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Colonoscopic evaluation of acromegalic patients: a single center experience

Yasemin Emür Günay[1], Serdar Durak[2], Arif Mansur Coşar[3], Murat Erkut[3], Sami Fidan[3]

[1]Department of Endocrinology and Metabolism, Giresun Training and Research Hospital, Giresun, Turkey
[2]Department of Gastroenterology, Trabzon Training and Research Hospital, Trabzon, Turkey
[3]Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, Karadeniz Technical University, Trabzon, Turkey

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ABSTRACT

Aims: To investigate the importance and necessity of colonoscopic screening in patients with acromegaly.

Methods: This study included 82 patients with acromegaly and, 82 healthy individuals as the control group who underwent screening colonoscopy in the Gastroenterology Department of Karadeniz Technical University, between January 2008-January 2021.

Results: The mean age of the patients was 45.71±12.61 years at the time of acromegaly diagnosis. 51.2% (n=42) of patients were female. Abnormal findings including evidence of polyps, and inadequate bowel preparation were significantly more common in the acromegaly group than the control($p<0,05$). The a growth hormone (GH) level measured at the time of diagnosis was significantly higher in patients with acromegaly diagnosed with inadequate bowel preparation ($p<0,05$). There was no significant difference between the two groups in non-polyp colonoscopy findings, polyp localization, histologic types and colorectal cancer.

Conclusion: The frequency of polyps is higher in patients with acromegaly than in the normal population and therefore colonoscopy screening should be performed. It would be reasonable to perform bowel preparation in patients with acromegaly (especially those with high GH at the time of diagnosis) using an approach different from standard bowel preparation, as the rate of inadequate bowel preparation is higher in this group of patients.

Keywords: Acromegaly, colonoscopy, growth hormone, colon polyps

INTRODUCTION

Acromegaly is a rare disorder caused by a GH-secreting tumor in the pituitary gland. The annual incidence is reported as 3-4 per million and the prevalence as 50-70 cases per million. Both sexes are affected equally and usually in the fifth decade of life.[1] GH secretion induces the production of insulin-like growth factor-1 (IGF-1). Both of these hormones promote protooncogene expression and cellular growth and proliferation.[2] Acromegaly is associated with higher mortality and neoplastic, cardiovascular, metabolic, and respiratory complications compared with the general population.[3]

The association between acromegaly and hyperinsulinemia resulting from abnormal glucose tolerance and insulin resistance is well established.[4] Studies have shown that people with diabetes have an increased risk of colorectal cancer than people without diabetes. Hyperinsulinemia is thought to be involved in the pathogenesis of this increase.[5] Patients with acromegaly had also been found to have an increased incidence of colon polyps.[6-8]

Earlier and more frequent colonoscopic screening is recommended because the risk of colorectal polyps and cancer is likely to develop earlier in patients with acromegaly than in the general population due to increased GH and IGF-1 levels. Guidelines for the management of acromegaly published by the American Society of Clinical Endocrinologists and the Society of Endocrinology recommend colonoscopy at the time of diagnosis of acromegaly.[9,10] Some guidelines also state that patients with acromegaly should undergo colonoscopy every 3-5 years, beginning at age forty.[7,11]

In this study, we aimed to determine the incidence of colon pathology, specifically colon cancer and colon polyps, the relationship between colon polyp location and pathology, and clinical and laboratory findings in patients with acromegaly who underwent colonoscopy and thus evaluate the need for colonoscopic screening.

Corresponding Author: Yasemin Emür Günay, yaseminemurgunay@gmail.com

METHODS

The study was carried out with the permission of Karadeniz Technical University Ethics Committee (Date: 10.03.2022, Decision No: 161). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Eighty-two patients with acromegaly who underwent colonoscopic examinations were included in this retrospective study at Gastroenterology Department of Karadeniz Technical University Farabi Hospital between January 2008 and January 2021. As a control group, we recruited 82 patients who had undergone colonoscopy in our gastroenterology clinic for screening purposes and had no comorbidities. The demographic, histopathologic, laboratory and colonoscopic results of all patients were obtained by the hospital's electronic database in this study,retrospectively.

Colonoscopy preparation was done with oral 250 ml of sennoside A+B. Specialist physicians with at least three years of experience performed colonoscopy with Olympus or Pentax colonoscopes. We determined the location of all polyps (e.g., rectum, sigmoid colon, descending colon, transverse colon, ascending colon, cecum) during the procedure. We defined the left colon as the rectum, sigmoid, descending colon, and the right colon as the transverse colon, ascending colon, and cecum. All polyps that underwent polypectomy were sent to the pathology laboratory for histologic diagnosis. We recorded localization, number, and histologic subtypes of polyps. Abnormal findings include polyps, hemorrhoids, colorectal carcinoma, diverticula, parasitosis, ischemic/inflammatory colitis, anal fissures and tapeworms. We assessed inadequate bowel preparation using the Boston Bowel Preparation Scale with scores of 0 and 3.

We measured serum IGF-1 with an enzyme-labeled chemiluminescent solid-phase immunometric kit (Immulite IGF-I, Siemens Medical Solutions Diagnostics, UK) using the IMMULITE 1000 system.

We measured serum GH levels with an immunoradiometric kit (IRMA) using commercially available kits (hGH- IRMA CT; RADIM, Rome, Italy). The reference ranges for GH were 0-16 ng/ml for women and 0-8 ng/ml for men.

Statistical Analysis

We used the SPSS Windows version 22 program for statistical tests. We evaluated continuous variables with histogram and Q-Q plot for normal distribution and with Shapiro-Wilk or Kolmogorov-Smirnov test for the number of variables. Normally distributed continuous variables are presented throughout the study as mean±standard deviation, and the t-test for independent variables was used to compare the two groups. Other continuous variables were presented as median (IQR), and the non-parametric Mann-Whitney U test was used to compare the groups. We presented categorical variables as frequency and percentage and used the Pearson chi-square test or Fischer exact probability test to compare the groups. Tests with a p-value of 0.05 and below at the 95% confidence interval were considered statistically significant.

RESULTS

The mean age at diagnosis of acromegaly in 82 patients who underwent screening colonoscopy was 45.71±12.61 years.51.2% (n=42) of the patients were female and 48.8% (n=40) were male. The mean age of the control group was 51.91±13.31 years, 52.4% (n=43) of the patients were female, and 47.6% (n=39) were male. There was no statistically significant difference between the acromegaly and control groups in terms of age and sex (p> 0.05) (Table 1).

Table 1. Demographic and clinical characteristics of the acromegaly and control groups

Variable	Acromegaly (n=82)	Control (n=82)	p
Age*, mean±SD	48.87±12.46	51.91±13.31	0.132
Male/Female, n (%)	40/42 (48.8/51.2)	39/43 (47.6/52.4)	1
Cases with polyps, n (%)	16 (19.5)	6 (7.3)	0.037
Surgery, n (%)	69 (84.1)		
Disease control, n (%)	45 (54.9)		
Somatostatin analog, n (%)	50 (61)		
Radiotherapy, n (%)	9 (11)		

*Based on age at the time of colonoscopy.

84.1% (n=69) of the patients with acromegaly had a history of pituitary surgery. In 13 patients who did not undergo surgery, medical treatment was given because they did not accept the operation or were at high risk for operation. The disease control was achieved in 54.9% (n=45) of the patients with surgery. While 61% (n=50) of the patients received somatostatin analogue treatment, 11% (n=9) received radiotherapy (Table 1).

Colonoscopy findings were normal in 37 (45.1%) patients with acromegaly who underwent colonoscopic examination, abnormal findings were noted in 34 (41.5%) patients, and no definite evaluation could be made in 11 (13.4%) patients because of inadequate bowel cleansing. While colonoscopy findings were normal in 75.6% (n=62) of subjects in the control group, abnormal findings were noted in 23.2% (n=19); no definite evaluation could be made in 1.2% (n=1) due

to inadequate bowel cleansing. The rates of abnormal findings [acromegaly group 42.7% (n=35) and control group 24.4% (n=20)] and inadequate bowel cleansing [acromegaly group 13.4% (n=11) and control group 1.2% (n=1)] and were statistically higher in cases with acromegaly compared to the control group (p=0.019 and p=0.005, respectively), and the detection rate for normal colonoscopic findings was significantly lower (p<0,001). (Table 2).

Table 2. Colonic localization and histological types of polyps and non-polyp findings in patients with acromegaly

	Acromegaly	Control	P
Polyp localization,n (%)			
Right colon	4 (25)	1 (16.7)	0.367
Left colon	11 (68.7)	3 (50)	0.047
Right and left colon	1 (6.3)	2 (33.4)	1
Polyp Histology, n (%)			
Tubular	15	8	0.403
Tubulovillous	3	1	0.620
Hyperplastic	2	3	1
Reactive	3	0	0.245
Inflammatory	2	0	1
Total	25	12	
Non-polyp finding,n (%)			
Hemorrhoids	13 (15.9)	10 (12.2)	0.654
Colorectal carcinoma	2 (2.4)	1 (1.2)	1
Diverticula	2 (2.4)	3 (3.7)	1
Parasitosis	2 (2.4)	0	0.497
Ischemic/inflammatory colitis	2 (2.4)	4 (4.9)	0.682
Anal fissure	1 (1.2)	2 (2.4)	1
Tapeworm	1 (1.2)	0	1
Inadequate colon cleansing	11(13.4)	1(1.2)	0.005

We detected polyps in 19.5% (n=16) of cases with acromegaly and 7.3% (n=6) of cases in the control group. The polyp detection rate was significantly higher in the acromegaly group than in the control group (p=0.037). The median number of polyps in the patients with polyps was 1 (1-4). There was no difference in age between the group with and without polyps in patients with acromegaly (p=0.562), whereas the age at polyp detection was statistically higher in the control group (mean age 60.17±4.53 vs. 51.26±13.56, p=0.002). There was no gender difference in polyp detection in the acromegaly or control groups. (p> 0.05). We found no significant difference in patients with acromegaly between cases with and without polyps in terms of time from diagnosis to colonoscopy (p=0.664). There was more than one polyp in 6 and 5 cases in patients with acromegaly and the control group, respectively.

We detected 25 polyps in 16 out of 82 patients with acromegaly who underwent colonoscopy. Of the acromegaly patients with polyps, polyps were located in the left colon in 11 (68.7%) of the patients, in the right colon in 4 patients (25%), and in both the right and left colon in 1 patient (6.3%). Rectal polyps are included in left colon polyps. If rectal polyps were evaluated separately, the most common site of polyps was the rectum with 8 (32%) polyps.

In the control group, we detected a total of 12 polyps in 6 cases, and the most common location of polyps was the sigmoid colon with four polyps (33.3%). Other polyp localizations were 1 in left colon, 3 in right colon and 2 in both right and left colon, respectively (Table 2).

Regarding the localization of polyps in the right or left colon, the left colon location of polyps was more frequent in the acromegaly group than in the control group (p=0.047) (Table 2). There was no statistically significant difference between the acromegaly and control groups in polyp localization in the rectum, sigmoid colon, descending colon, transverse colon, ascending colon, and rectum (p > 0.05).

When we evaluated the histological type of polyps, 60% (n=15) of polyps in patients with acromegaly were tubular adenomas, 12% (n=3) were tubulovillous adenomas, and 12% (n=3) were reactive polyps. There was no statistically significant difference in the evaluation of histological types of polyps in cases with and without acromegaly (p> 0.05) (Table 2).

The most common findings other than polyps in patients with acromegaly were: Hemorrhoids 15.9% (n=13), diverticula 2.4% (n=2) and parasitosis (Enterobius vermicularis) 2.4% (n=2) (Table 2). There was no statistically significant difference between the acromegaly and control groups in the frequency of non-polyp findings (p> 0.05) (Table 2).

In patients with acromegaly, we found no statistically significant difference in the presence or absence of polyps between patients depending on their concomitant systemic diseases, whether or not they underwent surgery, whether or not they were surgically cured, whether or not they received radiotherapy, and whether or not they were taking a somatostatin analog (p> 0.05) (Table 3).

When we evaluated IGF-1 and GH levels of patients with acromegaly for the presence/absence of polyps, we found no statistically significant difference in IGF-1 and GH levels at the time of diagnosis, at three months after surgery and before colonoscopy, and in GH levels at the time of diagnosis and three months after surgery (p> 0.05) (Table 3).

The GH level measured at the time of diagnosis was significantly higher in patients with acromegaly with inadequate bowel preparation (p=0.028).

Table 3. The association between the presence of polyps and the type of treatment, GH/IGF-1 levels and demographic data in patients with acromegaly

	Polyp (+)	Polyp (-)	P
Operation history, n (%)			0.711
Yes	13 (18.8)	56 (81.2)	
No	3 (23.1)	10 (15.2)	
Disease controle, n (%)			0.781
Yes	8 (17.8)	37 (82.2)	
No	8 (21.6)	29 (78.4)	
Radiotherapy history, n (%)			0.681
Yes	1 (11.1)	8 (12.1)	
No	15 (20.5)	58 (87.9)	
Use of somatostatin analogue, n (%)			0.777
Yes	9 (18)	41 (82)	
No	7 (21.9)	25 (78.1)	
Age, mean±SD	50.5±10.04	48.47±13.01	0.562
Gender, n (%)			0.583
Male	9 (22.5)	31 (77.5)	
Female	7 (16.7)	35 (83.3)	
IGF-1 (Diagnosis), mean±SD	689.27±348.73	770.58±308.51	0.445
IGF-1 (Postop 3rd month) mean±SD	385.81±279.01	340.02±206.82	0.471
IGF-1 (Colonoscopy), mean±SD	543.18±272.3	559.11±312.71	0.849
GH (Diagnosis), median (IQR)	3.62 (5)	4.12 (6)	0.83
GH (Postop 3rd month), median (IQR)	1.23 (2.77)	1.31 (1.96)	0.345

*IGF-1: Insulin-like growth factor 1, GH: Growth hormone

DISCUSSION

The frequency of polyps is higher in patients with acromegaly than in the normal population and therefore colonoscopy screening should be performed. Mortality in patients with acromegaly is higher than in the general population. With advances in treatment in recent years, mortality rates due to the disease itself have decreased. In recent studies, the most common cause of death in patients diagnosed with acromegaly is a malignancy (35%), followed by cardiac and cerebrovascular disease.[12,13]

The prevalence of colorectal polyps was 30.3% in the study by Koksal et al.[14] and 30.2% by Guistina et al.[3] In our study, this rate was 19.5%.

Studies show an increased risk of colorectal tumors and cancers in patients with acromegaly and associate this increase with high GH levels.[15,16] Although there was no significant difference in the detection rate of malignancy in patients with acromegaly compared to the control group in our study, the rate of polyps was higher in the acromegaly group than in the control group.

The difference in the rates of polyps or colorectal tumors in acromegaly patients might be related to the age at diagnosis of acromegaly, the age at which colonoscopy was performed, the timing of colonoscopy after diagnosis, and the follow-up period. Therefore, it is clear that longer follow-up studies with more patients are needed to evaluate the significance of the difference. We excluded the risk of follow-up and cancer development from the analysis because we aimed to analyze the initial screening results and not determine these details.

GH levels could be reached in only one of the patients with colon cancer, so it was not appropriate to evaluate the relationship between colon cancer and GH in our study. When we assessed the initial GH level for the presence of polyps, we found no significant difference.

Current guidelines recommend colorectal cancer screening at the time of diagnosis of acromegaly and starting at age 40 years.[17] The mean age of acromegaly patients (n=16) with polyps was 50.5±10.04 years, and the rate of patients younger than 40 years was 18.7% (n=3). These rates support the need for colonoscopic examination, regardless of age, at the earliest possible time when patients are diagnosed with acromegaly. Our two patients with acromegaly diagnosed with colorectal cancer during screening were 65 and 68 years of age.

Studies on the location of polyps in patients with acromegaly are controversial. Some studies have reported that polyps form more frequently in the right colon in patients with acromegaly.[18] In a 2020 study by Ochiai et al.,[19] significantly more polyps were detected in the sigmoid colon and rectum compared with the control group. We found no significant difference in the location and detection rate of polyps in the right and left colon in the acromegaly group compared with the control group in our study.

In another study by Wassenaar et al.,[20] it was found that the diverticulum rate was high in patients with acromegaly. In our study, it was found to be similar to the control group.

The length of the colon is increased in patients with acromegaly, and standard bowel preparation is often inadequate because the transit time of the colon is more than double.[21,22] In our study, we found that inadequate bowel preparation was significantly higher in the acromegaly group than in the control group. GH levels at the time of diagnosis were also significantly higher in patients with inadequate bowel preparation. In our study, it can be concluded that there was inadequate colon cleansing due to the increase in intestinal length and slowing of bowel movements with increased GH. Our study can be considered an original contribution to the literature and shed light on new studies on this topic because we could not find any other publication in the literature comparing GH levels in patients with acromegaly with and without inadequate bowel preparation.

This study's limitation can be a single-center and retrospective study. The inability to collect complete and sufficient data from all patients may be a problem because some of the patients were examined in our center only for colonoscopy and followed up and treated in other centers, and some patients were referred to our center for surgery from surrounding provinces and had their colorectal scans performed in the center from which they were referred. This has resulted in a small number of patients with complete data.

CONCLUSION

In this study, although the frequency of polyps was significantly higher in patients with acromegaly, we found no significant difference in colorectal cancer. We found no significant difference between the acromegaly and control groups in non-polyp colonoscopy findings, polyp location, and histological types. Since inadequate bowel preparation is more common in patients with acromegaly (especially in patients with high GH at the time of diagnosis), bowel preparation should be performed with a different approach other than standard bowel preparation. More data is required on the need for colonoscopic screening in patients with acromegaly who are at relatively higher risk for colorectal malignancy. For this reason, there is a need for multicenter and prospective studies in larger series that include colonoscopic findings, clinical and laboratory data, and compare patients with acromegaly with each other and with the control group.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Karadeniz Technical University Ethics Committee (Date: 10.03.2022, Decision No: 161).

Informed Consent: Because the study was designed retrospectively, no written informed consent from was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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