Hormonal changes in women with breast cancer infected with Toxoplasma gondii

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Abstract

Introduction: Acute Toxoplasmosis is more critical in immunocompromised patients with cancer. The present study was conducted to investigate the anti-Toxoplasma gondi antibodies and assess the toxoplasmosis risk in women with breast masses in western of Iran in 2012. This research was done as a case-control study on women who referred to the treatment centers in cities of Kermanshah and Ilam in 2011.
Materials and methods: 60 women with breast cancer were selected as cases, and also 60 healthy ones as the control group. They were evaluated in terms of IgG, IgM, estrogen and progesterone levels using immunoassay method. Women in this study were in the secretory phase and were under the age of menopause. Results were analyzed using SPSS software 16 with independent T test.
Results: Relationship between Toxoplasma gondii (T. gondii) infection and breast cancer was statistically significant (P<0.01). There was a significant relationship between anti-Toxoplasma IgG antibody and breast cancer (P=0.01). Women with breast cancer and healthy women were not reported positive in terms of IgM anti-Toxoplasma. Significant relationship was detected between estrogen and Toxoplasma in women with breast cancer (P<0.01). There was no significant relationship between the level of progesterone and anti-Toxoplasma antibodies. A total of 30 patients (50%) from the women under study had the tumor marker CEA 19-9 (Carcino embryonic antigen).
Conclusion: Patients with breast tumors may be at risk of opportunistic infections such as toxoplasmosis. Therefore, periodic examination of breast cancer patients should be conducted by clinicians to prevent the potential occurrence of toxoplasmosis.

Keywords: Hormones changes, Toxoplasma gondii, Breast cancer

Introduction

Toxoplasma gondii (T. gondii) is an intestinal parasite in cats with a wide range of interface hosts common in humans. The parasite is transmitted to humans through the ingestion of oocysts from cat or by eating meat infected with tissue cyst and fluids containing a single zooitt. A number of conducted studies show the relationship

between T. gondii and increased cancer risk, Parkinson's disease, schizophrenia, multiple sclerosis, Alzheimer's disease and numerous diseases. This relationship is due to the reaction of Toxoplasma with 3000 host genes or proteins .

Toxoplasma is seen in some malignancies like lymphoma, acute and chronic lusymia and myeloma. Recent studies show that Toxoplasma antibodies can be seen in women with breast and ovarian cancer. Although the mechanism behind this is unknown, but there is no doubt that Toxoplasmosis paves the way for tumor development (3-5). In recent years, approximately 8500 to 9000 people are diagnosed with breast cancer in a year which is a high figure in the country. (30 out of 100 thousand breast cancer in Iran). The factor that amplifies the danger is that the age of the disease is lower in Iranian women than worldwide standards and this makes the disease all the more significant. (6) Therefore, as to the importance of the issue and the lack of research in the country, the present study was conducted with the aim of studying women with breast masses to estimate the rate of T. gondii infection.

Materials and methods

This research was done as a case-control study on women who referred to the treatment centers in cities of Kermanshah and Ilam in 2011-12. Due to the prevalence of 33% and 5% in the similar areas, a group of 120 people between 18 and 40 years were studied (60 women as study group and 60 women as control). After filling the written consent, each individual completed a questionnaire. All women were in the ovary secretory phase. Observing aseptic conditions, blood sampling was conducted simultaneously and under the same conditions. Collected samples were centrifuged 10 minutes with 2000 g. At first ELISA Test were performed on all samples to examine the anti-Toxoplasma antibodies. Final results were recorded By ELISA- (reader) Multi Scan MS Lab System Finland) with 450 Nm wave length. Level of Toxoplasma antibodies were measured using a Pishromedical kit; samples with 1.1 in ml were evaluated as positive and samples with less than 0.9 as negative.

Controls group members were totally corresponding with those of study group in terms of age, sex and occupation. The two groups were evaluated by immunoassay method for estrogen and progesterone rates. Final results were recorded in a wavelength of 450 nm. Quantitative analysis of samples was implemented with a standard curve and using optical density and concentration of positive and negative controls. This method uses standard diagramming on the x-axis—as the concentration standard—and the y-axis of the optical density to draw the patients' optical density and then connects the dots to form the standard diagram; finally, these dots provide the amount of estrogen and progesterone. Descriptive-analytical statistics including independent T-test analysis were used to examine the relationship between Toxoplasma infection and the amount of estrogen and progesterone.

Results

Results of this study showed a relationship between T. gondii infection and breast cancer ($P<0.01$). There was a significant relationship between anti-Toxoplasma IgG antibody and breast cancer ($P=0.01$). Women with breast cancer and healthy women were not reported as positive in terms of IgM anti-Toxoplasma. Significant relationship was detected between estrogen and Toxoplasma in women with breast cancer ($P<0.01$). There was no significant relationship between the level of progesterone and anti-Toxoplasma antibodies. A total of 30 patients (50%) of the women under study had tumor marker CEA 19-9 (Carcinoembryonic antigen) (Table 1).

Table 1. The frequency of tumor markers in breast cancer among women with breast cancer

Tumor Marker	Frequency	Percent	Valid Percent	Cumulative Percent
CEA125	16	26.7	26.7	26.7
CEA19-9	30	50.5	50.5	76.7
CEA15-3	6	10.0	10.0	86.7
CEA	8	13.3	13.3	100.0
Total	60	100.0	100.0	

Discussion

In people with normal immune system, the infection is usually self-limited, but the parasites can survive for years in the host body in the form of tissue cysts. During this phase, tissue cysts are controlled by humoral and cellular immune system, including T lymphocytes and macrophages (7, 8). People with immunocompromised systems, especially those with higher chronic infection risk due to cellular immune deficiency, as well as patients with cancer, collagen tissue diseases, transplant recipients treated with immune suppressive drugs, or immune-deficient hemodialysis patients with chronic renal failure, are more susceptible to be infected with T. gondii (9).

Studies conducted in recent years indicate that (chronic) asymptomatic toxoplasmosis has the greatest impact on various aspects of human life (10). In other words, chronic Toxoplasma gondii is able to manipulate the host's performance (11). Overall, all forms of toxoplasmosis have serious effects on human health and leave heavy economic and social burdens throughout the world (12, 13).

In this study, IgG Toxoplasma in women with breast masses were more positive than that of the control group. Increase in IgG titer can be caused by the brain proliferation tachyzoites during chronic infections with Toxoplasma. Some researchers relate the high antibody titer IgG to the specific values of SAG1 mRNA of the brain tachyzoites (10). The increase in IgG and lack of increase in IgM can be expressed as a useful indicator of the occurrence of brain tachyzoites growth in immunocompromised people with Toxoplasma chronic infection (14).

Also, IgG increases and reactivation of Toxoplasma infection in chronic phase can be ascribed to the existence of antigens MIC6, GRA2, rhoptry protein ROP1, heat shock protein HSP90, one (putative) heat shock protein HSP70, and heavy chains of meiosis in the process of tachyzoites multiplication (15). In other studies, the amount of IgG Anti-Toxoplasma in patients with breast cancer have been reported 60% and IgM Toxoplasma 0% (16). In patients with cancer, immune function is impaired and this is the main reason for the increase of Toxoplasma antibodies. Furthermore, toxoplasmosis can be due to the use of anti-cancer drugs in patients with Lymphoma, leukemia, malignant tumors and patients with breast, ovarian and lung tumors (17).

Recently, considerable evidence show the effects of steroid hormones on toxoplasmosis in humans and animals. In these studies, female mice infected with toxoplasmosis showed a harder brain inflammation compared to the male ones. Estrogen affects the infection process in a hitherto unknown way. Available data suggest that estrogen may weaken the immune cells and destroy the activity of NK cells and cause neutrophil dysfunction. Estrogen is capable of producing systemic antibodies, but causes damage to the localized ones. Animal and human cell culture studies show that estrogen supplementation can make contraction and exacerbation of viral, bacterial, and parasitic infections.

Recent empirical evidences put forward the mechanisms of host exploitation by parasites titled "Transregulation". Within this system, the parasite directly uses

factors like growth and hormone of the host to promote its growth and proliferation (20-23).Some studies indicate that the host's steroid hormones influence the physiological aspects of parasites. Steroids such as estradiol, testosterone, progesterone, cortisol and DHEA can be bonded with the host by cytoplasmic specific receptor of the parasite. Receptor bonded to the host protein-receptors is regulated by genomic mechanisms, parasite growth, pathogenesis, proliferation and differentiation. Parasite is able to bind to host molecules and use them for their own benefit through Transregulation mechanism.

The host's endocrine system through regulating and changing the immune system of the host can not only affect the operation of parasites but also can be directly exploited by parasites (24).Accordingly, the host's hormones regulate the important processes of growth, differentiation, and proliferation of the parasite by genomic and non-genomic mechanisms through the Transregulation mechanism. In some cases this mechanism successfully established parasite infection. In some others, Transregulation is beneficial for the host in order to successfully reduce parasite infection (24).

Finally, parasites through the receptor, transporter, steroidogenic enzymes, and secondary message-carriers and using the host cytokines as growth factors and acquisition of essential amino acids for metabolism, exploit hormones and prevent surface bonding antibodies of the host (25). The immune system is stimulated by parasites' antigens and produces a lot of hormones. Some parasites produce steroid hormones which are able to change the host hormone levels (26). To prevent the occurrence of acute toxoplasmosis in patients with breast cancer, and to control chronic toxoplasmosis, it is essential that doctors regularly conduct periodical screening and anti-Toxoplasma tests in these patients. The increase in anti-Toxoplasma IgG, especially in patients with breast cancer, with history of Toxoplasmosis, is an alarm which cautions against parasite reactivation and acute Toxoplasmosis

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