

## Evaluation of the Relationship Between Thyroid Nodules and Disease Activity in Patients with Acromegaly

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### Abstract

**Introduction:** Development of thyroid nodules is common in acromegaly patients. However data related with the clinical course of these nodules is rare in literature. We aimed to evaluate the relationship between thyroid nodules and disease activity in acromegaly patients.

**Material and Methods:** Presence of nodular thyroid disease, papillary thyroid cancer and parameters related with nodule development were investigated in a total of 138 acromegaly patients (F:73, M:65). In patients who were being followed up during the study period (n:56), thyroid ultrasonography was performed by an experienced radiologist and changes in nodule size (Group -1: decrease by >20%, Group-2: stationary with 0-20% change, Group-3 increase by >20%) was compared with disease activity.

**Results:** Frequency of thyroid nodules was %69 (n=95; 20 solitary nodule/75 multiple nodules), FNAB biopsy (n:55) revealed 66% benign, 16% suspicious, 11% malignant and 7% nondiagnostic cytological results. Patients with thyroid nodules were older (p=0.05), had higher baseline IGF-1 % ULN (upper limit of normal) levels (p=0.01) and colon polyps were more frequent (p=0.017) (Table 1). Nodule size was stationary, decreased or increased in 45%, 30% and 25% of the patients, respectively. Presence of disease activity was significantly higher in patients with increased nodule size (p<0.0001) (Table 2).

**Conclusion:** Thyroid nodules are correlated with age and baseline IGF-1 levels in acromegaly patients. Thyroid nodules should be monitored regularly in patients with active acromegaly.

Table 1. Comparison of functional pituitary adenomas in terms of nodular thyroid disease and papillary thyroid carcinoma.

N=232	Acromegaly (n=138)	Prolactinoma (n=59)	Cushing's Disease (n=35)	p
Sex (Male/Female)	65/73	22/37	7/28	0.009*
Age at diagnosis (years) mean±SD	42±13	36±13	36±11	<0.001°
Prevalence of nodular thyroid disease (n, %)	95 (69)	21 (36)	12 (34)	<0.001°
Single nodule (n)/Multiple nodules (n)	20/75	7/14	6/6	NS
Dominant nodule size (mm) mean±SD	17.4±9.7	15.5±10.3	14.5±6.7	NS
FNA cytology (n, % of patients with nodules)	55 (58)	10 (48)	8 (67)	NS
Benign (n, %)	36 (66)	8 (80)	3 (38)	
Suspicious (n, %)	9 (16)	1 (10)	2 (25)	
Malignancy (n, %)	6 (11)	-	2 (25)	
Nondiagnostic (n, %)	4 (7)	1 (10)	1 (12)	
Surgery (n, % of patients with nodules)	27 (28)	3 (14)	5 (42)	NS
Suspicion of malignancy	13 (48)	2 (67)	5 (100)	
Increased nodule size	8 (30)	1 (33)	-	
Intrathoracic goiter	4 (15)	-	-	
Thyrotoxicosis	2 (7)	-	-	
Prevalence of papillary thyroid carcinoma (n, % of patients with nodules)	15 (16)	2 (10)	4 (33)	NS
Largest tumor diameter (mm) (mean±SD)	11±9 (1-30)	26±12 (17-35)	21±9 (14-9)	
High risk subtype (n, %)	1	0	1	
RAI therapy (n, %)	9	2	4	
Remission rate at last visit (n, %)	14 (93)	2 (100)	4 (100)	

p<0.05, statistically significant, Significant p values are shown in bold; FNA; fine needle aspiration, RAI; radioactive iodine therapy; \*: Acromegaly & Cushing's Disease; °: Acromegaly & Cushing's Disease, acromegaly & prolactinoma

Table 2. Comparison of patients with and without nodule in terms of clinical and laboratory findings

<b>N=232</b>	<b>Patients with nodule (n=128)</b>	<b>Patients without nodule (n=104)</b>	<b>p</b>
Sex (Male/Female)	52/76	42/62	NS
Age at diagnosis (years) mean±SD	42±13	37±13	0.01
Max. adenoma diameter (mm) mean±SD	16±10	17±12	NS
TSH levels <sup>o</sup> (mIU/L) mean±SD	1.9±3	1.9±1.8	NS
Glucose metabolism disorders* (n, %)	92 (72)	57 (55)	0.006
Fasting plasma glucose (mg/dl) mean±SD	116±41	102±32	0.014
HbA1c (%) mean±SD	7.1±1.9	6.4±1.4	NS
HOMA-IR mean±SD	4.9±5.1	4.1±3.3	NS
Baseline IGF-1 % ULN (patients with acromegaly) mean±SD	334±149	254±82	0.01
Baseline GH levels (ng/ml) (patients with acromegaly) mean±SD	19±17	19±14	NS
Colonic polyp (n, %) (patients with acromegaly)	29 (31)	5 (12)	0.017
Baseline PRL levels (ng/ml) (patients with prolactinoma) mean±SD	1343±2902	1329±2381	NS
Baseline ACTH levels (pg/ml) (patients with Cushing's disease) mean±SD	74±47	85±43	NS
Baseline cortisol levels (µg/dL) (patients with Cushing's disease) mean±SD	31±11	28±10	NS

p<0.05 statistically significant, Significant p values are shown in bold; <sup>o</sup>: TSH level was assessed in patients without central hypothyroidism; \*: Patients with diabetes mellitus or prediabetes; NS, not significant; TSH, thyroid stimulating hormone; HOMA-IR, homeostasis model assessment of insulin resistance; IGF-1, insulin-like growth factor-1; GH, growth hormone; IGF-1 % ULN; the % increase compared with the upper limit of normal, PRL, prolactin; ACTH, adrenocorticotrophic hormone.