Low titer of antibody against Toxoplasma gondii may be related to resistant to cancer

ABSTRACT

Context: Toxoplasma gondii is a protozoan parasite with a world-wide distribution. However, the majority of infected cases remain symptomless. There are raising scientific evidences indicating that parasitic infections induce antitumor activity against certain types of cancers. The inhibitory effect of T. gondii on cancer growth has also been shown in cell culture and mouse model.

Aims: Considering the anti-tumor effect of this parasite, in this study the relationship between low titer of antibodies against T. gondii and resistant to cancers has been investigated.

Subjects and Methods: In two separate experiments, anti T. gondii antibody was estimated in 150 patients with cancer and 120 normal people.

Statistical Analysis Used: Chi-square test was used for data analysis.

Results: The frequency of low titer antibody against Toxoplasma gondii in cancer patients was significantly higher than the frequency of low-titer antibody against this parasite in normal people.

Conclusions: Exposure to T. gondii may be related to resistance to cancer.

KEY WORDS: Antibody, cancer, Toxoplasma gondii

INTRODUCTION

Toxoplasma gondii is an intracellular protozoa with a global distribution.[1] Human infections with T. gondii occur in three ways including: Eating raw or undercooked meat containing T. gondii tissue cysts, ingesting oocysts from soil or acquiring congenital infection through the placenta.[2] Serological studies have shown that T. gondii infection is prevalent in meat-producing animals, especially pigs, sheep and goats.[3] In new cases of T. gondii infection in pregnant women, infection can be transmitted to the fetus which may result in serious disorders such as mental retardation, blindness, epilepsy, and death. Also, acute form of infection may cause severe encephalitis or reactivation of latent infection among immunosuppressed persons. Moreover in patients with acquired immunodeficiency syndrome toxoplasmosis is the most frequent severe neurologic infection. However, the majority of people with normal immune system are asymptomatic or show mild symptoms such as fever, which may be resolved spontaneously.[4] Although the distribution of T. gondii is worldwide, epidemiological surveys show wide variation in prevalence of infection in various geographic locations. In some parts of France and in most tropical area of Latin America and subsaharan Africa rates of infection may reach to 90%. However in hot and dry regions such as North Africa the prevalence does not go over 20%. Most seropositive individuals for T. gondii antibodies have no history of clinical manifestations. It means that the majority of T. gondii infected people are symptomless.[5]

Cancer is the main cause of death in developed countries. However, in underdeveloped countries infections and parasitic diseases considered as the main causes of death. There are many scientific evidences indicating that parasitic infections induce antitumor activity against certain types of cancers.[6] Suppression of neoplastic growth via infectious organisms has been shown for some bacteria, protozoa and helminthes.[7] Stimulation of the immune response by these organisms or inhibition of angiogenesis may explain the biologic basis of these observations. In animal models it has been shown that certain parasites or parasitic compounds were able to inhibit cancer growth.[8-12] Also, it is interesting to note that an antigenic similarity exist between various tumors and some parasites such as Echinococcus granulosus. For example, cancer-associated O-glycosylated Tn antigen has been extracted from some parasites.[13] Anti-tumor activities of T. gondii parasite have been shown in different investigations.[11,12,14-19] Injection of rats with Toxoplasma lysate antigen
resulted in a significant reduction in tumor formation. In another study a marked antitumor effect was observed when Toxoplasma-infected mice, injected with the tumor cells mixed with formalin-fixed Toxoplasma organisms. In another experimental study, significant reduction in the tumor size was observed in mice injected with T. gondii antigen absorbed in alum adjuvant. Also inhibition of Lewis lung carcinoma (LLC) growth by T. gondii has been shown. Finally, the inhibitory effect of T. gondii on cancer growth has also been shown in cell culture.

Toxoplasma gondii run a chronic and symptomless infection in the majority of the people in the world. Considering the anti-tumor effect of this parasite, in this study the relationship between low titer of antibodies against T. gondii and resistant to cancers has been investigated.

**SUBJECTS AND METHODS**

In this descriptive and analytical investigation, study population consisted of patients with different forms of cancers. In two separate experiments 150 cancer patient sera tested in comparison with normal sera as control groups [Table 1]. In the first experiment 90 sera from patients with breast, prostate and colon cancers were collected in 2011. These samples were considered as case group 1. Ninety sera samples from healthy blood donors that were similar with patients in terms of demographic characteristics were also collected as control group 1. In the second experiment 60 sera samples from patients with breast, prostate and colon cancers were collected in 2013 as case group 2. Thirty sera samples from healthy blood donors that were similar with patients in terms of demographic characteristics were also collected as control group 2. All the patients were in the earliest stage of cancer. Also, the age of patients was below 70 years. The patients with suppressed immune system or advanced cancer were removed from the study. All of the samples were examined using enzyme-linked immunosorbent assay (ELISA) test for estimation of antibody titers against T. gondii. Optical density (OD) results of the ELISA tests were classified to very low, low, moderate and high.

In this research, spare serum sample of patients in medical laboratories were collected and tested and, therefore, no bleeding was performed in this work. Chi-square test was used for data analysis.

**RESULTS**

In the first experiment, 65.5% of patients in the control group and 23.7% of patients in the case group had low OD which corresponded with low titer of antibody [Table 2]. In the second experiment, the similar results were achieved and 73.33% in control and 55.17% in the case group had low level of antibody [Table 3]. The results of ELISA test of experiments 1 and 2 have been summarized in Tables 2 and 3 respectively.

**DISCUSSION**

In the first experiment, 65.5% of patients in the control group and 23.7% of patients in the case group had low OD which corresponded with low titer of antibody. In the second experiment, the similar results were achieved and 73.33% in control and 55.17% in the case group had low level of antibody. The difference between low OD results in both experiments was significant ($P < 0.05$). Low-titer antibody against T. gondii may be associated with exposure to the parasite sometimes in the life time, so with this postulation everybody who infected with T. gondii may achieve resistant to cancer. How T. gondii cause possible tumor inhibition growth is not clear, one possibility may be related to stimulation of the immune system by this parasite. The raised immune system may nonspecifically interfere with the tumor growth. As an example, T. gondii infection inhibits the tumour growth in certain types of cancers in mouse models through induction of Th1 immune responses and antiangiogenic activities. Also, it has been shown that T. gondii stimulates host response especially production of IL-12 and interferon. These cytokines may contribute to antitumor activities. In another study, it has been suggested that T. gondii is a powerful agent for cancer immunotherapy and is useful as a stimulant of the
cellular immune responses,\textsuperscript{[11]} T. gondii as a nonspecific immune stimulant also used for cancer immunotherapy\textsuperscript{[11]} Kim et al. indicated that T. gondii activates Th1 immune responses and inhibits angiogenesis in LLC-bearing mice, leading to the induction of antitumor and antimetastatic activities.\textsuperscript{[11]}

Suzuki et al. also examined antitumor effect of formalin-fixed Toxoplasma organisms as an immunostimulant on EL4 lymphoma in toxoplasma-infected C57Bl/6 mice. They showed a potent antitumor effect, a marked suppression of tumor growth, as well as a prolongation of lifespan of examined mice.\textsuperscript{[19]}

Other possible mechanism of antitumor activity of T. gondii may be related to the effect of parasite metabolites on cancer cells. In this context, the inhibitory effect of this parasite on cancer growth has also been shown in cell culture.\textsuperscript{[8,14-23]}

CONCLUSION

Based on results of this work low titer of anti-Toxoplasma antibody was related to resistance to cancer. Hence, it may be concluded that asymptomatic infection of T. gondii stimulates the immune system which may show anti-tumor activity.

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REFERENCES


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