

ORIGINAL ARTICLE

ABO and Rh blood groups frequency in women with HER2 positive breast cancer

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Summary

Purpose: The role of genetic factors in the development of cancer is widely accepted. Data on the role of ABO blood group and Rh factor in breast cancer is inconclusive. The aim of this study was to investigate the presence of a possible association between HER2 (+) breast cancer in Turkish women and ABO blood groups and Rh factor.

Methods: In 294 female patients with HER2 (+) breast cancer, ABO blood groups and Rh factor were examined. The relationship of blood groups with age, menopausal status, and family history of cancer; estrogen receptor (ER), progesterone receptor (PR) and HER2 status of these patients was evaluated. Blood groups distribution of 22,821 healthy blood donors was also assessed and compared with the patients' blood groups distribution.

Results: The median patient age was 47 years (range

20-80) and 56% of the patients were premenopausal. ER and PR were positive in 50 and 60% of the patients, respectively. Overall, the ABO blood group distribution of the 294 HER2 (+) breast cancer patients was similar to that of the healthy blood donors ($p=0.36$). Likewise there was no correlation between blood type and ER, PR and menopausal status. Rh (-) patients had more frequent family cancer history and this difference was significant for patients with blood group B Rh (-) and O Rh (-) ($p = 0.04$).

Conclusion: In the present study we didn't find any relationship between HER2 status and ABO blood group and Rh factor. However, further studies with larger number of patients are needed to establish the role (if any) of blood groups in patients with breast cancer.

Key words: ABO blood group, breast cancer, HER2, Rh factor

Introduction

The role of genetic factors in the development of cancer is widely accepted. Since Aird et al. reported a relation between blood group A and cancer of the stomach, there have been a lot of studies published about the relation between ABO blood groups and diseases such as peptic ulceration [1,2]. Recently, a relationship between pancreatic cancer and ABO blood groups has been described [3-5]. It is well known that genetic factors (e.g. BRCA1/2) are involved in the etiology of some cases of familial breast cancer. ABO blood group genes are mapped at the chromosome 9q, in which genetic alterations are common in many cancers [6]. Apart from ABO blood groups, some authors suggested that

Rh factor was related with breast cancer risk [7]. Individualized current therapeutic strategies for patients with primary breast cancer are frequently determined by the size of the primary tumor, axillary lymph node status, pathologic disease stage, estrogen and progesterone receptors status and HER2 overexpression. In some previous studies, ABO blood groups have been reported as predisposing or prognostic factors in breast cancer [8-11]. Also it was suggested that A, B, H, and Lewis blood group antigens in human breast cancer are correlated with steroid hormone receptor and disease status [12].

The aim of this study was to investigate the presence of a possible association between HER2 (+) breast cancer in Turkish women and ABO blood groups and Rh factor.

Methods

This study was approved by the Institutional Review Board of Ankara University Faculty of Medicine. Included in the study were 294 female patients with HER2 (+) breast cancer. The relationship of blood groups with age, menopausal status, and family history of cancer, ER, PR and HER2 status was evaluated in the breast cancer patients. Patient blood groups distribution was compared with the blood groups of 22,821 healthy blood donors of Ankara University Medical School Blood Center in 2010.

Statistical analysis

Statistical analysis was carried out using the Statistical Package for the Social Sciences 13.0 for Windows (SPSS, Inc, Chicago, IL, USA). Descriptive statistics were calculated for all variables. Pearson’s chi square test analysis was used to detect statistical differences in proportions. All tests were two-tailed and a p value of less than 0.05 was considered significant.

Results

The median age was 47 years (range 20-80) in patients and 33 years (range 18-65) in healthy blood donors. Overall, the ABO blood groups distribution of the 294 HER2 (+) breast cancer patients was similar to that of the healthy blood donors (Table 1). Although the percentage of blood group A Rh (+) was higher in patients than in controls (49.3 vs. 43.5% respectively), the difference wasn’t statistically significant (p=0.09). Of the 294 patients 268 (91.2%) were Rh (+) and 26 (8.8%) Rh (-). The corresponding figures of the controls were 20,111 (88.1%) and 2,710 (11.9%) (p=0.11).

Fifty-six percent of the patients were premenopausal. ER and PR were positive in 50% and 60%, re-

spectively. ABO blood types weren’t correlated with age, ER, PR, or menopausal status. However, the difference of PR status according to ABO groups was close to the level of statistical significance (p=0.056; Table 2). Although not statistically significant (p=0.06), Rh (-) patients had more frequent family cancer history. Patients with blood group B Rh (-) and O Rh (-) had significantly higher family history of cancer (p=0.04). However, Rh status wasn’t statistically different in relation to age, menopause, ER, and PR status (Table 3).

Table 2. HER2 (+) patient characteristics according to ABO status

| Characteristics | ABO blood groups | | | | p-value |
|-----------------------|------------------|-----|------|-----|---------|
| | A % | B % | AB % | O % | |
| Age (years) | | | | | 0.66 |
| ≤ 35 | 15 | 12 | 10 | 15 | |
| >35 | 85 | 88 | 90 | 85 | |
| Menopausal status | | | | | 0.19 |
| Pre | 52 | 57 | 58 | 66 | |
| Post | 48 | 33 | 42 | 34 | |
| Family cancer history | | | | | 0.04 |
| Negative | 55 | 52 | 57 | 48 | |
| Positive | 33 | 31 | 24 | 38 | |
| Unknown | 12 | 17 | 19 | 14 | |
| ER status | | | | | 0.43 |
| Negative | 43 | 50 | 43 | 54 | |
| Positive | 56 | 50 | 52 | 46 | |
| Unknown | 1 | 0 | 5 | 0 | |
| PR status | | | | | 0.056 |
| Negative | 37 | 33 | 38 | 45 | |
| Positive | 62 | 67 | 52 | 55 | |
| Unknown | 2 | 0 | 10 | 0 | |

Table 3. HER2 (+) patient characteristics according to Rh status

| Characteristics | Rh + % | Rh - % | p-value |
|-----------------------|--------|--------|---------|
| Age (years) | | | 0.53 |
| ≤ 35 | 15 | 12 | |
| >35 | 85 | 88 | |
| Menopausal status | | | 0.66 |
| Pre | 57 | 60 | |
| Post | 43 | 40 | |
| Family cancer history | | | 0.01 |
| Negative | 54 | 35 | |
| Positive | 35 | 38 | |
| Unknown | 13 | 27 | |
| ER status | | | 0.10 |
| Negative | 46 | 58 | |
| Positive | 53 | 42 | |
| Unknown | 1 | 0 | |
| PR status | | | 0.64 |
| Negative | 38 | 42 | |
| Positive | 60 | 58 | |
| Unknown | 2 | 0 | |

Table 1. Blood group distribution of HER2 (+) patients and controls

| Blood groups | HER2 (+) patients (n = 294) | | Controls (n=22,281) | | p-value |
|--------------|-----------------------------|------|---------------------|-------|---------|
| | N | % | N | % | |
| A Rh (+) | 135 | 45.8 | 8795 | 38.54 | 0.09 |
| A Rh (-) | 10 | 3.4 | 1130 | 4.95 | |
| Total A | 145 | 49.3 | 9925 | 43.5 | |
| B Rh (+) | 37 | 12.6 | 3185 | 13.96 | 0.97 |
| B Rh (-) | 5 | 1.7 | 425 | 1.86 | |
| Total B | 42 | 14.3 | 3610 | 15.8 | |
| AB Rh (+) | 19 | 6.5 | 1581 | 6.93 | 0.78 |
| AB Rh (-) | 2 | 0.7 | 205 | 0.90 | |
| Total AB | 21 | 7.1 | 1786 | 7.8 | |
| O Rh (+) | 77 | 26.2 | 6550 | 28.70 | 0.54 |
| O Rh (-) | 9 | 3.1 | 950 | 4.16 | |
| Total O | 86 | 29.3 | 7500 | 32.8 | |
| Total | 294 | 100 | 22821 | 100 | 0.36 |

Discussion

Blood group antigens are present on many epithelial cells. However, the role of these antigens in the pathogenesis of cancer is unclear. The relation between ABO blood groups and the development of malignancy has been reported by Alexander in 1921. In 1953 Aird et al. reported that “the frequency of blood group A is greater and the frequency of blood group O is less in patients with gastric cancer”. They also reported that blood group O is strikingly high in patients suffering from peptic ulcer [1,2]. The relation between ABO/Rh blood groups and cancer was the subject of intensive research, especially until 1990 [1,2,6,9,10,12,13]. Recently, a significant association between pancreatic cancer and ABO blood groups was reported. Even though the role of ABO blood groups and Rh factor as prognostic factors in breast cancer has been examined in the past, still few data are available and the role of blood group remains controversial [2,8-10,13].

Research on breast cancer strongly indicates etiological heterogeneity and inherited and environmental factors influence the risk of breast cancer development [6]. Heredity play an important role in breast carcinoma and the role of genetic factors in breast cancer genesis is a very well known issue. ABO is a hereditary trait and determined easily in daily practice. Therefore, many studies were carried out to find possible relationships between ABO blood groups and malignant and non-malignant diseases. In the 1950s Aird et al. and Goldenberg et al. reported that they didn't find any significant relationship between breast carcinoma and blood groups [2,14].

In the present study the distribution of the ABO blood groups of the 294 HER2 (+) breast cancer patients was similar to that of the Turkish general population, without statistically significant difference ($p=0.36$) between groups; however, the ratio of patients with blood group A Rh (+) was higher compared with the control group, a finding compatible with the literature. Munzarova et al. analyzed retrospectively the clinical records of 551 breast cancer patients. Age at presentation, stage of disease, progression free survival, distant metastasis, mortality and survival were examined. The authors couldn't find any difference in these parameters in relation to ABO blood groups [10]. Also in the study of Holdsworth et al. the distribution of blood groups was not significantly different in breast cancer patients. However, they showed a difference in survival between patients with different blood groups. Patients with blood group AB and B (high risk group) had higher relative death and relapse rates than those with group O and A (low risk group). When they compared high and

low risk groups they found that survival and recurrence rates were significantly different (p -value= 0.015 and 0.023, respectively).

The data about family history for cancer and ABO/Rh are controversial. Tryggvadottir et al. [6] investigated Icelandic familial and sporadic breast cancer, bilateral breast cancer and distribution of ABO blood groups. The blood group distribution was similar but the familial cases had higher prevalence in group B and lower prevalence in group O and the odds ratio (OR) for B vs. all others was 2.1. Interestingly, non-affected first degree female relatives were only half as likely to belong to group B as were Icelandic women and the odds ratio for B vs. all others was 0.5 [6]. In a Greek study Stamatakos et al. showed a positive family history in Rh (+) and increased risk of metastasis in Rh (-) patients [11]. Ronco et al. reported a significant association between group O and family history (OR=1.98, $p=0.03$). Also a positive association was found among Rh (-) women (OR=3.11, $p=0.001$) when compared to Rh (+) women (OR=1.46, $p=0.15$). Additionally, when Rh (-) and (+) patients were compared, OR for family history of cancer (other than breast cancer) was 2.08 and p -value was 0.03 [7]. In this study, although not statistically significant ($p=0.06$), Rh (-) patients had higher family cancer history. However, in present study patients with blood group B Rh (-) and O Rh (-) had higher family history of cancer ($p=0.04$).

Idikio et al. studied A, B, H, and Lewis-a and b blood group antigens in human breast cancer. The expression of blood group antigens were different for all antigens and statistically significant differences were identified for H, Lewis-a and b ($p<0.05$) antigens. So the authors concluded that H, Lewis-a and b blood group antigens are reduced significantly in human breast cancer and the loss of these antigens reflects invasive behavior [12], whereas in the study of Nakagoe et al. immunohistochemical expression of Lewis-x antigen in tumor cells was significantly correlated with poor prognosis and survival. However, survival curves for A, B, H, Lewis-a antigens weren't different [8].

Although the sample size is a major limitation of this study, the results of the present study showed that the ABO/Rh blood group distribution of the 294 HER2 (+) breast cancer patients was similar to that of the Turkish general population. Also no correlation between ABO blood type and age, ER, PR, and menopausal status was established. Rh (-) patients had more frequent family history of cancer and this difference was significant for patients with blood group B Rh (-) and O Rh (-). Nevertheless further studies with larger number of patients are needed to establish the role of blood groups in patients with breast cancer.

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