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Role of Growth Hormone for Colonic Polyps in Non-Acromegalic Patients

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SUMMARY

The colorectal manifestations can be initial signs of an endocrine disease. The relationship between acromegaly and increased incidence of colonic polyps and cancer has been well established. On the other hand, there is no study yet reporting whether any polypoid lesion detected incidentally during colonoscopy should indicate a clinically inappearent growth hormone excess.

Twelve patients with polyps detected by colonoscopy and 12 control subjects with normal colonoscopy were investigated for growth hormone status. There was no statistically significant difference (p=0.95) between two groups in terms of growth hormone (GH) levels.

This study suggested that despite the increased incidence of colonic polyps associated with high GH levels in acromegaly, sporadically detected colonic polyps in clinically non-acromegalic patients could not establish any association with growth hormone excess.

Key Words: Acromegaly, Colonic polyps, Growth hormone

Non-Akromegalik Hastalardaki Kolon Poliplerinde Büyüme Hormonunun Rolü

ÖZET

Kolorektal bulgular endokrin hastalıkların ilk bulgusu olabilirler. Akromegali ile kolon polip ve kanserlerinin artmış insidansı arasındaki bağıntı belirgin bir şekilde ortaya konulmuştur. Bunun yanında kolonoskopi sırasında tesadüfen rastlanan polipoid lezyonların klinik olarak aşikar olmayan büyüme hormonu fazlalığının göstergesi olabileceğini belirten herhangi bir çalışma henüz bulunmamaktadır.

Kolonoskopi sırasında polip belirlenen oniki hasta ve normal kolonoskopi verilerine sahip oniki kontrol vakası büyüme hormonu düzeyleri bakımından değerlendirildi. İki gurup arasında büyüme hormonu düzeyleri bakımından istatistiksel olarak anlamlı bir fark bulunmamaktaydı (p=0.95).

Bu çalışma, akromegalilerde büyüme hormonu yüksekliği ile beraber kolon polip insidansının artmasına rağmen, klinik olarak akromegalisi bulunmayan hastalarda rastlantısal olarak saptanan kolon poliplerinin büyüme hormonu fazlalığı ile herhangi bir ilişkisi olmadığını düşündürmektedir.

Anahtar Sözcükler: Akromegali, Büyüme hormonu, Kolon polipleri

INTRODUCTION

It has been suggested that patients with acromegaly have increased risk of developing adenomatous and hyperplastic colonic polyps, therefore it has been recommended that all patients with acromegaly should undergo colonoscopic screening as part of their routines (1). This brings the question in mind whether the patients with gastrointestinal polyps incidentally detected may have increased incidence of growth hormone excess and should be screened for acromegaly.

The increased prevalence of the adenomatous polyps in acromegaly was hypothesized to be due to impairment of mucosal immune surveillance. due to the mitogenic effect of insulin-like growth factor-1 (IGF-1), and due to colonomegaly which prolongs colonic transit time and hence exposes the epithelium to several presumed pathogens (2-5).

This study was designed to determine whether there is an association between growth hormone excess and colonic polyps in non-acromegalic population, and whether the colonic polyps are initial signs of acromegaly.

MATERIALS AND METHODS

The study group included 7 men and 5 women aged 38 to 82 years (mean, 57 years) with colonic polyps detected during fiberoptic colonoscopy. The control group consisted of 12 subjects (3 men, 9 women, mean age 57 years) with normal colonoscopic findings investigated because of irritable bowel syndrome or constipation. Endoscopic polypectomy was done, and polyps were seperately recorded according to location, size, and pathology.

Since secretion of growth hormone is pulsatile single measurement would not be reliable, therefore, growth hormone levels were measured as fasting basal, and at 2 h after 100 gr oral glucose. The oral glucose tolerance test is accepted as the simplest and most specific dynamic test to detect growth hormone excess and acromegaly (6-7). The test assesses the suppressibility of growth hormone after glucose load. In healthy people it suppresses GH concentration to less than 2µg/L after 2 h.

Growth hormone levels were measured by immulite autoanalyser using DPC kit-system ($LKGH_1$) by two directional solid phase chemiluminescence enzyme immunometry method. Normal reference range was 0.05-4.3 µg/L.

Statistical analysis of continuous variables was performed by Mann-Whithney U test between two groups (Table 2), and Kruskall Wallis one way anova test between multiple groups (Table1). $P<0.05$ was accepted as statistical significance.

Table 1. The characteristics of the study group.

No. of patient	Location of polyps	Number, size (the biggest one, mm)	GH levels (µg/L) Basal	2 h after OGTT
1	Descending col	1, 10 mm	0.86	0.14
2	Descending col	1, 4 mm	0.25	0.06
3	Descending col	3, 12 mm	0.16	0.09
4	Descending col	1, 3 mm	0.48	0.06
5	Descending col	1, 4 mm	0.87	0.04
6	Splenic flexura	1, 4 mm	0.05	0.04
7	Descending col	1, 15 mm	0.95	0.58
8	Descending col	2, 8 mm	2.5	1.99
9	Descending col	5, 3 mm	3.10	0.36
10	Descending col	2, 25 mm	0.05	0.04
11	Descending col	2, 35 mm	0.33	0.04
12	Descending col	1, 10 mm	0.47	0.04

Table 2. The comparison of the parameters between the study and control groups.

	Study group	Control group	p
Sex			
Men	7	3	0.21
Women	5	9	
Age (Median,years)	57 (38-82)	57 (40-75)	0.59
Basal GH (Median, µg/L)	0.47 (0.05-3.10)	0.41 (0.06-3.90)	0.95
GH at 2 h after OGTT (Median, µg/L)	0.09 (0.06-9.30)	0.09 (0.05-0.42)	0.51

RESULTS

Polyps extracted by endoscopic polypectomy were adenomatous polyps in 6 cases, hyperplastic in 4 cases, and inflammatory in 2 cases and located at descending colon except one which was at splenic flexura. The sizes, locations, and number of polyps, and growth gormone levels in the study group were shown in Table 1.

There was no difference between the

parameters of the study and control groups as shown in Table 2.

The comparison of growth hormone levels between the patients with polyps <5 mm and those with >5 mm with each other, and with the control group did not reveal any significant difference (p=0.90 and 0.38, respectively) as well.

DISCUSSION

Endocrine diseases may initially present as a symptom or sign referable to colorectal disease. Thyroid disorders depending on the functional status of the gland may cause refractory constipation, diarrhea, or steathorrea; brittle diabetes may present with chronic and intermittant diarrhea; hyperparathyroidism has been associated with increased incidence of colonic malignancies; and acromegaly is evidently a risk factor for colonic neoplasia (5,8,9).

The mechanism for development of colorectal neoplasia in acromegaly is unclear, and seems to be multifactorial[2]. In sporadic neoplasms in the non-acromegalic population, several molecular changes have been described in the DNA of adenomatous polyps. Specific mutations in the *ras* proto-oncogene followed by deletions in chromosomes lead to altered proliferative pattern of the colonic mucosa. Especially, the loss of genetic material on the short arm of chromosome 17 is associated with mutation in tumor suppressor protein p53 (10,11). The occurance of similar mutations in the oncogenes (*ras, c-myc*) and tumor suppressor genes (p53, APC, MCC, DCC) in the acromegaly-associated tumors is under investigation (3).

Insulin-like growth factor-I (IGF-1) has been assumed to play role in the pathogenesis of neoplastic process. IGF-1 is the tissue biomarker of GH, and a mitogen which stimulates growth of colon cancer cell lines in vitro (12). IGF-1 receptors are found on the surfaces of both normal and neoplastic colonic mucosal cells[4]. It is reported that increased colonic mucosal epithelial proliferation is correlated with IGF-1, and thus with GH concentrations (13). Jenkins and colleagues suggested that tissue exposure to GH may result in colonomegaly with resulted prolonged colonic transit time that increases exposure of mucosa to oncogenes such as secondary bile acids (2). The altered colonic lamina propria lymphocyte pattern seen in acromegaly may also contribute to the pathogenesis of polyp formation (5).

In the study presented we investigated whether sporadically detected colonic polyps may be initial manifestations of acromegaly, and therefore may show a correlation with increased growth hormone levels. However, we could not establish such a relation in non-acromegalic patients. This indicated that some other pathogenetic factors such as intraluminal unconjugated bile acids, or other mitogenic factors (gastrin, transforming growth factor alfa) may still play the major role in non-acromegalic patients with colorectal neoplasia (12,14,15). Further large population-based studies in patients other than acromegalics are required to determine the influence of a mitogen like IGF-1 in the development of such polyps.

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