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Thyroid Nodules Colon Polyps and Gallbladder Polyps In Acromegaly Patients

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ABSTRACT

Acromegaly is a pituitary disease characterized by excess growth hormone (GH) secretion in adults which results in several comorbidities and increased mortality. Studies suggest an increased prevalence of both benign and malignant tumors including thyroid nodules, breast diseases and colon polyps in acromegaly. The risk of gallbladder polyps also seems to be increased in acromegaly. Coexistence of thyroid nodules, colon polyps and gallbladder polyps in acromegaly remains uninvestigated.

In this study we aimed to investigate the risk factors for the development of thyroid nodules, colon polyps and gallbladder polyps and we aimed to see whether the presence of thyroid nodules is associated with colon polyps or gallbladder polyps in patients with acromegaly.

Thirty eight acromegaly patients who are being followed up in the outpatient clinics of Endocrinology and Metabolism in a tertiary care center were involved in the study. Thyroid ultrasonography (US) was performed by the same experienced observer. Abdominal and hepatobiliary ultrasonography reports and colonoscopy reports of all patients with acromegaly were analyzed retrospectively.

The present study showed that the presence of thyroid nodules, colon polyps and gall bladder polyps in acromegaly does not depend on one another. In our study, we found that the presence of thyroid nodules, colon polyps and gallbladder polyps in acromegaly were not linked to each other. In other words, the presence of one or both of these comorbidities in a patient was not found to be associated with the others.

When clinically indicated, we recommend that each patient with acromegaly be evaluated separately for thyroid nodules, colon polyps, and gallbladder polyps.

Keywords:

Introduction

Acromegaly is a pituitary disease characterized by excess growth hormone (GH) secretion in adults, resulting in several comorbidities and increased mortality (1). Studies suggest an increased prevalence of both benign and malignant tumors including thyroid nodules, breast diseases, and colon polyps in acromegaly (2,3,4). The risk of gallbladder polyps also seems to be increased in acromegaly (5). The guidelines are inconsistent regarding the routine surveillance imaging procedures to be carried out in patients with acromegaly (6,7,8). However, colonoscopy, which is a more difficult and invasive procedure, is needed to detect colon polyps. The coexistence of thyroid nodules, colon polyps, and gallbladder polyps in acromegaly remains uninvestigated. It is not known whether the presence of thyroid nodules or gallbladder polyps may be a clue for the presence of colon polyps or not.

In this study, we aimed to investigate the risk factors for the development of thyroid nodules, colon polyps, and gallbladder polyps, and we aimed to see whether the presence of thyroid nodules is associated with colon polyps or gallbladder polyps in patients with acromegaly.

Materials and Methods

Thirty-eight acromegaly patients who are being followed up in the outpatient clinics of Endocrinology and Metabolism in a tertiary care center were involved in the study. Written informed consent was obtained from the

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participants prior to the study. The diagnosis of acromegaly was made on the basis of characteristic clinical features, elevated IGF-1 levels over normal values for age and gender, and failure of GH suppression below 1 ng/ml after a 75 g oral glucose load (9).

Demographic data and medical history of all subjects were recorded; physical examination and anthropometric measurements were performed. Weight and height were measured. The body mass index (BMI) was measured by dividing the weight by the square of the height (kg/m^2).

Serum IGF-1, GH, free T4, TSH were obtained from all patients. Growth hormone and IGF-1 levels were analyzed with the radioimmunoassays method by using the DIAsource analyzer(Belgium). Serum IGF-1 levels were compared to the age-gender adjusted normal range. Thyroid-stimulating hormone (TSH), free thyroxine (fT4), were measured with specific electrochemiluminescence immunoassays method by using the Roche Cobas 8000 analyzer (Rotkreuz, Switzerland).

Thyroid ultrasonography (US) was performed by the same experienced observer using high-resolution B-mode ultrasound images (Hitachi EUB-7000hv) with a 13-MHz linear array transducer. The volume of each thyroid lobe was calculated by the ellipsoid model formula (length x thickness x width x 0.52) (10). Abdominal and hepatobiliary ultrasonography reports of all patients with acromegaly were reviewed retrospectively. The ultrasonography was performed by senior residents in radiology. The colonoscopy reports of all patients with acromegaly were reviewed retrospectively. Colonoscopies were performed by consultant specialists in gastroenterology.

Remission is defined as the latest IGF -1 level within the reference range for age and sex (either with or without medical treatment).

Statistical Analysis: Statistical analysis was performed using SPSS Version 25. Normality distribution analysis of the data was performed by using Kolmogorov-Smirnov and Shapiro-Wilk tests. Normally distributed parametric data were presented as mean±SD and the significance of intergroup variance were analyzed using the Student-t-test. Data that did not fit to normal distribution were presented as mean (minimum-maximum). Non-normally distributed data were expressed as the median values and compared using the Mann–Whitney U-test. The Chi-square test was used to analyze categorical variables. The correlation between parameters that are in conformity with normal distribution was studied by using Pearson correlation analysis, and Spearman rho correlation test was used that was not normally distributed and Spearman rho correlation test was used for those without normal distribution, $p < 0.05$ was considered significant.

Results

A total of 38 acromegaly patients were included in the study. The mean age of the patients was 52.1±10.6 and 27 of the patients was female. Demographic and clinical features of the patients are summarized in Table 1. Median follow up period of the patients was 6,5 years after diagnosis. Half of the patients were receiving medical treatment (somatostatin analogues or pegvisomant) for control of acromegaly, whereas the others were in remission without medical therapy.

Thyroid Nodules: Twenty five patients had thyroid nodules. Fine needle aspiration (FNA) biopsy was performed in 16 nodules-selected according to the TIRADS score from 13 patients. Cytopathological analysis were as follows; ten were benign, two were nondiagnostic. These patients did not perform a second biopsy. One patient whose FNA biopsy was suspicious for malignancy underwent total thyroidectomy, the pathological diagnosis of this patient was consistent with papillary thyroid cancer.

Patients with thyroid nodules were older (median age: 54.92±9) than the patients without thyroid nodules (median age: 46 ±11.6) but the difference was not significant (p= 0.14). The prevalence of thyroid nodules was comparable in males and females (18/27 of females and 8/11 of males p=0,7).

Eleven of the 16 patients in remission had thyroid nodules whereas all of the 9 patients in the non-remission group had thyroid nodules (p= 0.01). Neither the number of nodules nor the volume was correlated with the IGF-1 levels at diagnosis (p=0.06 and p=0.95 respectively). However the latest IGF-1 level was significantly correlated with the number of thyroid nodules and the volume of the dominant thyroid nodule (p=0.04 r=0.46).

Colon Polyps: Nine patients had colon polyps. The histologic subtypes of polyps were as follows; tubular adenoma (4 patients), hyperplastic polyps (2 patients), inflammatory polyps (1 patient), tubulovillous adenoma (1 patient), tubular adenoma with malignant foci (1 patient). The

Table 1. Demographic and Clinical Characteristics of The Patients

Patients	Total N=38
Age (year)	52.1±10.6
Sex	
Female	27 (%71.1)
Male	11 (%28.9)
Follow-up (year) median (min- max)	6.5 (1-31)
Medical therapy	
No medical therapy	20 (%52.6)
Somatostatin	17 (%44.7)
Pegvisomant	1 (%2.6)
RT	7 (%18.4)
Colon polyps	9 (%23.7)
Gallbladder polyps	3 (%7.9)
Cholelithiasis	6 (%15.8)
Thyroid nodules	25 (%67.2)

RT: Radiotherapy

Table 2. Comparison of The Data of The Group With and Without Thyroid Nodules

	Thyroid nodule(+) N=25	Thyroid nodule(-) N=13	p value
First IGF-1 (ng/dl)	838.86±471.18	609.16±386.18	0.28
Latest IGF-1 (ng/dl)	252.42±137.16	115.35±87.63	0.008*
Medical therapy			0.73
No medical therapy	13 (%50)	7 (%58.3)	
Somatostatin	12 (%46.2)	5 (%41.7)	
Pegvisomant	1 (%3.8)	-	
Colon polyp	7 (%28)	2 (%20)	0.62
Gallbladder polyp	2 (%8)	1 (%8.3)	0.97
RT	4 (%15.4)	3 (%25)	0.47

IGF-1:İnsülin like growth factor-1 RT: Radiotherapy
*significantly different, p<0.01

polyps were located in descending colon in three patients, sigmoid colon in two patients, rectum in two patients, transverse colon in one patient, and cecum in one patient. The median age of the patients with colon polyps (56.44±5.5) was not different from the age of patients without colon polyps (51.46±10) (p= 0.17). Patients with colon polyps had a longer duration of disease (12 years (min, max: 1-21)) when compared to the patients without colon polyps (6 years (min,max:1-31)), but the difference was not significant(p=0,053). Eight of the nine patients with colon polyps were under treatment with somatostatin analogs, whereas 10 of the 29 patients without colon polyps were being treated with these agents. The risk for colon polyps in the non-remission group was not significantly different from the risk in patients in remission. (4/9 in the non-remission group vs. 5/20 in the remission group p= 0.17)

Gallbladder Polyps: Three patients had gallbladder polyps. Two of the three patients with gallbladder polyps were under treatment with somatostatin analogs. All patients with gallbladder polyps were in remission.

Table 2 shows the results of comparing the data of the groups with and without thyroid nodules. There wasn't any significant association between the presence of thyroid nodules and colon polyps, nor between the thyroid nodules and gallbladder polyps.

Discussion

Acromegaly is a chronic disease caused by GH hypersecretion and, in turn, overproduction of

IGF-1, which results in somatic overgrowth, increased risk for cardiovascular death, and an increased risk for neoplasms (11).

Studies suggest an increased incidence of thyroid nodules (12,13) and colon polyps4 in acromegaly. A study from the United Kingdom suggested an increased risk for gallbladder polyps in newly diagnosed acromegaly patients as well (14). , The development of thyroid nodules is shown to be associated with disease duration (15).

Results from several studies carried out about the risk of colon cancer and mortality from colon cancer in acromegaly patients are contradictory (16,17,18,19). Some authors suggest routine periodic colonoscopies in follow-up of acromegaly patients, whereas some others suffice with one colonoscopy20. Although a consensus on the risk of neoplasms in acromegaly is not achieved, most of the current guidelines advise routine follow-up of patients with thyroid ultrasonography every 1-2 years and colonoscopy every 2-3 years (21). Thyroid ultrasonography is an easy and noninvasive imaging procedure, whereas colonoscopy is invasive and may become complicated. The most common complications are perforation and bleeding. Perforation is a serious complication of colonoscopy, happening in up to 5% of therapeutic colonoscopies (22,23). The overall incidence for bleeding during or after colonoscopy ranges from 0.3% to 6.1% in clinical studies (24,25).

To date, any possible association between the coexistence of thyroid nodules, colon polyps, and gallbladder polyps in acromegaly has not been investigated. The main purpose of our study was to investigate this association together with some identifiable risk factors in this small cohort of acromegaly patients for thyroid nodules, colon polyps, and gallbladder polyps.

In this study, we found that (although age and sex do not seem to be risk factors) high IGF-1 level is a risk factor for the development and growth of thyroid nodules in patients with acromegaly. However, we couldn't find a similar association between IGF -1 and colon polyps or gallbladder polyps. Dworakowska et al. reported that the development of colon polyps was associated with high IGF -1 levels26. The small number of patients included in the study may have masked a possible association.

The present study showed that the presence of thyroid nodules, colon polyps, and gall bladder polyps in acromegaly does not depend on one another. In other words, the coexistence of one or two of these comorbidities in an individual patient does not seem to be associated with the other. Therefore, each acromegaly patient should be evaluated for the presence of thyroid nodules, colon polyps, and gallbladder polyps on its own when clinically indicated.

There are some limitations to our study. First, we included a relatively small number of patients with acromegaly, some of whom are in remission. Second, this study is retrospectively designed, so some of the data were unavailable to the researchers.

In this retrospective study, we found that the presence of thyroid nodules, colon polyps, and gallbladder polyps in patients with acromegaly were independent of each other. Therefore, we suggest that when clinically indicated, each acromegaly patient should be evaluated for thyroid nodules, colon polyps, and gallbladder polyps on their own.

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