealed 3 focuses at the thyroid region and radioactive iodine therapy was planned. Computerized tomography of the brain showed a 3 x 2.5 x 2 cm sized mass image in the sella extending to the cavernous sinuses. MRI of the sella also showed a pituitary macroadenoma destroying and widening the sella.

### Discussion

Pituitary adenomas are found in almost all patients with acromegaly. It takes approximately 10 years from the time that overproduction of GH begins, to become clinically evident. Moon et al. first reported the malignant potential of the GH in 1950. They found that rats treated with GH commonly developed pulmonary and lymphatic malignancies (3,4). Higuchi et al. investigated the incidence of malignant tumors retrospectively in 44 patients with acromegaly and with a total 670 years of the duration of disease. Male patients found to have a significantly higher ratio of malignancy than expected and they suggested that male patients with acromegaly might have high risk of malignancy and careful screening for tumors both

before and after surgical and medical treatment is necessary (5). Barzilay et al. studied records of 87 patients with acromegaly retrospectively and reported 2.45-fold increased rate of malignant tumors. They found 2 patients with papillary thyroid carcinoma and reported the rate of the thyroid carcinoma was excessive. Carcinoma of the thyroid was found during recurrent or active acromegaly. Among benign lesions, goiters, predominantly nodular, were seen in 25% of the patients in addition to a large number mesenchymal lesions. They suggested that this could be related to stimulatory effects of GH or IGF-I on receptors present in these organs (6,7). Balkany et al. also reported 3 cases in whom acromegaly and thyroid carcinoma were associated (8). And Ozgen et al. reported a case with acromegaly and follicular thyroid carcinoma (9). In our case the diagnosis was minimally invasive follicular carcinoma of the thyroid with microfollicular variant, in the patient with recurrent and active acromegaly similar with the literature.

In a multi-center study, Gasperi et al. investigated the prevalence of the thyroid diseases in 258 patients with active acromegaly. Two hundred and two out of 258 acromegalic patients (78%) were affected by thyroid disorders with a significantly higher prevalence with respect to the control group (27%,  $p < 0.0001$ ). Thyroid volume was correlated with the estimated duration of acromegaly, but not with age or serum levels of GH, IGF-I and TSH concentrations. The prevalence of thyroid carcinoma was slightly increased than in general population (10). In our case, the patient had been diagnosed as multinodular goiter and prescribed L-thyroxin but did not take the medication regularly, and finally developed thyroid carcinoma after twelve years of the diagnosis of acromegaly and multinodular goiter established. At the time of thyroid cancer were diagnosed, the levels of GH and IGF-I were found to be increased.

In patients with acromegaly the increased incidence of malignant diseases are thought to be associated with the increased level of IGF-I. IGF-I was reported to potentiates the TSH induced thyroid cellular growth in normal human thyroid cells (11) and IGF-I receptors were found to be present in neoplastic human thyroid tissues (12). Also, IGF-I was reported to stimulate DNA

synthesis and cell growth in a variety of cell types, especially mesenchymal origin (13). The cell growth results in benign proliferative pathology such as nodules or polyps, but is also more likely to generate tumorigenic mutations, activating oncogens such as ras, within these tissues (14). A further mechanism, by which IGF-I may serve to promote the development of malignancy, is by inhibition of apoptosis (15).

As a result, there are many reports suggesting the relationship between excessive GH levels and thyroid carcinoma. Generally, cases with papillary thyroid carcinoma were reported. In our case, the diagnosis was follicular thyroid carcinoma with microfollicular variant in association with acromegaly. Patient have recurrent acromegaly with macroadenoma. We conclude that the development of thyroid cancer may be related with long duration of excessive GH and IGF-I levels.

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