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RESEARCH ARTICLE

Blood Group Characteristics in Colorectal Cancers

Kolorektal Kanserlerde Kan Grubu Özellikleri

Şahin Kahramanca[1], Turgut Anuk[2], Ali Cihat Yıldırım[1], Oskay Kaya[3]

[1]Kars Harakani State Hospital, Clinic of General Surgery, Kars, Turkey
[2]Kafkas University Faculty of Medicine, Department of General Surgery, Kars, Turkey
[3]University of Health Sciences, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Clinic of General Surgery, Ankara, Turkey

ABSTRACT

Aim: Colorectal cancer (CRC) is the third most common cancer in the world. Tumors are most commonly located in the rectosigmoid region. There are many factors in the etiology such as age, geographical features, family history, obesity, diet, and history of malignancy. In the present study, we aimed to determine the effect of blood group characteristics, which play a role in the etiology of stomach cancer, on the etiology of CRC.
Method: We retrospectively reviewed the files of patients who were diagnosed with CRC and operated in our center or at other centers and were followed postoperatively at our centers. Age, gender, histologic TNM stage (tumor, lymph node involvement, and metastasis), tumor-bearing colon segment, ABO blood group, and Rh antigen were examined from the patients' records.
Results: There were 265 (54.5%) patients with lymph node involvement and 53 (10.9%) with liver metastasis. The most common tumor location was the rectum (n=203). When the blood group and Rh antigen subgroups were examined, blood group A was detected in 253 patients (52.1%), blood group B in 115 patients (23.7%), blood group O in 78 patients (16%), and blood group AB in 40 patients. The incidence of colon cancer was found to be significant in patients with A (+) blood group (p<0.001).
Conclusion: As in stomach cancer, our findings show that the A (+) blood group is a risk factor in colorectal cancers, which have multifactorial etiology. Further genetic studies are needed.
Keywords: Colorectal cancer, ABO blood group, Rh antigen

ÖZ

Amaç: Kolorektal kanserler (KRK) tüm dünyada 3. en sık görülen kanser tipidir. Tümör lokalizasyonu en fazla rektosigmoid bölge yerleşimlidir. Etiyolojisinde yaş, coğrafi özellikler, aile öyküsü, obezite, diyet, malignite öyküsü gibi birçok faktör rol oynamaktadır. Çalışmamızda mide kanseri etiyolojisinde rol oynayan kan grubu özelliklerinin, kolorektal kanser etiyolojisi üzerine etkisini ortaya koymayı amaçladık.
Yöntem: KRK tanısı ile tarafımızdan opere edilen ve dış merkezlerde opere edilip merkezlerimizde takip altında olan hastaların dosyaları retrospektif incelendi. Hastaların; yaş, cinsiyet, histopatolojik TNM (tümör, lenf nodu tutulumu ve metastaz varlığı) evreleri, tümörlü kolon segmentleri, hastaların ABO kan grupları ve Rh antijenleri incelendi.
Bulgular: Çalışmamızdaki hastaların 265'inde (%54,5) lenf nodu pozitifliği, 53'ünde (%10,9) karaciğer metastazı tespit edildi. En sık tümör yerleşimi rektum (n=203) idi. Kan grubu ve Rh antijen alt grupları incelendiğinde; 253 hastada (%52,1) A kan grubu, 115 hastada (%23,7) B kan grubu, 78 hastada (%16) O kan grubu ve 40 hastada (%8,2) AB kan grubu saptanırken, 370 hastada (%76,1) Rh antijeni pozitif olarak tespit edildi. A (+) kan grubuna sahip hastalarda kolon kanseri görülme sıklığının anlamlı olduğu gözlendi (p<0,001).
Sonuç: Birçok etiyolojik faktörün risk faktörü olarak kabul edildiği kolorektal kanserlerde, genetik çalışmalara ihtiyaç olmakla birlikte, A (+) kan grubunun mide kanserinde olduğu gibi risk faktörü olduğu sonucuna ulaştık.
Anahtar Kelimeler: Kolorektal kanser, ABO kan grubu, Rh antijeni

Address for Correspondence/Yazışma Adresi: Şahin Kahramanca MD
Kars Harakani State Hospital, Clinic of General Surgery, Kars, Turkey
Phone: +90 531 429 84 84 **E-mail:** drkahramancasahin@gmail.com **ORCID ID:** orcid.org/0000-0002-4080-640X
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Introduction

Colorectal cancer (CRC) is the third most common cancer and ranks third in males and fourth in females among causes of cancer-related mortality.[1] There are a number of etiological factors such as age, gender, obesity, diet, geography, and hereditary characteristics. Forms of CRC with proven genetic bases include the polyposis syndromes and hereditary nonpolyposis syndromes. However, the CRCs associated with these inherited and acquired etiologic factors account for a relatively small proportion of all CRC cases. In the majority of patients the responsible factors are still undetectable. Blood groups are one of the controversial etiologic factors in CRC. Blood group antigens, discovered by Karl Landsteiner in 1901, have been the subject of numerous cancer studies since 1953, when Aird declared that blood group A was associated with stomach cancer.[2] Today, there are literature data suggesting that blood group A plays a role in the development of stomach, uterus, kidney, and neurological malignancies; blood group B in esophagus cancers; and blood group O in melanoma.[3,4,5] In this study, we aimed to determine differences in blood group distribution among patients with CRC.

Materials and Methods

Ethical approval for the study was obtained from the Kafkas University Faculty of Medicine Ethics Committee (approval number 105, 26 October 2016) and the study was conducted in accordance with the criteria of the Declaration of Helsinki. Informed consent forms were obtained from all patients included in the study. Data were collected by retrospective chart review of CRC patients diagnosed and followed postoperatively in the Kars State Hospital and Kafkas University Medical Faculty Hospital between June 2013 and September 2016. All patients included in the study presented to the general surgery outpatient clinic and emergency department with complaints of abdominal pain, changes in bowel habits, rectal bleeding, and malaise, and underwent surgery either in our center or other centers after receiving CRC diagnosis. The following data were recorded from the patients' records: age and gender, surgery type (elective/emergency), TNM (tumor, lymph node involvement, and distant metastasis) staging according to the pathology report, tumor location (segment), and ABO blood groups and Rh antigens.

Statistical Analysis

Statistical analyses of the data were done using SPSS for Windows version 22 (Chicago, IL, USA) software package. The Kolmogorov-Smirnov test was used to determine whether continuous variables showed normal distribution. Descriptive statistics were expressed as mean ± standard deviation for continuous variables, and number and percentage for categorical variables. Categorical variables were assessed by nonparametric chi-square test. Results were considered statistically significant for $p<0.05$.

Results

The study included 486 patients with a male/female ratio of 1.52:1. Two hundred and sixty-five patients (54.5%) had lymph node positivity and 53 patients (10.9%) had liver metastasis. The most common TNM stages were 3B (n=96), 3C (n=96), 2A (n=87), and 2B (n=80). The most frequent tumor locations were the rectum (n=203) and sigmoid region (n=138). Sixty-two patients underwent emergency surgery. The demographic characteristics of the patients are shown in Table 1. Analysis of blood group and Rh antigen subgroups revealed that 253 patients (52.1%) were blood group A, 115 patients (23.7%) were blood group B, 78 patients (16%) were blood group O, 40 patients (8.2%) were blood group AB, and 370 patients (76.1%) were Rh positive (Table 2). The incidence of colon cancer was significant among patients in the A (+) blood group

Table 1. Demographic characteristics of colorectal cancer patients

Demographic characteristics		Patient number (n) and percentage
Age (years)		61.4±12.3
Gender (male/female)		293/193
TNM stage	Stage 1	42 (8.4)
	Stage 2A	87 (17.9%)
	Stage 2B	80 (16.5%)
	Stage 2C	2 (0.4%)
	Stage 3A	17 (3.5%)
	Stage 3B	96 (19.8%)
	Stage 3C	96 (19.8%)
	Stage 4A	47 (9.7%)
	Stage 4B	20 (4.1%)
Tumor location	Right colon	105 (21.6%)
	Transverse colon	19 (3.9%)
	Left colon	138 (28.4%)
	Rectum	203 (41.8%)
	Anal canal	8 (1.6%)
	Synchronous/ metachronous	13 (2.7%)

TNM: Tumor, lymph node involvement, distant organ metastasis

(p<0.001). Although ABO blood groups were not associated with lymph node involvement or TNM grade (p=0.239 and p=0.055), there was a significant relationship between blood group and risk of liver metastasis, particularly for blood group A (p=0.020). No statistically significant relationships were observed between Rh antigen and TNM stage, lymph node involvement, or liver metastasis (p=0.579, p=0.849, and p=0.140).

Discussion

This study investigated the relationship between ABO blood groups and Rh antigens and rates of CRC, which involves numerous etiological factors. Our results show that the prevalence of blood groups A and B, as well as Rh antigen positivity were significantly higher among CRC patients. Despite being an archive study, it was of a retrospective design, which is a drawback in terms of the strength of the evidence. ABO blood group antigens were discovered by Karl Landsteiner in 1901 and Rh antigens by Huang et al.[2] in 1940. The ABO blood group antigens are encoded on chromosome 9q34. Although these antigens are biochemical components of the erythrocyte membrane, they have also been identified in epithelial cells of the gastrointestinal mucosa.[6] There is an intriguing hypothesis regarding the pathophysiological link between ABO blood groups and malignancy. Dysregulation of the enzymatic activities of glycosyltransferase A and glycosyltransferase B, which are responsible for cell membrane-mediated signaling and intercellular adhesion during the immune response, may increase plasma levels of von Willebrand factor, thereby leading to angiogenesis, apoptosis, and tumorigenesis. In addition, the association shown between ABO antigens and tumor necrosis factor-α, E-selectin, P-selectin, and intercellular adhesion molecule-1 also supports the hypothesis that ABO alleles influence the formation and spread of malignancy.[7] In line with these pathophysiological mechanisms, Huang et al.[2] first demonstrated the relationship between stomach cancer and blood group A Rh antigen in 1953. This first step led to the theory that blood group antigens could be a predisposing factor in many types of malignancies and continues to guide new studies in this area even today. Aird's findings regarding the association between gastric cancer and blood group were later corroborated by Etemadi et al.[8] who reported that individuals in the non-O blood groups (those carrying at least one A or B allele) had a higher incidence of gastric cancer and a 1.09-fold higher rate of total mortality. Xu et al.[9] also reported that gastrectomy patients with blood group A alleles had poorer prognosis. Beckman and Angqvist[10] reported that blood group O had a protective effect on tumor growth and spread, while Qiu et al.[11] also reported that blood group O reduced lymphatic invasion. Pancreatic cancer is usually advanced at time of diagnosis and has a very poor prognosis even after surgery. Wolpin et al.[12] reported that pancreatic cancer was more common in the non-O blood groups, and Greer et al.[13] reported that the incidence of pancreatic cancer was especially high in blood group A. CRC is the third most common cancer worldwide, and similar data have been reported in Turkey. Henderson et al.[3] reported that blood group A was more frequent in patients with CRC, and in Turkey, Urun et al.[1] also found that the incidence of CRC was higher among patients with non-O blood groups, especially those carrying the blood group A allele. Our finding that 52.1% of the CRC patients in this study had blood type A is consistent with the literature. In 2001, Nakagoe et al.[14] evaluated nonpolypoid syndromes, one of the hereditary syndromes involved in CRC development, and reported that blood group A was associated with nonpolypoid CRC. Despite improved early diagnosis, treatment modalities, and industrial advances, CRC remains one of the main causes of cancer-related death. In addition to comorbid factors, causes of cancer-related mortality include tumor grade, distant organ metastasis, and lymph node invasion. Nakagoe et al.[14] showed that CRC patients with blood group A had higher risk of lymph node metastasis. Cao et al.[6] investigated the overall postoperative survival and found that mean survival time was 99.8 months for blood group A (shortest survival), 103.4 months for blood group B, and 113.9 months for blood group AB (longest survival). As with A and B antigens, Rh antigen positivity has been associated previously with the spread of malignancy.[15] However, we observed no relationship in the present study between Rh antigen and lymph node metastasis, liver metastasis, or TNM stage. ABO was also not associated with lymph node involvement or TNM stage, but we found that risk of liver metastasis was higher in blood group A.

Table 2. Distribution of ABO blood groups and Rh antigen among colorectal cancer patients

ABO blood group				Rh antigen	
A	B	O	AB	Rh +	Rh -
253/486	115/486	78/486	40/486	370/486	116/486
52.1%	23.7%	16.0%	8.2%	76.1%	23.9%
p<0.001				p<0.001	

In summary, CRC is the most common malignancy of the gastrointestinal system and various acquired and inherited factors play a role in its etiology. Polyposis and nonpolyposis syndromes are the most common hereditary forms of CRC. In the present study, we investigated blood group and subgroup distributions in many gastrointestinal system malignancies. Although the patient population in this study was not sufficient to reach a definitive conclusion, we found that blood group A and Rh antigen positivity had a higher

frequency among the patients with CRC followed up in our center.

Ethics

Ethics Committee Approval: It was taken from Kafkas University Faculty of Medicine (date and aproval number 26.10.2016/105).

Informed Consent: Informed consent forms were obtained from all patients included in the study.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Ş.K., O.K., T.A., Concept: T.A., A.C.Y., Design: Ş.K., Data Collection or Processing: A.C.Y., Analysis or Interpretation: Ş.K., Literature Search: O.K., T.A., Writing: Ş.K.

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