RESEARCH ARTICLE

Relationships between Skin Cancers and Blood Groups - Link between Non-melanomas and ABO/Rh Factors

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Abstract

Background: This investigation focused on possible relationships between skin cancers and ABO/Rh blood groups. Materials and Methods: Between January 2005 and December 2012, medical data of 255 patients with skin cancers who were admitted to Kayseri Training and Research Hospital, Radiation Oncology and Plastic Surgery Outpatient Clinics were retrospectively analyzed. Blood groups of these patients were recorded. The control group consisted of 25701 healthy volunteers who were admitted to Kayseri Training and Research Hospital, Blood Donation Center between January 2010 and December 2011. The distribution of the blood groups of the patients with skin cancers was compared to the distribution of ABO/Rh blood groups of healthy controls. The association of the histopathological subtypes of skin cancer with the blood groups was also investigated. Results: Of the patients, 50.2% had A type, 26.3% had O type, 16.1% had B type, and 7.5% had AB blood group with a positive Rh (+) in 77.3%. Of the controls, 44.3% had A type, 31.5% had 0 type, 16.1% had B type, and 8.1% had AB blood group with a positive Rh (+) in 87.8%. There was a statistically significant difference in the distribution of blood groups and Rh factors (A Rh (-) and 0 Rh positive) between the patients and controls. A total of 36.8% and 20.4% of the patients with basal cell carcinoma (BCC) had A Rh (+) and B Rh (+), respectively, while 39.2% and 27.6% of the controls had A Rh (+) and B Rh (+), respectively. A significant relationship was observed between the patients with BCC and controls in terms of A Rh (-) (p=0.001). Conclusion: Our study results demonstrated that there is a significant relationship between non-melanoma skin cancer and ABO/Rh factors.

Keywords: ABO blood group - skin cancer - Rh factor - basal cell carcinoma - squamous cell carcinoma

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Introduction

Skin cancers are the most common form of all neoplasms (Tursen et al., 2005). Non-melanoma skin cancer accounts for 10% of all cancer types and for less than 0.1% of cancer-related deaths (Jemal et al., 2011; Vincenzo et al., 2011).

The incidence of skin cancers has been globally increasing over the years. Basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), which are two main types of non-melanoma skin cancer, represent the most common malignant neoplasm of all skin tumors. Individuals with fair skin are at high risk for BCC. The incidence of the disease increases with the increasing age. On the other hand, an increasing trend is observed in favor of SCC in individuals at the age of ≥65. These are usually slow-growing and localized tumors with a very low rate of metastatic spread (Armstrong and Kricker, 1995; Tursen et al., 2005; Otley, 2006).

The underlying etiopathogenesis of skin cancers is still unknown. Sun exposure, ultraviolet B (UVB) radiation in particular, is strongly associated with the development of skin cancers. Other possible causes include exposure to ionizing radiation, arsenic, polyaromatic hydrocarbons, and compromised immune system. In addition, genetic factors are also known to play a role in susceptibility to skin cancers (Armstrong and Kricker, 1995; Vincenzo et al., 2011).

ABO/Rh is the blood group system which is commonly used in Turkey and worldwide. Shattock and Karl Landsteiner are the first to discover that human blood varied from one individual to another in respect of physiological characteristics. They also discovered the A, B and AB blood groups. In later years, Decastello, Sturli and Hectoen discovered 0 blood groups, whereas Landsteiner and Wiener discovered the Rh factor. Currently, a number of blood groups including Kidd, P, Lutheran, Lewis, Duffy, Dieego, MN Ss, I, Xg, Sutter,

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Auberger, Kell-Cellan and Dombrock are available. However, they are not well-recognized as much as ABO and Rh, as they do not interfere with the blood transfusion. ABO blood group system is divided into four groups including A, B, AB, and 0, while Rh system is divided into two groups including Rh positive (+) and Rh negative (-). There are a total of eight blood groups, as both systems are combined (Coon and Weinstein, 1986; Ichikawa et al., 1998; Hosoi, 2008; Iodice et al., 2010).

Today, the relationship between ABO and Rh blood group systems and several diseases including cancers and the role of these systems in the etiopathogenesis of the diseases is still under investigation (Ichikawa et al., 1998; Rolfe et al., 2002; Adamian, 2005; Tursen et al., 2005; Greer et al., 2010; Iodice, 2010; Vincenzo et al., 2011). However, there is a limited number of clinical studies reporting the role of blood group systems in the etiopathogenesis of the diseases (Tursen et al., 2005; Vincenzo et al., 2011).

In this study, we aimed to investigate a possible relationship between skin cancers and ABO/Rh blood groups.

Materials and Methods

Between January 2005 and December 2012, medical data of 255 patients with skin cancers who were admitted to Kayseri Training and Research Hospital, Radiation Oncology and Plastic Surgery Outpatient Clinics were retrospectively analyzed. Age, histopathological subtype of skin cancer and blood groups [A, B, AB, 0 with Rh (+) or Rh (-)] were recorded. Patients with unknown blood group were excluded. The control group consisted of 25.701 healthy volunteers who were admitted to Kayseri Training and Research Hospital, Blood Donation Center between January 2010 and December 2011.

The statistical analysis was performed using the SPSS software, version 10.0 (SPSS, Inc., Chicago, IL, USA). Qualitative variables were expressed in percentage. Pearson chi-square and Monte Carlo tests were used to determine the correlation among the categorical variables. The distribution of the blood groups of patients with skin cancer was compared to the distribution of ABO/Rh blood groups of healthy controls. The association of the histopathological subtypes of skin cancer with the blood groups was also investigated. A p value of <0.05 was considered statistically significant.

Results

A comparison between the blood groups and Rh factors of the patients and controls is shown in Table 1. Of the patients with skin cancer, 50.2% had A blood group, 26.3% had 0 blood group, 16.1% had B blood group, and 7.5% had AB blood group. However, 44.3%, 31.5%, 16.1% and 8.1% of the controls had A, 0, B and AB blood group, respectively. The percent of A Rh (-) group was higher in the patient group, compared to the controls, while a higher number of controls had 0 Rh (+) blood group. There was statistical significance in blood groups and Rh factors between the patients and controls (p<0.001).

Of the patients with SCC 46.3% had A Rh (+) blood group compared to 36.8% among the BCC group. In addition, of the patients with SCC 22.2% had 0 Rh (+) blood group, compared to 20.4% in the BCC group. The rarest blood group was AB Rh (-) including 2.5% in the BCC group, 0% in the SCC group. A higher number of patients with SCC had A Rh (+) blood group, while they had less A Rh (-) blood group. However, it did not reach statistical significance. No significant difference in the distribution of 0 and A blood groups was observed between the SCC and BCC group (p=0.663) (Table 2).

The distribution of ABO blood groups among the patients with BCC and controls is summarized in Table 3. On the other hand, a significant difference in ABO/Rh

Table 1. A Comparison between the Blood Groups and Rh Factors of the Patients and Controls (n: number of the patients)

			Control group		Skin cancer group	
			n	%	n	%
ABO/Rh blood	0 Rh	(-)	990	(3.9)	14	(5.5)
		(+)	7096	(27.6)*	53	(20.8)*
	A Rh	(-)	1299	(5.1)*	29	(11.4)*
		(+)	10087	(39.2)	99	(38.8)
	AB Rh	(-)	306	(1.2)	5	(2.0)
		(+)	1784	(6.9)	14	(5.5)
	B Rh	(-)	506	(2.0)	10	(3.9)
		(+)	3633	(14.1)	31	(12.2)
Total			25701 (100)		255 (100)	

*Different symbol is statistically significant (p<0.05)

Table 2. A Comparison between the Blood Groups/ Rh Factors and Cancer Subtypes (n: number of the patients)

			BCC		SCC	
			n	%	n	%
ABO/Rh blood	0 Rh	(-)	11	(5.5)	3	(5.6)
		(+)	41	(20.4)	12	(22.2)
	A Rh	(-)	25	(12.4)	4	(7.4)
		(+)	74	(36.8)	25	(46.3)
	AB Rh	(-)	5	(2.5)	0	(0)
		(+)	12	(6.0)	2	(3.7)
	B Rh	(-)	9	(4.5)	1	(1.9)
		(+)	24	(11.9)	7	(13.0)
Total			201 (100)		54 (100)	

*Different symbol is statistically significant (p<0.05)

Table 3. A Comparison among the Patients with BCC and Controls in Terms of ABO/Rh Factor (n: number of the patients)

			BCC group		Control group	
			n	%	n	%
ABO/Rh blood	0 Rh	(-)	11	(5.5)	990	(3.9)
		(+)	41	(20.4)	7096	(27.6)
	A Rh	(-)	25	(12.4)*	1299	(5.1)*
		(+)	74	(36.8)	10087	(39.2)
	AB Rh	(-)	5	(2.5)	306	(1.2)
		(+)	12	(6.0)	1784	(6.9)
	B Rh	(-)	9	(4.5)	506	(2.0)
		(+)	24	(11.9)	3633	(14.1)
Total			201 (100)		25701 (100)	

*Different symbol is statistically significant (p<0.05)

factor was observed between the BCC group and control group (p=0.001). Of the patients with BCC, 36.8%, 20.4%, 12.4% and 11.9% had A Rh (+), 0 Rh (+), A Rh (-), and B Rh (+), respectively. Among the controls, 39.2%, 27.6, 5.1% and 14.1 had A Rh (+), 0 Rh (+), A Rh (-), and B Rh (+), respectively. A higher number of controls had B Rh (+), AB Rh (+), A Rh (+) and 0 Rh (+), compared to the BCC group. There is statistical significant difference in A Rh (-) blood group was observed among the BCC and controls (p<0.001).

Discussion

It is well-established that human gene frequencies for the ABO blood groups vary in a society, thereby leading to a risk factor for many diseases. Recently, there has been a trend of linking blood groups and several diseases. Genetic studies have demonstrated that individuals with A blood group are more resistant to the influenza virus, despite a higher risk profile for acute rheumatism, whereas individuals with 0 blood group are highly resistant to the viruses despite a higher risk profile for gastric cancer, ulcer and other forms of cancer. In addition, although it has been reported that several forms of cancer are associated with subtypes of ABO blood groups, the exact mechanism of this association remains to be elucidated (Rolfe et al., 2002; Adamian, 2005; Hosoi, 2008; Xie et al., 2010).

The ABO blood group antigens, which are the primary antigens in human blood, are located on the surface of red blood cells and various epithelial cells. The ABO blood group system is associated with the chromosome 9. Genetic changes may present on the chromosome 9 in case of several forms of cancer. Therefore, it has been reported that genetic changes on the chromosome 9 may have an effect on the release of ABO blood group antigens. Several studies have shown that changes in the ABO/Lewis blood group antigens may be associated with the malignant transformation for some tumors (Aird et al., 1953; Jordan and Lynch, 1983; Rolfe et al., 2002; Adamian, 2005; Tursen et al., 2005; El Hajj et al., 2007; Hosoi, 2008; Edgren et al., 2010; Iodice et al., 2010).

In 1953, Aird et al. (1953) first reported such a relationship between A blood group and gastric cancer. Subsequent studies confirmed that the incidence of gastric cancer was higher (nearly 20%) in individuals with A blood group. In addition, a higher incidence of gastric cancer in individuals with 0 blood group was reported in another study (El Hajj et al., 2007; Edgren et al., 2010). Several studies also demonstrated that the incidence of laryngeal and hypopharyngeal cancer, acute myeloid leukemia, ovarian, pancreatic, breast, vulvar and gastric cancer was higher in individuals with A blood group (Henderson et al., 1993; Su et al., 2001; Rolfe et al., 2002; Vadivelu et al., 2004; El Hajj et al., 2007; Edgren et al., 2010; Greer et al., 2010). There are also various studies indicating that the incidence of esophageal squamous cell carcinoma, gastric cancer, acute lymphoblastic leukemia and malignant melanoma was higher in individuals with 0 blood group, while the incidence of endometrial cancer and advanced esophageal cancer was higher in individuals with AB blood group and the incidence of pancreatic cancer, Hodgkin's lymphoma and cardial cancer was higher in individuals with B blood group (Karakousis 1986; Su et al., 2001; Alavi et al., 2006; El Hajj et al., 2007; Vincenzo et al., 2011). So far, no relationship has been observed between the ABO blood groups in patients with brain cancer, cervical cancer, salivary gland cancer, testicular cancer and skin cancer, and the blood subtypes in healthy individuals (Mittal, 1970; Jordon et al., 1989; Pinkston and Cole, 1996; Mehrazin, 2006).

In addition, studies in which the relationship between ABO blood groups and several forms of cancer and parameters including diagnosis, metastasis, prognosis, stage, and histopathological diagnosis was defined are available in the literature. Several studies investigated a possible association of the blood groups and its frequency with clinicopathological parameters and prognosis of the diseases in patients with esophageal, cardiac, gastric, pulmonary, hypopharyngeal, salivary gland, gynecological, colorectal, pancreatic, bone, bladder, urethral, and renal cancer (Mittal, 1970; Slater et al., 1993; Pinkston and Cole, 1996; Su et al., 2001; Nozoe et al., 2004; Adamian, 2005; Mehrazin, 2006; El Hajj et al., 2007). Jordon et al. reported that blood group antigens might be useful in the differential diagnosis of malignant pleural mesothelioma (MPM) and adenocarcinoma (Jordon et al., 1989). Although different reports are available in the literature, Guleria et al. demonstrated that the incidence of breast cancer was higher with a worse prognosis in patients with A blood group, as confirmed by many studies (Guleria et al., 2005). Similarly, Nakagoe et al. and Moldvay et al. found a relationship between the blood group antigens and metastatic disease and its prognosis (Moldvay et al., 2000; Nakagoe et al., 2000).

However, there are a limited number of studies investigating the relationship between Rh factor and different forms of cancer.

Slater et al. (1993) reported that a higher number of patients with advanced colorectal cancer had Rh positive. Similarly, Adamian (2005) observed that the incidence of endometrial cancer was higher in patients with AB Rh negative. Cerny et al. (2006) also found that a higher number of patients with lung cancer had Rh negative. However, no relationship between the Rh factor and skin cancer and salivary gland cancer was reported (Karakousis et al., 1986; Pinkston and Cole, 1996; Vincenzo et al., 2011).

On the other hand, the exact relationship between ABO blood groups and skin cancer remains to be elucidated, although several studies have investigated this relationship over the last three decades. In our study, we aimed to investigate a possible relationship between skin cancers and ABO/Rh blood groups.

Descriptive epidemiological studies have shown that environmental factors are the main determinants of the risk for skin cancers. In addition, genetic factors have been reported to be associated with the development of skin cancers. Several studies demonstrated that individuals with compromised immune systems (i.e. renal transplantation, non-Hodgkin's lymphoma, or chronic lymphocytic leukemia) were at a higher risk for non-melanoma skin cancer with an aggressive prognosis. These

findings suggested that immunosuppression might play a role in the underlying etiology of skin cancers. On the other hand, no increased incidence of BCC in patients with compromised immune systems was reported, whereas the incidence of SCC was higher in patients with mutations in the Tp53 gene (Armstrong and Kricker 1995; Otley, 2006).

Furthermore, ABO blood group and Rh factor have been associated with the etiopathogenesis of skin cancers. However, limited data are available on this possible association. In our study, we observed that the distribution of A Rh (+) was higher, while the distribution of 0 Rh (+) was lower in patients with BCC compared to the control group. There was a statistically significant difference in the distribution of A Rh (-) factor between the BCC group and control group. These findings were consistent with the literature data reported by Iodice et al. and Tursen et al. investigated the possible relationship between the blood groups and malignant and benign skin lesions in 98 patients and 419 healthy controls. The authors reported that a higher number of patients with skin cancer had A blood group, while a lower number of patients had 0 blood group. However, it did not reach statistical significance (Tursen et al., 2005; Iodice et al., 2010). Similarly, Iodice et al. demonstrated that most of the patients with non-melanoma skin cancer had A Rh positive (Iodice et al., 2010). In another study, Xie et al. (2010) investigated the relationship between the blood groups and incidence of skin cancer in participants with 0 blood group and non-0 blood group. The authors reported that participants with non-0 blood group had a reduced risk by 14% for developing SCC and by 4% for developing BCC. However, the reduction in the risk for melanoma for non-0 blood group was not statistically significant. As a result, the risk for developing skin cancer was lower in participants with non-0 blood group (Xie et al., 2010). In another study investigating the possible relationship between the ABO and cutaneous malignant melanoma (CMM), Vincenzo et al. reported an increased risk for developing CMM in individuals with 0 Rh (-) (Vincenzo et al., 2011). In another study involving 168 patients with malignant melanoma, Karakousis et al. (1986) revealed that a higher number of patients with 0 blood group had malignant melanoma. However, the results did not indicate statistical significance. The median survival was 46.6 months and 67.7 months in patients with 0 blood group (p=0.04) and A blood group, respectively. The authors reported that the overall survival was improved in women and patients with A blood group, compared to the 0 blood group (Karakousis et al., 1986).

In conclusion, we observed a significant relationship between non-melanoma skin cancer and ABO/Rh factors. We suggest focus on the non-melanoma skin cases belonging to the blood groups A Rh-negative in future studies. However, further large-scale studies are required to investigate the effects of blood groups on the histopathological subtypes of skin cancer.

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