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Kolorektal Polipte Kronik Obstrüktif Akciğer Hastalığı Sıklığı ve Sistemik İnflamasyonla İlişkisi

Chronic Obstructive Lung Disease Frequency in Colorectal Polyp and Relationship with Systemic Inflammation

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ÖZ

GİRİŞ ve AMAÇ: *Çalışmamızda kolorektal polip olgularında Kronik Obstrüktif Akciğer Hastalığı sıklığı (KOAH) ve bu durumun sistemik inflamasyonla ilişkisi araştırılmıştır.*

YÖNTEM ve GEREÇLER: *Aralık 2016 -2017 tarihleri arasında Gastroenteroloji kliniğinde kolonoskopi yapılan ve kolorektal polipozis tanısı konulan olgulardan özgeçmiş sorgulamasında KOAH tanısı olan 35 olgu ile yine özgeçmiş sorgulamasında herhangi bir kronik hastalığı olmayan 163 kontrol olgu alındı. Tüm olguların yaş, sigara öyküsü (paket-yıl) gibi demografik verileri, patoloji sonuçları, lezyonun anatomik yeri ile lökosit, nötrofil lenfosit oranı (NLO) ve ortalama trombosit hacmi (MCV) parametrelerinden oluşan hemogram verileri kaydedildi.*

BULGULAR: *Olguların 137 (%69,2)'si erkek, 61 (%30,8)'i kadın ve yaş ortalaması 63,56±11,68 (20-89) olarak bulundu. 129 olgunun sigara öykülerine ulaşılabildi ve bunlardan 62 (%48,1)'sinin sigara öyküsü vardı. Son 1 yılda kolorektal polipozis tanısı konulan olgular arasında KOAH sıklığı %8 olarak bulundu. KOAH olanlarda kontrol grubuna göre lökosit, NLO ve MCV değerleri istatistiksel olarak anlamlı olarak daha yüksek bulundu (sırasıyla p= 0,001, <0,001, <0,001). Polipler histopatolojik olarak neoplastik ve non-neoplastik olarak karşılaştırıldığında bu inflamasyon değerleri iki grupta da benzer bulundu. Lökosit, NLO ve MCV değerlerinin sigara öyküsü ile pozitif korele olduğu görüldü.*

TARTIŞMA ve SONUÇ: *KOAH ve adenomatöz polipler sistemik inflamasyonla ilişkili olup, çalışmamızda adenomatöz polip saptanan olgular arasında sıklığı %8 bulunmuştur ve bu olgularda sistemik inflamasyon belirgin yüksektir. KOAH tanısı olan polipli olgularda neoplastik ve non-neoplastik polip alt grubunda inflamasyon değerlerinin inceleneceği prospektif çalışmalara ihtiyaç vardır.*

Anahtar Kelimeler: *Kronik Obstrüktif Akciğer Hastalığı, kolorektal polip, sistemik inflamasyon, MPV, NLR*

ABSTRACT

INTRODUCTION: *The prevalence of chronic obstructive pulmonary disease (COPD) in patients with colorectal polyps and its relationship with systemic inflammation was investigated in our study.*

METHODS: *A total of 35 cases with COPD diagnosis (COPD group) and 163 control groups without chronic disease in medical history among patients who were diagnosed colorectal polyposis by colonoscopy between December 2016-December 2017 were included to the study. Demographic data such as age, smoking history, pathology results, anatomic location of the lesion, hemogram data such as leukocyte, neutrophil lymphocyte ratio (NLR) and mean platelet volüme (MPV) were recorded.*

RESULTS: *137 (69.2%) of the cases were male and the mean age was 63.56 ± 11.68 (20-89) years. Smoking history was available in 129 cases, of which 62 (48.1%) had a smoking history. The prevalence of COPD was 8% among patients with colorectal polyposis in the previous year. Leukocyte, NLR and MPV values were statistical significantly higher in patients with COPD compared to healthy group (p = 0.001, <0.001, <0.001, respectively). When the polyps were histopathologically categorized as neoplastic and non-neoplastic polyps, no significant difference was found in the comparisons of inflammation parameters between the groups.*

DISCUSSION and CONCLUSION: *COPD and adenomatous polyps are associated with systemic inflammation and its prevalance among adenomatous polyps was found to be 8%. Prospective studies are needed to examine the inflammation values of neoplastic and non-neoplastic polyp subgroups in patients with polyps with COPD.*

Keywords: *Chronic Obstructive Lung Disease, colorectal polyp, systemic inflammation, MPV, NLR*

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a disease presenting with systemic inflammation with high mortality and morbidity, characterized with limitation of the airway that is not fully reversible (1). It is estimated to become the fifth most fatal disease around the world by 2020 (2). While the most important cause of COPD is smoking, it may develop due to advanced age, genetic and environmental factors, and air pollution, independent from smoking, in some cases (3).

Colorectal polyps are proliferative lesions originating from the mucosa and submucosa epithelia and forming masses protruding into the intestine lumen. They are grouped as non-neoplastic (hyperplastic, hamartomatous, and inflammatory polyps) and neoplastic polyp adenomas (tubular, tubulovillous, and villous) (4,5). Similar to COPD, there is an important relationship between the incidence of adenomatous polyps and smoking (6). Risk of adenomatous polyp development was found to be 2-3 times higher in people who smoke than those who do not. Similar to adenomatous polyps, the association of hyperplastic polyps with smoking time and amount was also demonstrated (7).

Contraction of the airways in COPD causes local inflammation, and systemic inflammation response develops with the release of acute phase reactants (C-reactive protein [CRP], fibrinogen, serum amyloid A, surfactant protein D, and leukocytes) (8). It is characterized with inflammation in many cancer types such as colorectal cancer besides COPD, and proinflammatory cytokines were shown to have increased (9). However, these biomarkers are expensive tests that cannot be used in routine practice. Leukocyte, neutrophil leukocyte ratio (NLR), mean platelet volume (MPV), which are currently tested routinely, were studied both in COPD and colorectal, breast, stomach and renal cell carcinomas as inflammatory markers (10). It is known that adenomatous polyps and some hyperplastic nodules can transform into colorectal carcinoma (6). However, there are limited studies about both systemic inflammation in colorectal polyps and its biomarkers, and the frequency of adenomatous polyps in COPD. Our study investigated the frequency of COPD and its association with systemic inflammation in colorectal polyp cases, which are two diseases having common risk factors.

MATERIALS and METHODS

After the study was granted approval by the ethics committee, file data of cases who underwent colonoscopy at the Gastroenterology clinic between December 2016-December 2017 and subsequently diagnosed with colorectal polyposis were scanned retrospectively. The study enrolled 35 cases diagnosed with stable COPD and 163 control cases having no chronic disease (cancer, cardiovascular, neurovascular and metabolic diseases) in their medical history. The leukocyte, neutrophil, lymphocyte platelet counts and mean platelet volume (MPV) were recorded from Complete blood count (CBC) parameters in laboratory tests, and the neutrophil lymphocyte ratio (NLR) values were calculated from these parameters. For COPD cases, pulmonary function test results were recorded. Pulmonary function tests were performed according to the ATS/ERS standards using Jaeger MasterScope PC. Every measurement was repeated three times, and the best values were selected. Forced expiratory volume in one second (FEV1), Forced vital capacity (FVC), and FEV1/FVC were used as spirometric parameters.

Statistical Analysis

For the statistical analysis of the data, SPSS Statistics, version 20.0 (SPSS Inc., Chicago, Ill., USA) was used. Variables were expressed as mean±standard deviation, and percentage and frequency values. Also, homogeneity of variances, a preliminary condition of parametric tests, was controlled with the “Levene” test. Assumption of normality was checked with the “Shapiro-Wilk” test. When the differences between the two groups were to be evaluated, “Student’s t Test” was used if the parametric test’s preliminary conditions were met, or “Mann Whitney-U test” was used otherwise. The association of two continuous variables was evaluated with Pearson Correlation Coefficient and with Spearman Correlation Coefficient when the parametric test’s preliminary conditions were not met. The level of statistical significance was accepted as $p < 0.05$ and $p < 0.01$.

RESULTS

The study scanned the file data of 415 cases pathologically diagnosed with colorectal polyposis. A total of 198 patients with colorectal polyposis were included in the study, 35 of them were COPD group, and 163 were as controls. 137 (69.2%) of the cases were male and 61 (30.8%) were female and the mean age was 63.56 ± 11.68 (20-89) years. Smoking history was available in 129 cases, of which 62 (48.1%) had a smoking history. The mean size of polyps was 4.24 mm (2-40 mm). With regard to the location of colorectal polyps, 55 (27.8%) were detected in the rectum, 39 (19.7%) in the sigmoid colon, 35 (17.7%) in the transverse colon, 34 (17.2%) in the ascending colon, 25 (12.6%) in the descending colon and 10 (5.1%) in the caecum. According to the histopathological results, 150 cases (75.7%) had tubular, 24 (12.2%) had tubulovillous, 20 (10.1%) had hyperplastic, and 4 (2%) had inflammatory polyps. Among the cases diagnosed with colorectal polyposis in the last 1 year (415 cases), the frequency of COPD was 8%.

Forced expiratory volume in 1 second (FEV1), force vital capacity (FVC), and FEV1/FVC values were found to be 66.99±14.52%, 87.32±16.46% and 61.63±5.77%, respectively. The mean age of COPD cases was 67.97±9.14 years, and the female/male ratio was 1/34. The mean age of the healthy group was 62.61±11.98 years, and the female/male ratio was 60/103. The values of leukocyte, NLR and MPV were statistically significantly higher in the COPD group than controls (p=0.001, <0.001, <0.001, respectively). When the hemogram data neutrophil, lymphocyte and platelet results were evaluated, it was found that neutrophil count was statistically higher in COPD group (p=0.033) but lymphocyte and platelet counts were similar (0.294, 0.445, respectively). The demographic and laboratory data of both groups are given in (Table 1).

Table 1. Comparison of demographic and laboratory data of COPD and control groups

Variables	COPD group (n=35)	Control group (n=163)	p
Age (years)	67.97±9.14	62.61±11.98	**0.013**
Sex (F/M)	1/34	60/103	**0.001**
Smoking (pack/year)	31.59±21.26 (n=34)	8.38±14.61 (n=95)	**0.001**
White blood cell (×10^9 /L)	8577.43±1791.78	7366.32±1988.20	**0.001**
NLR	3.14±1.35	1.62±0.51	**<0.001**
MPV (fL)	10.45±0.98	8.67±0.50	**<0.001**
Neutrophil count (×10^9 /L)	5415.54±1617.01	4721.28±1760.91	**0.033**
Lymphocyte count (×10^9 /L)	1966.86±685.97	2103.01±702.83	0.294
Platelet count (×10^9 /L)	257776.91±121827.17	289662.58±239796.32	0.445

Abbreviations: NLR: Neutrophil lymphocyte ratio, MPV: Mean platelet volume

According to the histopathological results of polyps, tubular and tubulovillous polyps were classified as "neoplastic," and hyperplastic and inflammatory polyps as "non-neoplastic." The mean age in the neoplastic polyp group (64.3±10.81 years) was significantly higher compared to the non-neoplastic group (58.21±16.03 years) (p=0.016).

There was no difference between the two groups regarding sex and smoking (pack/year) (p=0.775, 0.076 respectively). Leukocyte, NLR, and MPV values and neutrophil, lymphocyte, and platelet counts were comparable in both groups (p=0.301, 0.614, 0.209, respectively) (Table 2).

Table 2. Comparison of Neoplastic and Non-neoplastic Polyps			
Polyp type	**Neoplastic polyps (n=174)**	**Non-neoplastic polyps (n=24)**	**p**
Age (years)	64.3±10.81	58.21±16.03	**0.016**
Sex (F/M)	53/121	8/16	0.775
Smoking history (pack/year)	15.47±19.95 (n=117)	5±10 (n=12)	0.076
White blood cell (×10^9 /L)	7635.23±2046.75	7182.92±2363.13	0.301
NLR	1.88±0.91	1.98±1.11	0.614
MPV (fL)	9.02±0.94	8.76±0.72	0.209
Neutrophil count (×10^9 /L)	4841.51±1724.70	4862.08±1983.73	0.957
Lymphocyte count(×10^9 /L)	2094.2±702.79	1968.33±684.46	0.410
Platelet count (×10^9 /L)	286937.89±236991.84	262916.67±72396.20	0.620
Abbreviations: NLR: Neutrophil lymphocyte ratio, MPV: Mean platelet volume			

When the inflammatory markers leukocyte, NLR and MPV were analyzed in terms of correlation, there was a positive correlation between smoking history and leukocyte, NLR, and MPV. There was no correlation detected between the other parameters and inflammatory markers (Table 3).

Table 3. Association of Smoking History with Inflammation Markers		
Variables	**Smoking history**	
	R	**p**
Leukocyte count (×10^9 /L)	0.256	0.03
NLR	0.325	<0.001
MPV(fL)	0.413	<0.001
NLR: Neutrophil lymphocyte ratio, MPV: Mean platelet volume		

DISCUSSION

Our study found that COPD frequency in colorectal polyposis cases was 8%, and leukocyte, NLR, MPV values in polyposis cases with COPD were significantly higher compared to the control group. There was no difference between neo-plastic and non-neoplastic polyps in terms of inflammation markers. Also, it was detected that smoking had a positive correlation with leukocyte, NLR and MPV.

Although the mean age of the patients with colorectal polyp was found 50 years in a study from Turkey, we found 63,6 years in our study. The frequency of colorectal polyps is more frequent in males compared to females, and 69.2% of cases in our study were male while 30.8% were female (11).

The most frequently histopathologically seen polyp among colorectal polyps is adenomatous polyps from the neoplastic polyp group and of these, the most frequent ones are tubular adenomas, villous adenomas, and tubulovillous adenomas, respectively (12,13). Korkmaz et al. found in their study where they evaluated 360 colorectal polyposis in 304 cases that the most frequent polyp type was tubular adenoma. The others, according to the order of their frequency, were hyperplastic, tubulovillous, inflammatory polyp (11). Consistent with the literature, our study found that the most frequently seen polyp type was tubular adenoma. The others were tubulovillous, hyperplastic and inflammatory polyps, respectively.

It is known that colorectal polyps are mostly seen in the rectosigmoid area, and its frequency decreases as it gets closer to the caecum (14). In the study by Dölek et al. it was reported that the polyps in the colon were most frequently seen in the rectum, then in transverse colon, ascending colon, descending colon, caecum, and sigmoid colon, respectively (15).

The study of Korkmaz et al. also reported that the most frequent localizations were rectum, sigmoid colon, descending colon, transverse colon, ascending colon, and caecum, respectively (11). The most frequent localization was rectum in our study, consistent with the literature data. The others were sigmoid colon, transverse colon, ascending colon, descending colon, and caecum, respectively.

Smoking is an important risk factor for colorectal polyposis and cancer development (16, 17). Long-time smoking increases the colorectal adenoma risk by 2-3 fold (18). Shin et al.'s study showed that adenomatous polyp developed 1.31 and 1.70 times more frequently in former and active smokers compared to those who never smoked (19). 48.1% of the cases in our study had a smoking history.

Smoking increases susceptibility to infections and continuously triggers inflammation (20). The most important cause of COPD is exposure to smoking, and it is a disease presenting with systemic inflammation (8). Our study detected positive correlation between smoking history and the inflammation values leukocyte count, NLR, and MPV.

Although there are studies showing that there is a relationship between smoking and colorectal polyp development, there are only few studies demonstrating the association of COPD with colorectal polyp and malignancy. The study by Chun et al. enrolled 333 cases undergoing post-bronchodilator spirometry and colonoscopy and detected that 82 of these had COPD. 60% of the cases had no smoking history. The prevalance of colorectal polyp was 39% in the group with no COPD, and 66% in the group with COPD. Colorectal malignancy risk in the COPD group was higher compared to the group with no COPD. (21).

It has been demonstrated that many cancers like colorectal cancer had an association with systemic inflammation. Although adenomatous polyps are almost fully precancerous lesions, their association with systemic inflammation is unknown (10, 22). However, it is known that the prevalance of adenomatous polyp dramatically increases with advanced age. Karaman et al.'s study of a total of 125 cases, including 67 neoplastic and 58 non-neoplastic cases, compared the age, neutrophil count, lymphocyte count, NLR, and MPV values and found that NLR value was higher in the neoplastic group (p=0.002) and that the other parameters were comparable. It was emphasized that NLR might be a marker of the presence of neoplasia in colon polyps (22). In our study, the mean age of neoplastic polyp cases was higher than that of the non-neoplastic group consistent with the literature. There was no difference in terms of NLR, MPV, and leukocyte values. This may be attributed to the small number of cases in the non-neoplastic group.

When the polyp cases were evaluated as COPD and non-COPD, the mean age and the rate of smoking history in the COPD group were significantly higher. The inflammatory indicators neutrophil count, leukocyte count, NLR, and MPV were significantly higher among the COPD cases. As our study was retrospective and the number in the COPD group was small, a subgroup analysis of the polyps in the COPD group could not be carried out. In this case, the higher inflammation values in the COPD group may be associated with the systemic inflammation present in COPD.

The first limitation of our study was that it was a retrospective study and there was only a small number of COPD cases. Inability to form a polyp subgroup of the COPD cases was the second limitation of this study.

CONCLUSION

COPD and adenomatous polyps are associated with systemic inflammation, and our study found that the frequency of COPD was 8% in the cases with adenomatous polyps. Smoking history is an important predictor of inflammation. While there was no difference in terms of inflammation markers between neoplastic and non-neoplastic polyps, systemic inflammation was markedly higher in the polyp cases with COPD. There is a need for prospective studies which will examine the inflammation values in the subgroups of neoplastic and non-neoplastic in polyp cases diagnosed with COPD.

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