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Association of colon adenomas and skin tags: coincidence or coexistence?

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Abstract. – OBJECTIVES: Skin tag (STs) are benign connective tissue tumors of the dermis. Some researchers have argued that there is a relationship between skin tag and colon polyps, although the physiopathological mechanisms underlying this relation were not well elucidated. In this study we aimed to investigate the co-existence of colonic adenomatous polyps and ST, additionally to shed light on the physiopathological mechanisms underlying this coincidence.

PATIENTS AND METHODS: A total of 45 patients aged between 18 and 60 diagnosed with adenomatous colonic polyps and 45 sex, age, and socio-demographically matched subjects, had no polyps, were enrolled as the control group. Routine blood analysis of all participants, including serum glucose, total cholesterol, low-density lipoprotein cholesterol (LDL-C), (high-density lipoprotein cholesterol (HDL-C), triglyceride, insulin, IGF-1, and EGF, were performed. The chi-square and independent sample t or Mann Whitney U test were used to determine differences between groups.

RESULTS: The number of participants with ST was significantly higher in the patient group (OR 7.067, $p < 0.01$). Serum levels of IGF-1 and EGF were statistically similar between the groups. In the subgroup analyses, no difference was found in serum levels of insulin, IGF-1, or EGF between patients with and without ST. However, higher serum levels of insulin and EGF were found in control subjects with ST ($p < 0.01$ and $p < 0.01$, respectively). For the entire study group, 67 participants had ST and 23 patients did not. Serum insulin, and IGF-1 were similar, while serum EGF levels were higher in patients with ST ($p < 0.01$).

CONCLUSIONS: Findings of the present study may show a co-existence of colonic polyps and ST. Although previous studies have indicated that insulin resistance may play a role in the pathogenesis of both lesions in diabetic and obese patients, we found no indication of a relationship in nondiabetic and nonobese patients with increased levels of EGF in patients with ST, suggesting an alternative pathogenesis in this patient group.

Key Words:
Adenomatous polyps, Skin tag, Acrochordon, IGF-1, Insulin, EGF.

Introduction

Acrochordon also known as skin tag (STs)are benign connective tissue tumors of the dermis and are particularly common in elderly adults.Clinically, ST appear as soft, skin-colored or hyperpigmented, usually pedunculated lesions often occurring on the major flexures of the body, such as neck, axilla, and inguinal region[1].

Adenomatous colonic polyps are a prevalent subgroup of colonic polyps that account for approximately 10% in sigmoidoscopy studies and more than 25% in colonoscopy studies. Some researchers have argued that there is a relationship between skin tag and colon polyps[3,4], although the physiopathological mechanisms underlying this relation were not well elucidated. However, high insulin concentrations were shown to play an important role in the development of both ST and adenomatous colonic polyps[5,6]. Insulin directly and indirectly activates insulin-like growth factor-1 (IGF-1) as well as epidermal growth factor (EGF) receptors in cells, such as keratinocytes and fibroblasts, and induces their proliferation[7]. In light of these data, in this study we aimed to investigate the co-existence of colonic adenomatous polyps and ST. Additionally to shed light on the physiopathological mechanisms underlying this coincidence, serum levels of insulin, IGF-1, and EGF in nondiabetic and nonobese patients were evaluated.

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Patients and Methods

This prospective clinical study was conducted at the Namik Kemal University Faculty of Medicine, Departments of Gastroenterology, Dermatology, and Internal Medicine, between April 2012 and January 2014. A total of 45 patients aged between 18 and 60 diagnosed with adenomatous colonic polyps by the Outpatient Clinics of Gastroenterology after colonoscopic and histopathological evaluation were enrolled in the study. Forty-five subjects, who were sex, age, and socio-demographically matched with the patient group, had no polyps, and who did not meet exclusion criteria were enrolled as the control group. Control subjects were selected from the same Outpatient Clinics, and all underwent colonoscopy. The study was approved by the Ethical Committee of Human Studies of Namik Kemal University and written informed consent was obtained from each patient.

All participants were nonsmokers and were examined for history and clinical and laboratory findings of any acute or chronic disorders, including endocrinological, inflammatory, infectious, and malignant diseases. Subjects who had any of these were excluded. All participants underwent dermatological evaluation, and ST were recorded according to number and location. Routine blood analysis of all participants, including serum glucose, total cholesterol, low-density lipoprotein cholesterol(LDL-C), (high-density lipoprotein cholesterol(HDL-C), triglyceride, insulin, IGF-1, and EGF, were performed.

Blood samples were obtained in the morning after a 10-12 h fasting. After centrifuging the blood samples at 2000 × g for 10 min, serum samples were collected and kept at −80°C until analyses. Serum glucose and lipids (total cholesterol, triglycerides, LDL-C, and HDL-C) were estimated with commercially available kits (Roche Cobas C 501; Roche Diagnostics GmbH, Tokyo, Japan). Insulin was measured by Human Insulin enzyme-linked immunosorbent assay (ELISA) kit (Sunred Biological Technology Co., Ltd, Shanghai, China). IGF-1 concentrations were measured by Human IGF-1 ELISA kit (Sunred Biological Technology Co., Ltd). EGF (USCN Life Science, Hubei, China) was measured in serum by commercial ELISA assays according to the manufacturer's instructions.Results were expressed as mIU/L for insulin, ng/ml for IGF-1 and pg/ml for EGF.

Statistical Analysis

All the statistical analyses were performed with SPSS 18 (SPSS Inc., Chicago, IL, USA). The chi-square and independent sample *t* or Mann Whitney *U* test were used to determine differences in demographic and laboratory results between control and patient groups and subgroups. $p < 0.01$ was accepted as significant.

Results

The patient group consisted of 45 subjects (51.1% male, mean age 50.96, mean BMI 26.6) of which 39 (86.7%) patients had ST and six (13.3%) did not. The control group consisted of 45 subjects (37.8% male, mean age 50.42, mean BMI 26.8) of which 28 (62.2%) had ST and 17 (37.8%) did not. The number of participants with ST was significantly higher in the patient group compared to the control group (OR 7.067, $p < 0.01$). Serum levels of glucose, total cholesterol, LDL-C, HDL-C, triglyceride, insulin, IGF-1, and EGF were statistically similar between the groups (Table I).

In the subgroup analyses, no difference was found in serum levels of glucose, total cholesterol, LDL-C, HDL-C, triglyceride, insulin, IGF-1, or EGF between patients with and without ST. However, higher serum levels of insulin and EGF were found in control subjects with ST ($p < 0.01$ and $p < 0.01$, respectively) (Table II).

For the entire study group, 67 participants had ST (49.3% male, mean age 51.52, mean BMI 26.9) and 23 patients did not (30.4% male, mean age 48.26, mean BMI 26.2). Serum glucose, total cholesterol, LDL-C, HDL-C, triglyceride, insulin, and IGF-1 were similar, while serum EGF levels were higher in patients with ST ($p < 0.01$) (Table III).

Discussion

Although adenomatous colonic polyps are a common subgroup of colonic polyps and the pathogenesis of the tumorous lesion has been well studied by many researchers, the exact pathophysiology has not been well elucidated. Cigarette smoking, alcohol consumption, and genetics have been blamed for having a role in the development of the lesions[8]. An increased number of colonic polyps in acromegalic patients led researchers to investigate the role of insulin resis-

Table I. Age, BMI, serum levels of glucose, total cholesterol, LDL, HDL, triglyceride, insulin, IGF-1 and EGF in patient and control groups.

	Patient (N = 45)	Control (N = 45)	p
Age	50.96 ± 9.14	50.42 ± 7.86	0.34
BMI	26.6 ± 2.6	26.8 ± 2.2	0.11
ST (+)	39 (87%)	28 (62%)	
ST (-)	6 (13%)	17 (28%)	
Glucose (mg/dl)	95 (75-158)	94 (77-144)	0.31
Total cholesterol (mg/dl)	196.4 ± 33.7	189.3 ± 51.7	0.44
LDL (mg/dl)	120.2 ± 30.5	117.3 ± 46.9	0.72
HDL (mg/dl)	48.2 ± 13.7	49.6 ± 13.9	0.64
Triglyceride (mg/dl)	104 (42-424)	103 (34-285)	0.11
Insulin (mU/L)	4.9 (1.3-15.5)	5.4 (2.8-28.2)	0.58
IGF-1 (ng/ml)	4.3 (1.2-15.56)	4.9 (1.7-18)	0.54
EGF (pg/ml)	16.1 (1.8-80.8)	15.6 (4-75.5)	0.74

Patient grou p = Subjects with colon polyps; Control group = Subjects without colon polyps; ST+ = Subjects with skin tag, ST- = Subjects without skin tags; BMI = Body mass index. Independent sample *t* test used to determine differences in serum levels of total cholesterol, LDL, HDL results between groups. Mann Whitney U test used to determine differences in serum levels of glucose, triglyceride, insulin, IGF-1 and EGF results between groups.

tance in the etiology of colonic polyps[9]. Kim et al[10] showed that metabolic syndrome, which is complicated with insulin resistance, might be a risk factor for colorectal adenoma. Similarly, Kim et al[11] argued that metabolic syndrome was associated with an increased risk of colorectal adenomas in Korean men.

Although Gould et al[12] suggested no relation between colonic polyps and ST, the presumed role of insulin resistance in both lesions led us to investigate the co-existence of these lesions and potential role of insulin, IGF-1, and EGF. The results of our study have demonstrated that the occurrence of colonic polyps increases in nondiabetic and nonobese patients with ST.

A relation between hyperinsulinemia and colonic polyps has been reported[9] in patients with acromegaly; however, in another study[13] no statistical difference in insulin serum concentration of non-acromegalic patients and control subjects was found. Similar to this latter study, we found no relation between insulin serum concentrations and colonic polyps. Matyja et al[14] reported that an increased number of colonic adenomas

Table II. Age, BMI, serum levels of glucose, total cholesterol, LDL, HDL, triglyceride, insulin, IGF-1 and EGF in between patients with and without skin tags, controls with and without skin tag subgroups.

	Patient			Control		
	ST+ (n = 39)	ST- (n = 6)	p	ST+ (n = 28)	ST- (n = 17)	p
Age	51.52 ± 7.94	48.26 ± 9.67	0.53	51.32 ± 7.65	48.94 ± 8.2	0.91
BMI	26.9 ± 2.4	26.2 ± 2.4	0.77	27 ± 2.1	26.4 ± 2.4	0.30
Glucose (mg/dl)	95 (75-158)	91 (84-108)	0.26	95 (82-136)	92 (77-144)	0.45
Total Cholesterol (mg/dl)	195.2 ± 33.5	204.3 ± 36.8	0.54	194 ± 57.1	180 ± 41.5	0.40
LDL (mg/dl)	122.6 ± 30.3	111.2 ± 33.7	0.44	119 ± 52.9	114 ± 36.0	0.69
HDL (mg/dl)	47.2 ± 12.5	55.2 ± 19.9	0.19	52 ± 12.7	45 ± 15.0	0.09
Triglyceride (mg/dl)	103 (56-424)	177 (42-339)	0.59	98.5 (34-285)	104 (42-205)	0.61
Insulin (mU/L)	4.8 (1.3-27.8)	5.4 (3.9-8.3)	0.79	5.6 (3.1-28.2)	4.1 (2.9-19.8)	0.01
IGF-1 (ng/ml)	4.2 (1.2-15.5)	5.8 (4-7.9)	0.21	5.7 (1.8-18.0)	3.7 (1.7-13.1)	0.07
EGF (pg/ml)	16.1(1.9-80.8)	16.4 (8.8-40.6)	0.64	21.5 (4.0-75.5)	11.6 (7.7-70.6)	0.006

Patient group = Subjects with colon polyps; Control group = Subjects without colon polyps; ST+ = Subjects with skin tag, ST- = Subjects without skin tags; BMI = Body mass index. Independent sample t test used to determine differences in serum levels of total cholesterol, LDL, HDL results between groups. Mann Whitney U test used to determine differences in serum levels of glucose, triglyceride, insulin, IGF-1 and EGF results between groups.

Table III. Sex ratio, age, BMI, serum levels of glucose, total cholesterol, LDL, HDL, triglyceride, insulin, IGF-1 and EGF in between subjects with and without skin tags.

	ST+ (n = 67)	ST- (n=23)	*p*
Sex (female/male)	34/33	16/7	0.11
Age	51.52 ± 7.94	48.26 ± 9.67	0.53
BMI	26.9 ± 2.4	26.2 ± 2.4	0.77
Glucose (mg/dl)	95 (75-158)	92 (77-144)	0.16
Total cholesterol (mg/dl)	194.9 ± 44.5	187. ± 40.9	0.45
LDL (mg/dl)	120.7 ± 40.9	113 ± 34.7	0.42
HDL (mg/dl)	49.3 ± 12.8	47.8 ± 16.6	0.63
Triglyceride (mg/dl)	103 (34-424)	110 (42-339)	0.77
Insulin (mU/L)	5.4 (1.3-28.2)	5.2 (2.9-19.8)	0.10
IGF-1 (ng/ml)	4.7 (1.2-18.0)	4.6 (1.7-13.1)	0.53
EGF (pg/ml)	18.0 (1.9-80.8)	11.6 (7.7-70.6)	0.02

ST+ = Subjects with skin tag; ST- = Subjects without skin tags; BMI = Body mass index. Independent sample *t* test used to determine differences in serum levels of total cholesterol, LDL, HDL results between groups. Mann Whitney U test used to determine differences in serum levels of glucose, triglyceride, insulin, IGF-1 and EGF results between groups.

may be related to increased levels of IGF-1 in acromegalic patients, while Renehan et al[15] and Kaczka et al[13] did not find any relationship in non-acromegalic patients. Similarly, we found no statistically significant relationship between colonic polyps and IGF-1.

Given the proliferative effects of EGF on gastrointestinal mucosa, some authors[16] hypothesized that EGF may play a role in the development of colonic polyps. EGF receptor overexpression has been associated with advanced colorectal adenomas; however, no relation between polyp formation and EGF was found in an animal study[17]. Furthermore, EGF-like growth factors may frequently be associated in tumor progression rather than premalignant lesions, such as adenomas[18]. Our findings showed no relation between colon adenomas and increased serum levels of EGF.

Studies[5,19,20] have investigated the correlation between serum levels of insulin, IGF-1, and ST. Jowkar et al[5] showed increased insulin levels in nondiabetic patients and the importance of the insulin effect in the pathogenesis of ST; however, they did not find any relationship between IGF-1 levels and ST. Conversely, the role of both insulin resistance and IGF-1 has been shown in the development of ST in chronic HCV infection[19]. In our work, we found no correlation between serum insulin levels and ST. This may be a result of patient characteristics since our study group was neither diabetic nor obese. Additionally, we found no relation between IGF-1 and ST.

The proliferative effects of EGF on human keratinocytes led us to hypothesize that EGF may have a role in the development of ST[7]. Scanning medical literature we found no studies investigating the relation between serum EGF levels and ST. However, Nanney et al[21] showed a correlation between EGF receptor distributions and increased levels in the epidermis and the clinical growthof ST. In the present study, EGF serum levels were significantly elevated in patients with ST. This elevation, however, was not found in a subgroup of patients with both ST and colon polyps.

Conclusions

Our findings may show a co-existence of colonic polyps and ST. Although previous reports have indicated that insulin resistance may play a role in the pathogenesis of both lesions in diabetic and obese patients, we found no indication of a relationship in nondiabetic and nonobese patients with increased levels of EGF in patients with ST, suggesting an alternative pathogenesis in this patient group. Further studies are needed to illuminate the potential role of EGF in the development of ST and its relation to colonic polyps.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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