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A Review Article in:

The Relationship between Toxoplasmosis And colorectal cancer

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Abstract

Cancers are characterized by uncontrolled growth of abnormal and transformed cells, which can invade adjacent tissues.

And while multiple factors can significantly contribute to carcinogenesis (WHO, 2015). Meetings of experts from diverse fields of cancer research held at the International Agency for Research on Cancer (IARC) from 2008 to 2009 have reassessed and classified human carcinogens into "discrete" groups including infectious pathogens (Bouvard et al., 2009, IARC, 2012).[1]

With the breeding of animals nowadays and despite the benefits of pets in the psychological side and their attribution in improving mental health and bring happiness to their owners , many studies emerged to see the connection between having a pet and certain diseases

For example, several studies have supported the idea that pets can carry carcinogenic pathogens. German researchers, for instance, found that 38% of a group of Bavarian women with breast cancer had lived with a dog for at least 10 years. In contrast, only 15% of women in a matched control group without cancer had a dog.[2]

In this article we will be focussing on cats as the second most breeding animal .

According to the British newspaper “Daily Mail”, the study found that the parasite “Toxoplasma gondii”, which is carried by about 30% of cats and remains in their feces, may alter more than 1,000 genes linked to cancer, but we will be focussing on one type of cancer

1. Introduction

Colorectal cancer (CRC) is one of the most common malignancies, with the morbidity increasing steadily in recent years [3]. However, the outcome of CRC patients has improved substantially because of anticancer treatments such as surgery, chemotherapy, and targeted treatment [4].Parasites, especially those that cause opportunistic infections, have received relatively little attention in malignancy patients.

Toxoplasma gondii is one of the most common parasites to cause opportunistic infections, and nearly one-third of humans suffer from chronic infection worldwide [5]. The human immune system can prevent the propagation of T. gondii, and thus, an acute acquired infection is generally self-limiting and asymptomatic in healthy humans [6]. However, in immunocompromised patients, T. gondii may cause a serious, life-threatening infection. Several studies demonstrate a latent relationship between toxoplasmosis and malignancy [7–8] .Cats are the only definitive host, and the oocysts they shed can be viable in soil for many years Many factors are associated with toxoplasmosis in cancer patients and some studies linked the incidence with specific age groups, residence and occupation. However, in patients with CRC, data on T. gondii infection are rare, and as a result, the prevalence of T. gondii infection and the associated risk factors in patients with CRC are unclear. in this article that is considered one of the most common cancers worldwide.

Toxoplasmosis:[9]

It is a disease caused by the single-celled parasite Toxoplasma gondii (T. gondii).

Family : Sarcocystidae

Class : Conoidasida

Genus : Toxoplasma; Nicolle & Manceaux, 1909

Species : T. gondii

Is one of the most common parasitic diseases and infects nearly all warm-blooded animals, including pets and humans .

Animals affected include :cattle, poultry, sheep, goats, cats, various other animals kept as pets, and various captive zoo and wild animals

Mode of transmission:

Toxoplasma can be transmitted to humans by 4 principal routes: a) ingestion of raw or inadequately cooked infected meat.

b) ingestion of oocysts, an environmentally resistant form of the organism that cats pass in their feces, with exposure of humans occurring through exposure to cat litter or soil (e.g., from gardening or unwashed fruits or vegetables).

c) a newly infected pregnant woman passing the infection to her unborn fetus.

d) blood transfusion and organ transplants.

.Epidemology:

around 30% of the human population, globally, is estimated to be infected [10–12]. Current estimates of human infection range from a relatively lower prevalence in countries like the UK (10%), China (10%) and the USA (10–20%) [10, 13] to areas where prevalence can exceed 40% (e.g. parts of continental Europe and South America) [11].

Course of the disease:

In humans, the result of infection may range from asymptomatic to severe disease. Asymptomatic infection occurs both congenitally and by ingestion of infected material in immunocompetent individuals. [12, 13, 14] In immunocompetent patients, toxoplasmosis lymphadenitis is self-limited. While in immunecompromised individuals symptoms can be severe or persistent.

Lymphadenitis is the most common clinical form of the disease, [10, 14,15, 16] with 3-7% causing clinically significant lymphadenopathy, particularly cervical lymphadenopathy,and may be accompanied by a number of nonspecific symptoms in a portion of individuals with lymphadenopathy, such headache, fever, malaise, fatigue, sore throat, and myalgia. [10, 14, 15, 13]

Diagnosis:

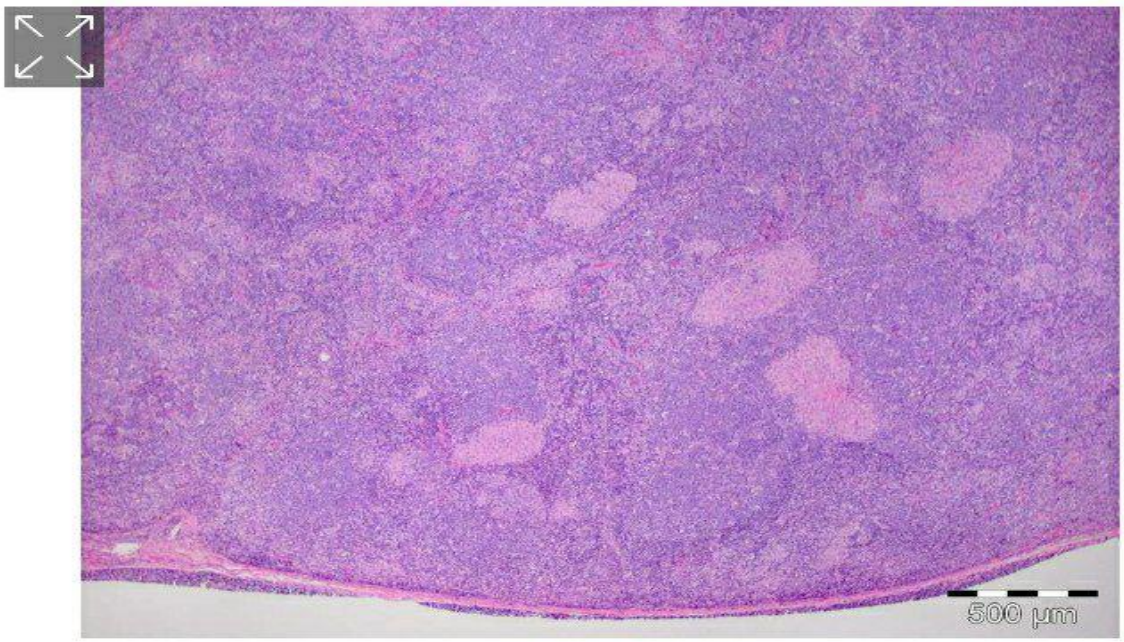
The differential diagnosis for toxoplasmosis lymphadenitis is very large , because the disease has very nonspecific, if any, symptoms.

However, the diagnosis may well be suggested by the histomorphology of a biopsied lymph node.

Such studies included the toxoplasma immunoglobulin (Ig) M serology, the Sabin-Feldman dye t est (which determines if toxoplasma IgA, IgG, and IgM antibodies are present), [17] and complement fixation titer

Pathology :

Toxoplasmosis changes the cells in a specific way that is commonly referred to as the "toxoplasmosis triad" includes follicular hyperplasia, the presence of monocytoid cells in subcapsular and trabecular sinuses, and the presence of clusters of epithelioid histiocytes . [18]



Toxoplasmosis Pathology. This low-power photomicrograph shows the large, irregularly shaped germinal centers and clusters of epithelioid histiocytes found in toxoplasmosis lymphadenitis.

The Association between Toxoplasmosis and colorectal Cancer

The susceptibility to the infection with toxoplasmosis in immunocompromised could be due to many reasons such as the geographical variation, customs, habits, difference in genetic susceptibility and the acquisition method of Toxoplasma infection [19, 20]. Persistent infections may promote cancer because long-term host defensive responses induce inflammation, which increases mutation rates [21]. IgG antibodies indicate chronic infection and an increased titer of IgG antibodies might show reactivation [22]. These chronic infections probably persist throughout the life and may remain undiagnosed until or unless it is reactivated as a result of severe immune suppression [23]. In this study, raised serum IL-6 was present in CA. Breast and CRC patients in compare with healthy control. T. gondii patients had a higher level of IL-6 as compared to healthy subjects, which seems to confirm the presence of an inflammatory state. Recent years focused on the identification of cytokines as prognostic factor .In addition, intracellular pathogens may disrupt cell barriers to cancer, allowing oncogenic mutations to accumulate through time [24]. An association

between serum IL-6 and size of tumor in patients with cancer has been reported [25]. With increasing tumor size, IL-6 is a pleiotropic cytokine that plays a significant role in the growth and differentiation of cells [26]. IL-6 is required for protective immunity agains T. gondii infection [27]and it is contributes in the progress of specific cellular and humeral

immune responses, including cell differentiation,m immunoglobulin secretion and T cell activation Human tumor cell lines have been reported to produce IL-6 [25]. Patients with

high IL-6 were more often found to have advanced disease [25]. IL-6 has a direct correlation with the stage of the disease it may indirectly correlate with the -their environment might actually shift from growth inhibition and differentiation to proliferation and antiapoptosis [28-29]

Prevention

In most regions of the world, the main source of infection is undercooked meat with live tissue cysts. Other prominent causes of infection in areas with poor water hygiene include ingestion of oocyst contaminated soil and water, as well as contact with infective oocysts.

Recent research has found that oocyst infection is more essential than previously considered. Toxoplasmosis prevention is mostly focused on health education on minimizing personal exposure to the parasite. Many countries have implemented education programs targeted at lowering congenital toxoplasmosis rates. Development of an effective vaccine against T. gondii appears to be an achievable goal, as primary infection results in a life-long protection against the parasite. The most effective approach for vaccine development has been the use of non-virulent mutated strains of the parasite [30]

Conclusion

Taking together, these results demonstrate that the increased incidental rate of toxoplasmosis may consider as an indication to the high risk of cancer due to the fact that the latent .Toxoplasma may be trigger long term infection

Moreover, the increased levels of anti- T. gondii IgG and IL-6 was significantly higher in .patients with colorectal cancer that infected with T. gondii in compare with healthy controls

Thus, anti- T. gondii IgG test and circulating levels of inflammatory cytokines has to be taken into consideration as marker for staging of the cancer

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