International Journal of Biology and Life Sciences
ISSN: 2957-9511 | Vol. 1, No. 1, 2022

The relationship between some species of parasites and cancer and their pathogenesis: A literature Review

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Abstract: Cancer is the second most common cause of death worldwide, and one of the pathogenesis is some species of parasites. At present, the main types of parasites for cancer are: Echinococcus granulosus (tapeworm), Toxoplasma gondii, Plasmodium, Trypanosoma cruzi, Schistosoma, liver fluke and so on. Different types of parasites cause different types of cancer. In recent years, many scholars have done related research and experiments on the mechanism of parasite-induced cancer infection, but the specific mechanism has not been clear so far. This article reviews the relationship between schistosomiasis, liver flukes and Toxoplasma gondii and cancer and their pathogenesis.

Keywords: Cancer; Pathogenesis; Parasite; Schistosomiasis; Liver fluke; Toxoplasma gondii.

1. Introduction

Cancer is the second leading cause of death in the world according to the World Health Organization. The pathogenesis of cancer has not yet been fully elucidated, and the currently relatively clear carcinogenic factors can be roughly divided into exogenous and endogenous. Among them, one type of exogenous factors is biological carcinogens, such as parasitic infection. The classification of carcinogens is maintained by WHO through its cancer research organization, the International Agency for Research on Cancer (IARC). Three kinds of parasites, Orchid fluke, Clonorchis sinensis and Schistosoma aegypti, have been listed as first-class biological carcinogens, that is, dangerous carcinogens. [1] At present, the main types of parasites for cancer are: Echinococcus granulosus (tapeworm), Toxoplasma gondii, Plasmodium, Trypanosoma cruzi, Schistosoma, liver fluke, etc. This article reviews the relationship between schistosomiasis, liver flukes and Toxoplasma gondii and cancer and their pathogenesis.

2. Schistosoma

2.1. Introduction

Schistosoma is a dioecious parasitic schistosome belonging to a variant of the flatworm that has a mammalian host and an intermediate invertebrate host: the freshwater snail. [2] Including Schistosoma aegypti, Schistosoma japonicum, Schistosoma mansoni, Schistosoma interstitium and Schistosoma mekong. According to the World Health Organization, schistosomiasis is an acute and chronic parasitic disease caused by Schistosoma schistosome, which is endemic in 78 countries around the world, in 2019, with at least 236.6 million people in need of preventive treatment. It is infected and parasitic on the host through feces entering the water, the presence of snails, and contact with infected water [3]. Schistosomiasis was widely prevalent in my country and affected national health. At this stage, although schistosomiasis has been basically eliminated, secondary diseases caused by schistosomiasis still exist [4]. For example, schistosomiasis is associated with several types of cancer, such as bowel, liver, gallbladder and bladder cancers.

2.2. Pathogenesis

2.2.1. Intestinal cancer

From existing experiments [5], we can know that there may be a relationship between Schistosoma japonicum and colorectal cancer. Chronic schistosomiasis is one of the causes of malignant tumors. By down-regulating Bax gene and up-regulating Bcl-2 gene expression, tumor cell apoptosis is inhibited. Death. However, there are also studies [6] that show that the pro-apoptotic protein Bax has no correlation with schistosomiasis infection. Therefore, the pathogenesis of schistosomiasis and colorectal cancer is not clear at present, and its specific action pathway needs to be further studied.

2.2.2. Liver cancer

In recent years, studies on schistosomiasis and liver cancer have shown that schistosomiasis causes schistosomiasis liver disease, of which hepatic fibrosis is the most common, and is often clinically caused by viral hepatitis, alcoholic liver, fatty liver and autoimmune diseases. Severe fibrosis can develop into liver cancer.

Among them, there are three mechanisms for schistosomiasis to cause hepatocellular carcinoma.

Firstly, schistosoma and its hepatic granulomatous inflammation and fibrosis are related to cancer.

The incidence of liver cancer in schistosomiasis-infected animals was significantly increased and parasites were detected early in infection. Animals infected with egg promoter gene-negative animals with less egg variability were less able to metabolize carcinogens. Eggs can embolize the liver retrogradely, forming egg nodules, which can lead to cirrhosis through fibrosis.

Secondly, the interaction of different cytokines regulates liver fibrosis, resulting in the mutation of proto-oncogenes or the inactivation of tumor suppressor genes (which can also occur at the same time), resulting in liver cancer. TGF-β1, MMP-1, and TIMP-1 have been shown to play a close role in the mechanism of hepatic fibrosis in some studies. A positive correlation was observed between TGF-β1 and TIMP-1 content in liver tissue and serum and the degree of hepatic fibrosis, and it also indicated that TGF-β1 has a positive regulatory effect relative to TIMP-1. The function of MMP-1 is to degrade the ECM (extracellular matrix). The main cause

of liver fibrosis is the continuous increase of TIMP-1, whose function is to degrade the ECM. [7]

Thirdly, combined viral chronic hepatitis has a mutual promotion effect on the formation of HCC. [7]

2.2.3. Bladder cancer

Existing data agree that Schistosoma aegypti infection is closely related to the occurrence of bladder cancer. [8] Schistosoma causes bladder cancer mainly through bladder irritation, inflammation and concurrent chronic bacterial infection [8]. Through the development of a mouse model of urogenital schistosomiasis, egg deposition is sufficient to reproduce several important aspects of urogenital schistosomiasis, even in the absence of other life stages of this essential human pathogen. [9] After the larvae of schistosomiasis are infected with the human body through the skin in the water, the adult worms parasitize around the skin of the bladder and lay the eggs on the skin wall of the bladder, thereby causing bladder cancer. Epithelium caused by the eggs Injury, chronic inflammation, and oxidative stress processes may play an essential role in the development of bladder cancer. [10] There have been many clinical cases of schistosomiasis related to bladder cancer, but the specific pathogenesis still needs to be further elucidated.

3. Liver flukes

3.1. Introduction

Clonorchis sinensis (C. sinensis), also known as liver fluke (liver fluke), Chinese liver leech. On October 27, 2017, in the preliminary reference to the list of carcinogens published by the World Health Organization's International Agency for Research on Cancer, Clonorchis sinensis has been included in the list of Class I carcinogens. Clonorchis sinensis adult parasitic in the human liver bile duct, can cause Clonorchiasis (Clonorchiasis), also known as liver fluke disease. Some data show that liver fluke infection is closely related to the occurrence of cholangiocarcinoma and liver cancer. Its ultimate pathogenic mechanism may be closely related to the damage of DNA in proliferating cells and the production of endogenous nitric oxide. [7]

3.2. Pathogenesis

3.2.1. Hepatocellular carcinoma

Clonorchis sinensis is related to cellular liver cancer, which can cause inflammation around the bile duct, severe epithelial cell proliferation, and progressively cause liver diseases such as liver fibrosis and liver cirrhosis. The identification methods of Clonorchis sinensis include: hepatic bile duct cancer, common hepatolithiasis with recurrent suppurative cholangitis, Caroli disease, sclerosing cholangitis, and Fasciola hepatica infection. Sclerosing cholangitis is one of the influencing factors of intrahepatic bile duct dilatation and concentric thickening of the intrahepatic and extrahepatic bile duct tree. [11]

There are two mechanisms by which parasites cause liver cancer.

Firstly, the presence of carcinogens is already present with parasite-induced cell necrosis and cell proliferation that triggers priming. Parasite-induced cell necrosis and proliferation have occurred following carcinogen production, and these cell proliferations may trigger priming. In the mechanism by which carcinogens cause DNA cell damage and pain, gene mutation, recombination and translocation will only be damaged and fixed in the cell, and then cause the activation of oncogenes. Cell proliferation is essential during DNA damage fixation.

Secondly, the parasite-induced chronic cell necrosis and regeneration can lead to the further development of tumorigenesis. Cell proliferation caused by chronic persistent inflammatory and necrotic responses may also nonspecifically cause liver pain. [12]

The etiology and cancer mechanism of hepatocellular carcinoma are extremely complex. Although Clonorchis sinensis has been shown to be related to liver cancer, more experiments are still needed to prove it.

3.2.2. Cholangiocarcinoma

High infection of liver flukes can cause cholangitis, cholangiohepatitis, and further induce biliary cirrhosis, multiple intrahepatic stones, and eventually cholangiocarcinoma. Further studies showed that the secretion of Clonorchis sinensis could promote the proliferation and invasion of cholangiocarcinoma cells. [11]

There are three mechanism:

(1) Mechanical irritation or injury

After being ingested by the human body, the larvae follow the bile and move to the bile duct, where they gradually mature and become adults. In the larval stage, liver flukes can cause mechanical damage inside the bile duct. When the number of adults reaches a certain level, a large number of adult worms and eggs block the bile duct, causing the bile duct wall to thicken and the pressure in the bile duct to rise, further leading to inflammatory reactions or Bile duct epithelium ulceration. Adult eggs can spread to the surrounding bile duct from the ulcerated site, and gradually develop into eosinophilic granulomatosis, which can eventually lead to peribiliary fibrosis.

Not only that, the hallmarks of abnormal bile duct epithelial cells or precancerous and adenomatous changes are the chronic stimulation, mechanical damage and chronic inflammation caused by liver flukes leading to pathological hyperplasia. [13]

(2) Toxic effects of excreta

While Clonorchis sinensis causes mechanical damage inside the bile duct, it continuously secretes excretory secretory products (ESPs), which play an important role in the process of Clonorchis sinensis infection.

Matrix metalloproteinases (MMPs) are collagen hydrolases that damage the tissue barrier of cancer cell invasion, and they play a essential part in the invasion and metastasis of tumors.

The findings of Pak et al. showed that the enhancement and induction of matrix metalloproteinases and nuclear factor kappa B (NF-κB) promoted the invasion and migration of bile duct epithelial cells, and further led to the development of CCA. [14]

Free radicals (active oxygen and reactive nitrogen) are one of the causes of the pathogenesis of many human diseases. Studies have shown that free radical production during liver fluke infection disrupts host redox homeostasis, while the prolonged endogenous crosstalk between free radicals and TLR activation exacerbated the chronic inflammation circumstance in the bile duct epithelium and surrounding hepatic tissue. At this point, it is easy to lead to the development of hepatobiliary diseases, including CCA associated with chronic inflammation. [15-16] Furthermore, Bahk et al. [16] showed that free radicals enzymatically produced by ESPs from Clonorchis sinensis induce inflammation induced by NF-κb in cholangiocarcinoma cells. Not only that, HuCCT1 cells treated with natural ESPs can

induce Toll-like receptor (TLR) mRNA levels to change in a time-dependent manner, and free radicals are also generated, which indicates that free radicals triggered by ESPs are in the It plays an important role in the process of TLR signal transduction. Not only that, but depending on the level produced, free radicals can cause varying degrees of severe cellular damage and induce some diseases.

(3) Immune inflammatory response

Cytokines play a key part in in inflammatory or immune responses. After binding to cell membrane receptors, cytokines activate signal transduction pathways and result in proliferation, cell survival, differentiation, immune cell activation, migration and death. Inflammatory cytokines are generally divided into pro-inflammatory cytokines: IL-1, IL-12, IL-6, IL-15, IL-17, IL-23, and TNF-α, and anti-inflammatory cytokines: IL-4, IL-10, IL-13, and IFN-alpha. In a mouse model, infection with liver flukes results in increased levels of proinflammatory cytokines such as TNF-α and IL-6. At the same time, in the context of chronic inflammation-related diseases, the persistence and dysregulation of cytokines play a catalytic role in regulating antitumor responses and inducing malignant cell transformation. [17] The TNF-α and IL 1β signaling pathways induce NF-jB to be activated, which further drives the expression of pro-inflammatory mediators, leading to further enhancement of the inflammatory response. [18] Not only that, when IL-1 accumulates to a certain amount, it will induce extensive inflammation, affecting the growth and invasiveness of malignant cells. And because of its paracrine effect on tumor stromal cells, tumor invasiveness and metastasis will be rapidly enhanced. [18] Up to this point, the increase of pro-inflammatory cytokines TNF-α and IL-6 easily triggers chronic inflammation, and accompanied by the immunosuppression caused by the increase of immunosuppressive molecules such as TGF-β and IL-10, cholangiocarcinoma continues to develop.

4. Toxoplasma gondii

4.1. Introduction

Toxoplasma gondii, also known as three corpses, is an intracellular obligate parasite that mainly causes neurological diseases and kills individuals with low immune function. Toxoplasmosis, also known as toxoplasmosis and toxoplasmosis, is a A zoonotic parasitic disease that infects numerous warm-blooded animals. The World Health Organization says the spread of toxoplasmosis through undercooked or raw meat and fresh produce raises a very important food safety issue in Central and South America. In addition, studies have shown that toxoplasmosis causes damage to parts of the visual system.

4.2. Pathogenesis

4.2.1. Nervous system

A series of studies have shown that toxoplasmosis causes increased the level of miRNAs derived from mir-17,92 in primary human preputial fibroblasts, and this increase is a specific response.

mir-17,92 plays an important role in biological development. Amplification and overexpression of miR-17,92 has been demonstrated experimentally in human cancers, and its oncogenic role has been demonstrated in a mouse model of B-cell lymphoma. [19] In addition, mice overexpressing miR-17,92 in lymphocytes had enhanced lymphocyte proliferation, decreased activation-induced cell death, developed lymphoproliferative disorders and autoimmune conditions, and premature death [20].

So far, Toxoplasma gondii can promote tumor expansion by altering mir-17,92-derived miRNA levels, even playing a central role in cancer and infection.

Vision System

Ocular toxoplasmosis is divided into acute and congenital, most of which occur in the retina, and some cases occur in the choroid, vitreous, anterior chamber, and optic nerve head. [21] The main complications are fibrous bands, secondary serous or rhegmatogenous retinal detachment, optic neuritis and neuropathy, cataracts, elevated intraocular pressure during active infection and choroidal neovascular membranes. [22]

Among patients infected with Toxoplasma gondii, elderly patients and children may be more likely than ordinary patients. Elderly patients are often accompanied by punctate extraretinal toxoplasmosis, retinal vasculitis, retinal vascular occlusion, rhegmatogenous serous retinal detachment, unilateral pigmentary retinopathy similar to retinitis pigmentosa, neuroretinitis, and other forms of epithelium. Symptoms such as neuropathy, peripheral retinal necrosis, and scleritis (Smith & Cunningham 2002, Bonfioli & Orefice 2005). Pediatric patients are accompanied by choroidal neovascularization, cataracts, glaucoma, optic atrophy, and retinal detachment (Bosch-Driessen et al. 2000). [21]

Therefore, although the research results between toxoplasmosis and cancer are not exact, it can be known that Toxoplasma gondii is related to immune function or other immunology and other fields of basic biology, which contributes to the development of Toxoplasma gondii. further research.

5. Conclusion

As the second leading cause of death worldwide, the pathogenesis of cancer has not been fully understood, but there is evidence that parasitic infection is one of the factors that cause cancer. The relationship between parasites and cancer is complex, and different types of parasites can cause a variety of diseases at the same time, with more permutations and combinations. A variety of parasites have been classified as first-class biological carcinogens, that means, dangerous carcinogens. Now studies have shown that schistosomiasis is associated with various types of cancer, such as colon cancer, liver cancer, gallbladder cancer and bladder cancer; liver fluke is associated with bile duct cancer and liver cancer; Toxoplasma gondii is associated with neurological diseases and visual system. The main problem to overcome, however, is that parasites can co-occur with other factors that contribute to cancer. Therefore, if we want to explore the specific mechanism of parasites in the pathogenesis of cancer, we need to disentangle the influence of other variables at the same time.

References

[1] Brindley, P. J., da Costa, J. M., & Sripa, B. (2015). Why does infection with some helminths cause cancer?. Trends in cancer, 1(3):174-182.

[2] Kuper, H., Adami, H. O., & Trichopoulos, D. (2000). Infections as a major preventable cause of human cancer. Journal of internal medicine, 248(3): 171-183.

[3] Meng, Q., Chen, W. (2006). Prevention and Control of Common Parasitic Diseases. China Society Press, China Society Press, Beijing.

[4] Rong, Z., Huang, C. (2019). Research progress of schistosomiasis associated colorectal cancer. Modern Oncology Medicine ,02: 335-339.

[5] Liu, J., Lu, G., Li, J., et al. (2017). Expression and significance of Bcl-xL, Bax and Bcl-2 proteins in colorectal cancer associated with schistosomiasis. Chinese Tropical Medicine, 10: 1027-1030.

[6] Yang, D., Qiu, C., Sun, W., et al.(2014). Multigene protein expression in chronic schistosomiasis complicated with colorectal cancer was detected by tissue microarray. Chinese journal of schistosomiasis prevention and control ,4: 405-409.

[7] Huang, S., Li, Y. (2009). The relationship between parasitic infection and hepatocellular carcinoma and its molecular mechanism. Chinese journal of schistosomiasis prevention and control, 02: 158-160.

[8] Fu, C., Odegaard, J. I., Herbert, D. R., et al. (2012). A novel mouse model of Schistosoma haematobium egg-induced immunopathology. PLoS pathogens, 8(3): e1002605.

[9] Mostafa, M. H., Sheweita, S. A., O'Connor, P. J. (1999). Relationship between schistosomiasis and bladder cancer. Clinical microbiology reviews, 12(1):97-111.

[10] Wang, X., He, X., Pan, W. (2019). Parasitic infection and cancer. Chinese Tropical Medicin, 04: 392-395+400.

[11] Lim, J. H. (1990). Radiologic findings of clonorchiasis. American journal of roentgenology, 155(5): 1001-1008.

[12] Wang, J., Yao, Z. (1990). The relationship between parasitic infection and the incidence of hepatocellular carcinoma and cholangiocarcinoma. Journal of Practical Internal Medicine, 06: 321-322.

[13] Kim, T. S., Pak, J. H., Kim, J. B., et al. (2016). Clonorchis sinensis, an oriental liver fluke, as a human biological agent of cholangiocarcinoma: a brief review. BMB reports, 49(11): 590-597.

[14] Pak, J. H., Shin, J., Song, I. S., et al. (2017). Clonorchis sinensis excretory-secretory products regulate migration and invasion in cholangiocarcinoma cells via extracellular signal-regulated kinase 1/2/nuclear factor-κB-dependent matrix metalloproteinase-9 expression. International journal for parasitology, 47(1): 51-59.

[15] Pak, J. H., Son, W. C., Seo, S. B., et al. (2016). Peroxiredoxin 6 expression is inversely correlated with nuclear factor-κB activation during Clonorchis sinensis infestation. Free radical biology & medicine, 99: 273-285.

[16] Bahk, Y. Y., Pak, J. H. (2016). Toll-Like Receptor-Mediated Free Radical Generation in Clonorchis sinensis Excretory-Secretory Product-Treated Cholangiocarcinoma Cells. The Korean journal of parasitology, 54(5): 679-684.

[17] Maeng, S., Lee, H. W., Bashir, Q., et al. (2016). Oxidative stress-mediated mouse liver lesions caused by Clonorchis sinensis infection. International journal for parasitology, 46(3):195-204.

[18] Apte, R. N., Voronov, E. (2002). Interleukin-1--a major pleiotropic cytokine in tumor-host interactions. Seminars in cancer biology, 12(4): 277-290.

[19] Ventura, A., Young, A. G., Winslow, M. M., et al. (2008). Targeted deletion reveals essential and overlapping functions of the miR-17 through 92 family of miRNA clusters. Cell, 132(5): 875-886.

[20] Xiao, C., Srinivasan, L., Calado, D. P., et al. (2008). Lymphoproliferative disease and autoimmunity in mice with increased miR-17-92 expression in lymphocytes. Nature immunology, 9(4): 405-414.

[21] Commodaro, A. G., Belfort, R. N., Rizzo, L. V., et al. (2009). Ocular toxoplasmosis: an update and review of the literature. Memorias do Instituto Oswaldo Cruz, 104(2): 345-350.

[22] Delair, E., Latkany, P., Noble, A. G., et al. (2011). Clinical manifestations of ocular toxoplasmosis. Ocular immunology and inflammation, 19(2): 91-102.