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Original Article

Association of ABO blood group and breast cancer in Jodhpur

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Abstract

There is a large amount of evidence that the ABO blood group system may play a role in disease etiology. However, in relation to breast cancer, these findings are inconsistent and contradictory. Present study was conducted for analysis to access ABO blood groups potential role of in breast carcinoma. The study was conducted on 206 clinically diagnosed breast cancer patients from Radiotherapy Department of Mathura Das Mathur Hospital in Jodhpur, from September 2006 to December 2007. The standard agglutination test was used to determine the blood groups. Association of ABO blood groups and risk of breast cancers was found out with Odd Ratios (ORs) with 95% Confidence Interval (CI). In reference of proportion of breast cancer in blood group AB [OR 1 with 95% CI 0.476 to 2.103), the breast carcinoma in blood group A [OR 7.444 with 95% CI 4.098 to 13.5222) was found at 7.4 times at higher risk than in blood group 'AB'. Breast cancer was found minimum in blood group 'AB' and maximum in blood group 'A'.

Introduction

Breast cancer is a worldwide malignant disease. Over one million new cases of breast cancer are diagnosed every year (1). Although there are several other factors having the risk of breast cancer but ABO blood groups also has been associated with risk and survival of several malignancies, including pancreas cancer (2) and stomach cancer (3), the mechanism is complex and unclear. It may be due to influence of blood group antigens on systemic inflammatory response (4) which has been associated with the malignancies. The ABO antigen expressed on the surface of malignant cells appears to be different from the antigen expressed on normal tissue (5). The different expression of antigens on the surface of cancer cells might alter motility, apoptosis and immune escape (6). These mechanisms might influence the initiation and spread of malignancies.

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In some tumors, alteration of ABO/Lewis-related antigens is associated with malignant transformation (7). The ABO blood type, an easily accessible factor in patient's genetic makeup, has been associated with many diseases, though the explanation for the association between ABO blood groups and some disease is still unclear. Since the first report showing an association between blood group A and gastric cancer (3), numerous other reports have documented a relation between susceptibility to cancer and blood group. High incidence of blood group A in various cancers, including neurologic tumors, salivary gland, colon, uterus, ovary, pancreas, kidney, bladder and cervix (8), and consistent relation to O blood group in skin and melanoma (9) has been reported.

ABO blood group genes are mapped at 9q34.2 region in which genetic alteration is common in many cancers. The loss or presence of blood group antigens can increase cellular motility or facilitate the interaction between tumor cells and endothelial cells of distant organs (10). In many cancers, the deficiency of A or B epitope has been reported which is associated with accumulation of their precursor, which causes enhanced malignancy. Blood group carbohydrate antigens on the surface of cancer cells can be regarded as an end product of tumor progression that can be used as useful prognostic and diagnostic markers (11).

The present study is an attempt to correlate ABO blood groups frequency and to assess the utility of ABO blood group in relation to breast cancer as a preclinical tumor marker. Thus, the objectives of this study were to document ABO blood group of patients suffering from malignancies of breast and to describe the association of malignancy with ABO blood group in Jodhpur in Western Rajasthan.

Material and Method

This is a retrospective hospital based study conducted in Mathura Das Mathur Hospital in Jodhpur, Rajasthan from September 2006 to December 2007. A total of 206 consecutive, newly and confirmed diagnosed breast cancer patients were enrolled in this study as patient group. The study was approved by ethical committy and Institutional Review board of Dr. Sampurnanand Medical College, Jodhpur under Rajasthan University of Health Science, Jaipur.

A written informed conscious consent was obtained from all subjects before their participation. The data of age, sex, ABO blood group and pathological status of cancer were collected from the Radiotherapy Department of Mathura Das Mathur Hospital, Jodhpur.

Inclusion criteria for the cases were as follows :

Pathologically confirmed diagnosis of breast cancer, Laboratory data available for ABO blood type and detailed record of disease, course and history

Exclusion criteria

Familial cancer history, oral contraceptive pills used, menopausal status had been taken.

Initially all patients were completed a detailed questionnaire regarding diets and habits, submitted to thorough history taking and detailed physical examinations and performed routine radiological and laboratory investigations including complete blood count (CBC), tumor markers for breast cancer.

Blood samples were obtained into vacuum glass tubes containing EDTA.

ABO blood tying was carried out with standard agglutination method. ABO blood groups were determined by using antiserum A and Antiserum B (12).

Standard Agglutination Method: In agglutination test firstly we prepare red cell suspension in a test tube and then in under aseptic precautions add a drop of blood. Then a drop of each antiserum (antiserum A, antiserum B) on is placed on glass slide with the help of dropper and a drop of isotonic saline (used as control) also placed on the slide. The slide is accordingly labeled as anti- A, anti- B and control. After 10 minutes, examined for the presence of agglutination (clumping of RBC) under low power microscope, if there is no agglutination (RBC remain separated and evenly distributed), and if agglutination occurs the RBC are massed together in clumps.

Sample size determination

The sample size was determined (13) by using the formula for comparing the difference of means between the groups with $\alpha = 0.05$, power = 80% and es = 0.3

es = largest difference between any two groups to be detected/expected within the group Standard Deviation

es = diff / SD

Sample size = 173

Accordingly we found that the sample size of 206 breast cancer patients would be more useful for our study purpose.

Statistical analysis

For each factor, we calculated the adjusted Odds Ratios (OR) and 95% confidence Interval (CI) using maximum likelihood estimation.

Results

In this study we found that there was an association exists between blood groups A with breast cancer in sample population.

Above table described a total of 206 breast cancer cases. Maximum cancer cases were found in blood group A (n=76), followed by blood type B (n=67), O (n=48), and least were found in blood type AB (n=15).

In 206 breast cancer cases, in reference to blood group AB [ORs 1 with 95% CI, 0.476-2.103], blood group A [ORs 7.444 with 95% CI, 4.098-13.522] having 7.4 times higher association with breast cancer.

In reference to blood type A, blood group B [ORs 6.138 with 95% CI, 3.365-11.195], having 6.1 times higher risk for the breast cancer. Both blood type A and B having strong association with breast cancer.

Blood type O [ORs 3.868 with 95% CI, 2.087-7.169], having 3.8 times higher risk for the breast cancer.

Blood group AB having very least association to breast cancer in Jodhpur, Western Rajasthan (India).

Discussion

The association of blood group A is an interesting one in view of the suggestion of earlier immunologist that the heightened surveillance and overactive immune activity tend to result in less malignancy, whereas overly tolerant immune activity tends to encourage it. These observations suggest that a more general hypothesis that in the tissues of all people, both normal and cancerous, there are A- like antigens present on the biochemical level that are usually inaccessible to the immune system. However, when stimulated by an autoimmune process, or the immune response to a growing cancer, the antigen becomes accessible. At that point, blood group A person, who cannot make anti-A antibodies will be more likely to tolerate cancer, and blood group A person's immune system will be less likely to attack the body's own tissues (14).

The present study reported that blood group A have the highest association of breast cancer in women

TABLE I: Association of risk of breast cancer in relation to ABO blood groups in ORs with 95% CI.

Breast cancer cases	*Blood group A*		*Blood group B*		*Blood group O*		*Blood group AB*	
	No of cases	*ORs with 95% CL*	*No of cases*	*ORs with 95% CL*	*No of cases*	*ORs with 95% CL*	*No of cases*	*ORs with 95% CL*
206	76	7.444 (4.098-13.522)	67	6.138 (3.365-11.195)	48	3.868 (2.087-7.169)	15	1 (0.476-2.103)

*(ORs = Odd Ratios) with 95% (CI = Confidence Interval)

in Jodhpur in Western Rajasthan. Blood group AB had found the least association with breast cancer. Blood type B and O also has association with breast cancer but slightly less than blood type A.

A study performed by Guleria (15) showed that group A was significantly associated with breast cancer when compared to control. In Iceland a study in 1988 looked at the risk of bilateral breast cancer in 184 familial and 572 sporadic cases with regard to ABO typing.

A study of rapidly progressive breast cancer in Tunisian women found a slightly increased risk of a positive diagnosis in blood type A was reported by Mourali (16). The increased rate of blood type A as compared to controls has been reported in breast cancer patients by Anderson and Has (17). There are also some contradictory reports available about the association of blood group with breast cancer. Jayant K (20) reported no relation among breast cancer to blood groups whereas Surekha et al (18) have reported a high incidence exist between breast cancer and blood group B individuals.

In the last 25 years, there has been a tremendous amount of work published on the chemistry of blood group antigens and tumor immunology. As cells (e.g. in tissue) become malignant, they tend to lose normal antigens and acquire new antigens; these are so called tumor antigens. It has been proven that ABO antigens diminish on malignant cells as the malignancy progresses; the loss of A, B and H antigen is proportional to the metastatic potential of the tumors (19, 20).

The reason that deletion or reduction of the A or AB antigens in tumors of A or B individuals correlate with malignancy and metastatic potential may be due to lack of adhesiveness that a cancer cell achieves when it losses blood group antigens. The loss of blood antigens result in the tumor cells gaining the ability to move and circulate through the body, because blood type antigens loss the ability to express many of cell adhesion proteins, such as integrins, which normally express an A like antigen on their receptor and control cell movement (21).

Many malignant cells (such as those found in breast and stomach cancer) develop a tumor marker called Thomsen- Friedenrich (T) antigen, which is suppressed in normal healthy cells, Tn antigen (precursor of T antigen) only becomes unsuppressed as a cell become malignant. T and Tn antigens show some structural similarity to A antigen (22). Blood group A individuals have the least aggressive antibody immune response against the T and Tn antigens and they are actually immunologically considered similar because of their shared terminal sugar (N- acetyl-galactosamine), and so might be readily confused by immune system of blood group A individuals. Blood group A cancer patients had the greatest and most uniform suppression of the level of Tn antigens, irrespective of age, cancer stage, or tumor morphology and lower level of anti-B-isohemagglutinnins. This is probably at least a part of the explanation for the poorer outcomes in many cancers among blood group A individuals (23).

Hakomori suggested that if the immune surveillance theory is correct and we recognize tumor antigens as foreign, leading to attack of the tumor, then the “A-like” properties of tumor antigens may not be recognized by group A patients (24). Tumor Immune Surveillance in the immune system can specifically identify and eliminate tumor cells on the basis of their expression of tumor specific antigens or molecules induced by cellular stress whereby immune system identifies the cancerous or precancerous cells and eliminates them before they can cause harm (25).

In another study by Bennett Malisa (2008) found that blood group A exhibits increased levels of P-glycoprotein which may indicate why individuals may not respond to conventional chemotherapy as well as other blood groups. It would be interesting to know that the percentage of patients in this particular study were of Blood Group “A” (26). It appears that a more integrated treatment protocol should be considered using conventional modalities as well as dietary modifications. Or better yet, change the diet prior to diagnosis to alter the odds of cancer metastasis.

Blood Group "A" individuals have a very low immunologic response to T and Tn antigens because they share the same sugar (N-acetygalactosamine). This allows the cancer cells to bypass the immune system and replicate with little interference from the type A antibodies. Breast cancer in general can be very invasive depending on how well-differentiated the cancer cells appear. The more differentiated a cancer cell becomes; the greater its ability to adhere to other cells. A blood group "A" individual with a breast cancer diagnosis must primarily focus on creating a nutritional strategy which will have an effect on cancer survivorship (26).

The cancer and blood group A link is far from absolute. There are several tumors that show a consistent association with blood group O and B. This implies that cancer is a condition associated with derangement of blood type activity in general, and the expression of A-like antigens on the surface of tumors is just simply the most common of these arrangements (14).

Because of resource constrain, the identification of genetic and environmental factors among racial and ethnic groups should offer some insights into the observed epidemiological data and advance opportunities to better understand the control and development of cancer. Collectively, we could hypothesize that tumors have more chance to thrive and maximum found in blood group A patients than those in other blood groups.

Conclusion

In conclusion, evidence for association of blood groups with breast cancer is controversial, some blood groups showed positive association and others were negative. It appears that different blood groups are associated with breast cancer; Blood group A apparently increases the risk for cancer. Breast cancer has the strongest association with blood type A. Blood type needs to be considered together with other risk factors to understand. This study concludes that, in case of breast cancer, high frequency of breast cancer was found in blood group A followed by B and O. Further studies on blood groups in large series are needed to elucidate the relationship between blood group and disease. However, in comparison to trends of cancer occurrence from past few year reports, there has been a noticeable change in the pattern of cancer in this study. From this study some clues can be drawn for understanding the trends in cancer occurrence.

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