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MALIGNANT TUMORS WITH PARASITES

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ABSTRACT

Background: Certain parasites that can live inside the human body can also raise the risk of developing some kinds of cancer. Several parasites infest liver or biliary tree, either during their maturation stages or as adult worms. Multiple factors can significantly contribute to carcinogensis. **Material and Methods**: Parasitic pathogens and infection associated malignancy may be blood flukes, liver flukes, plasmodia species, *strongyloides stercoralis*, *trypanosome curizi* and sometime intracellular protozoan parasites like *leishmania* and *toxoplasma gondii*. **Results:** Adult worms are usually found in human hosts; their interactions with the host and parasite-derived products including their eggs strongly induce carcinogenesis. These malignancies included basal cell carcinoma, squamous cell carcinoma, and lymphoma. Although some parasitic infections have been very strongly associated with specific cancers, the available reported data have potentially linked leishmaniasis infection with the development of malignancy in humans and in animals. **Conclusion**: Although there are some parasites itself is not classified carcinogenic, but their risk more than the cancers as leishmaniasis, toxoplasmosis, amebiasis, hydatid cysts and *fasciola hepatica.*

KEYWORD: tumors, liver flukes, blood flukes, parasites, schistosomiasis, *strongyloides*, plasmoides, *trypanosome curizi*, leishmaniasis, toxoplasmosis, amebiasis, carcinoma, and lymphoma.

INTRODUCTION

Certain parasites that can live inside the human body can also raise the risk of developing some kinds of cancer. Several parasites infest liver or biliary tree, either during their maturation stages or as adult worms. Multiple factors can significantly contribute to carcinogensis.[1] Parasitic pathogens and infection associated malignancy may be blood

flukes, liver flukes, plasmodia species, *strongyloides stercoralis*, *trypanosome curizi* and sometime intracellular protozoan parasites like *leishmania* and *toxoplasma gondii*.[2]

1- Schistosomiasis and Cancer

Schistosomiasis is considered the most important helminth parasite of humans in terms of morbidity and mortality. Most human infections are due to *S. haematobium*, *S. mansoni*, and *S. japonicum*. Of those, *S. haematobium* is the most ubiquitous species in Egypt and in sub-Saharan Africa and causes urogenital schistosomiasis (UGS).[3][4] Adult worms are usually found in human hosts; their interactions with the host and parasite-derived products including their eggs strongly induce carcinogenesis.[5][6] Liver and colorectal cancers and lymphoid tumors may be associated with chronic schistosomiasis. Further important risk factors for the induction of bladder cancer are host immune responses and host genetic factors. Several mechanisms may account for the role of infection with *S. haematobium* in urinary bladder cancer, among them epithelium damage, chronic inflammatory processes and oxidative stress.[5][4] Nitrosamines and increased levels of urinary b-glucuronidase and cyclooxygenase-2 derived from adult schistosomes are also recognized as bladder carcinogens. A liquid chromatography-mass spectrometry analysis of urine samples from UGS patients revealed numerous estrogen-like metabolites including catechol estrogen quinones (CEQ), CEQ-DNA-adducts and novel metabolites derived from 8-oxo-7, 8-dihydro-2′-deoxyguanosine (8-oxodG).[7][8] The *S. haematobium*-derived carcinogens may lead to DNA damage and somatic mutations through chronic inflammation and oxidative stress in oncogenes.[9][10] Although evidence is sparse, infection with *S. japonicum* has been implicated in the etiology of colorectal cancer. Epidemiological and clinical studies in China and Japan suggested that *S. japonicum* may act as a carcinogen. Soluble egg antigen (SEA) from *S. japonicum*, which has a strong immunogenic activity, may contribute to carcinogenesis through stimulation of chronic inflammation. Cell-mediated responses are depressed during intestinal schistosomiasis and the degree of suppression apparently correlates with the development of hepatosplenomegaly. Anti-idiotype antibodies produced during chronic schistosomiasis may modulate immune responses and *S. mansoni* egg antigens can effectively modify subpopulations of T helper cells. Carcinogenic properties and mechanisms of *S. intercalatum*may possibly be inferred due to the similarity of *S. intercalatum* and *S. haematobium* in both morphology and life cycle of the parasite. However, compelling evidence indicating carcinogenicity of *S. intercalatum*and *S. mekongi* is still tenuous.[11]

2- Liver fluke infections and cholangiocarcinoma

There are three major liver trematodes that are responsible for infections in humans: *Chlonorchis sinensis*, *Opisthorcis* species, and *Fasciola hepatica*.

The life cycle of the trematodes can be completed in two different classes of hosts: definitive (humans, domestic, and wild animals) and intermediate (i.e. freshwater fish or snails).[12]

The flukes enter the bile ducts within the liver and gallbladder and can reside there for 20-30 years. The presence of flukes causes chronic inflammation of the bile ducts that can result in scarring and enlargement of the ducts.

Most infections are asymptomatic but those people with severe infection can have abdominal pain and fatigue. Other sequelae of a chronic long-term infection can include the formation of stones within the gallbladder and bile ducts, superimposed bacterial infections and cancer of the bile ducts.

Individuals suffering from severe infections can have an enlarged liver with abdominal discomfort, intense itching, loss of appetite or no appetite, weight loss, nausea, vomiting, and indigestion. Jaundice may occur from either the flukes plugging up the bile ducts or from stones or cancer (cholangiocarcinoma) which results after a prolonged chronic infection. It is important to note that occasionally, intense itching is the initial symptom of bile duct cancer. Cholangiocarcinoma (CCC) is a cancer of the bile ducts within the liver and outside the liver. Chronic inflammation from a parasitic infection is a known cause of CCC. Liver flukes are small, flat parasitic worms that can infect the liver, gallbladder and bile ducts. People become infected when they eat raw or undercooked freshwater fish that have the parasites, according to the Centers for Disease Control and Prevention (CDC). Most people who become infected with liver flukes have no symptoms, but some may experience indigestion, abdominal pain, diarrhea and constipation, according to the CDC. However, over long periods, infection with liver flukes can cause chronic inflammation in the bile ducts, resulting in scarring of the ducts and destruction of nearby liver cells, according to the WHO. What's more, the inflammation and scarring of the bile duct can lead to cancer of the bile ducts, which is called cholangiocarcinoma.[13][14] Symptoms of the cancer can include jaundice (yellowing of the skin), pain in the abdomen, dark urine, fever, itchy skin, vomiting and unexplained weight loss, according to the Veterans Affairs. For people with early-stage bile-duct cancer, about 15 to 30 percent survive at least five years following their diagnosis, according to the American

Society of Clinical Oncology. However, if the cancer has spread to a distant part of the body, the five-year survival rate is 2 percent). Pathologic conditions associated with opisthorchiasis are mainly hepatobiliary, specifically caused by bile duct fibrosis, cholangitis and other manifestations such as obstructive jaundice, hepatomegaly, abdominal pain, and nausea. After consumption of raw fish carrying *opisthorchiid metacercariae,* parasites excyst in the duodenum, migrate to the bile ducts and canaliculi following chemotactic stimuli, and adult worms feed on biliary epithelia and bile ingredients, eventually leading to biliary epithelial hyperplasia and fibrosis. Complex factors including genetics, environments, concomitant liver diseases, chronic infectious diseases and the parasitic infections (opisthorchiasis and clonorchiasis) are major risks for cholangiocarcinoma. The association of cholangiocarcinoma with opisthorchiasis and clonorchiasis has been evidenced by experimental, epidemiological and clinical data. Proposed mechanisms of carcinogenesis are biliary epithelium damage by parasites, long lasting immune-mediated pathogenesis, and effects of parasite-derived products on the bile ducts with subsequent modification of host cell proliferation.[5][4][15][16] A mechanism that can explain the association between *O. viverrini* infection and bile duct cancer is that parasite-derived molecules can lead to uncontrolled growth of host cells. Long-lasting interactions between *O. viverrini* and host responses initiate carcinogenesis. *O. viverrini* extracts could stimulate the production of inflammatory cytokines and *O. viverrini* derived products are internalized by cholangiocytes, which consequently induced cell proliferation and IL-6 production. Host immunological factors play also a crucial role in determining the outcome of opisthorchiid infection and in initiation of cholangiocarcinogenesis. The association between infection with *C. sinensis* and cholangiocarcinoma has been convincingly documented, and these helminths have been classified as highly carcinogenic agents. The exact mechanisms by which *C. sinensis* contribute to carcinogenesis are not clearly understood, although similar mechanisms to those of *O. viverrini*-induced carcinogenesis (*via* inflammation, parasite-derived products and physical damage) may be anticipated. Pancreatic ducts may harbor *C. sinensis,* which can lead to squamous metaplasia and mucous gland hyperplasia, and a well-differentiated ductal adenocarcinoma of the pancreas.[17][18]

3- *Strongyloides stercoralis* and Cancer

Strongyloides stercoralis, an intestinal nematode, can cause strongyloidiasis and gastrointestinal ulcer.[19] Infection with *S. stercoralis* may be complicated by autoinfection, which results in a hyperinfection syndrome and is associated with sustained infection, high

worm burden and high mortality. A recent epidemiological study investigated the association of co-infection with *S. stercoralis* and HTLV-1 with cancers in a large cohort of 5209 cancer patients and showed that *S. stercoralis* infection was associated with an increased occurrence of cancers.[20][21] These findings suggest that *S. stercoralis* is a cofactor for the development of HTLV-1- induced lymphoid cancers. *S. stercoralis* may not only serve as a cofactor for induction of HTLV-1-related lymphoid cancers, but also stimulates induction of colon adenocarcinoma probably by interacting with the host and/or activating the host immune response.[22]

Malaria and Burkitt lymphoma

Five species of the protozoan parasite *Plasmodium* - *Plasmodium falciparum*, *P. vivax*, *P. ovale*, *P. malariae*, and *P. knowlesi* affect humans. *P. falciparum* is the most virulent and widespread in regions endemic for malaria. Burkitt lymphoma is a monoclonal B cells cancer and the fastest growing tumor in humans in malaria endemic areas of sub-Saharan Africa. Burkitt lymphoma is classified into the clinical types of endemic, sporadic and immunodeficiency-associated Burkitt lymphoma.[23] Burkitt lymphoma is clearly associated with EBV infection, and in non-malaria-endemic areas it is associated with HIV/AIDS.

Although malaria itself is not classified carcinogenic, endemic Burkitt lymphoma in sub-Saharan Africa is geographically associated with holoendemicity of *P. falciparum* malaria. Co-infection with *P. falciparum* malaria and EBV is the main risk factor for endemic Burkitt lymphoma. *P. falciparum* infection is associated with enhanced proliferation and transformation of EBV-infected cells in both children with acute or asymptomatic malaria. The fact that *P. falciparum* can inhibit EBV-specific T cell immunity could explain how EBV and *P. falciparum* infections are associated with the increased risk of Burkitt lymphoma. Failure of EBV-specific T cells to control EBV-infected cells in malaria patients leads to the expansion and abnormal proliferation of EBV-infected B cells. Furthermore, elevated plasma EBV viral loads were associated with the development of endemic Burkitt lymphoma. Molecular mechanisms to explain how *Plasmodium* infection promotes Burkitt lymphomagenesis.[24][25] Widespread chromosome translocations were also observed in *Plasmodium*-induced germinal center B cells and the rearrangements occurred more frequently in genic regions. Taken together, malaria is not a direct trigger of cancer, but *P. falciparum* infection rather modifies the lymphoma phenotype to favor more mature B cell lymphomas by stimulating prolonged AID expression in germinal center B cells.[26][27]

The chromosome translocation between the *c-Myc* oncogene and immunoglobulin (*Ig*) gene loci that leads to deregulation of c-*M*yc expression together with *p53* gene mutations are known to be most relevant in the pathogenesis of Burkitt lymphoma.[28][29] Burkitt lymphoma is clearly associated with EBV infection, and in non-malaria-endemic areas it is associated with HIV/AIDS. Co-infection with *P. falciparum* malaria and EBV is the main risk factor for endemic Burkitt lymphoma. In a cohort of 711 Kenyan Burkitt lymphoma cases, the rates were higher in regions with chronic and intense malaria transmission compared to regions with no or sporadic malaria transmission. The mechanisms proposed are expansion of the EBV-infected B cell population, suppression of EBV-specific T-cell immunity, reactivation of EBV and activation-induced cytidine deaminase (AID)-dependent genomic translocation. Interaction of *P. falciparum* and B cells is considered as a key factor. B cell activation and hyper-gammaglobulinemia in malaria have been well described both experimentally and clinically.[30][31] A study has shown that *P. falciparum*-infected erythrocytes directly adhere to and activate B cells through the CIDR1α domain of *P. falciparum* erythrocyte membrane protein 1 (PfEMP1). Binding of PfEMP1 and CIDR1α induces expression of Toll-like receptor (TLR)7 and TLR10 and sensitizes B cells to TLR9 signaling leading to persistent activation of B cells and subsequently to impairment of their functions in chronic malaria. Increasing proliferation of polyclonal B cell populations might enhance the risk of expansion and transition of EBV-infected B cells, which could lead to the emergence of a malignant B-cell clone. Clinically, *P. falciparum* infection is associated with enhanced proliferation and transformation of EBV-infected cells in both children with acute or asymptomatic malaria. The fact that *P. falciparum* can inhibit EBV-specific T cell immunity could explain how EBV and *P. falciparum* infections are associated with the increased risk of Burkitt lymphoma. Failure of EBV-specific T cells to control EBV-infected cells in malaria patients leads to the expansion and abnormal proliferation of EBV-infected B cells. that cell-free EBV-DNA levels in plasma of children and pregnant women with malaria were increased compared to those without malaria, showing that EBV can be reactivated during malaria infection. Molecular mechanisms to explain how *Plasmodium* infection promotes Burkitt lymphomagenesis remain controversial. *P. chabaudi*was used to establish chronic malaria in an animal model; the infection resulted in an increased and prolonged clonal expansion of B cells in germinal centers and primarily induced expression of AID in *Plasmodium*-induced germinal center B cells.[26] In a mouse model of chronic malaria, AID induced genomic instability of germinal center B cells, mostly in immunoglobulin (*Ig*) regions and in highly transcribed genes.[32]

5- **Chagas Disease in Carcinogenesis**

Chagas disease (CD), a parasitic disease caused by the flagellated protozoan *Trypanosoma cruzi*. Successful transmission of *T. cruzi* primarily occurs through triatomine insects (kissing bugs). The *T. cruzi* containing insect feces contaminate mucous membranes, conjunctivae, or skin breaks, and initiate human infection. Approximately 40% of persons infected with *T. cruzi* are asymptomatic or present with indeterminate forms. About 2–5% progress annually to symptomatic forms with irreversible cardiac and/or digestive disorders, mostly presenting as megaorgans < 1% develop severe acute disease with the clinical manifestations of acute myocarditis, pericardial effusion, and/or meningoencephalitis.[33] An association of CD with gastrointestinal cancer has been had developed esophageal leiomyosarcoma, uterine leiomyoma, chagasic megacolon and development of colon cancer. The assumed *T. cruzi*-related carcinogenesis is most likely due to host genetic factors, and the parasite-host interaction resulting in chronic inflammation in particular tissues. Immunization with *T. cruzi* epimastigote lysate strongly inhibited tumor development *in vivo* by inducing the activation of both CD4(+) and CD8(+) T cells as well as by increasing numbers of CD11b/c (+) His48(−) MHC II(+) cells, which correspond to macrophages and/or dendritic cells.[34] Antibodies against *T. cruzi* lysate recognized various rat and human tumor cell types such as colon and human breast cancer cells and thus mediate tumor cell killing through antibody-dependent cellular cytotoxicity (ADCC).[35][2] the oxidative stress response of *T. cruzi* may also be of importance in protection of host chromosomes during chronic inflammation and, thus, in reduced cancer development. *T. cruzi* may exert both carcinogenic and antitumor effects.

Although there are some parasites itself is not classified carcinogenic, but their risk more than the cancers as leishmaniasis, toxoplasmosis, amebiasis and hydatid cysts.

1- Leishmaniasis

Leishmaniasis, a widely prevalent disease throughout tropical and subtropical regions of the world. The intracellular protozoan parasites of the genus Leishmania can cause human leishmaniasis, resulting in various visceral, cutaneous, and mucocutaneous manifestations. Visceral leishmaniasis (VL), which is lethal if left untreated, and cutaneous leishmaniasis (CL), which can affect the skin and/or mucous membranes with a broad spectrum of clinical manifestations, including dissemination (disseminated CL), are the most common clinical entitie. To maintain a chronic infectious state within its host, Leishmania parasites have

developed some successful strategies to prevent activation of effective immune responses and maintain the antimicrobial activities of host cells. These include remodeling the host cells'phagosomal compartments, interfering with the intracellular signaling pathways, alteration of toll-like receptor pathways, modulation of cytokines and chemokines, modification of T-cell responses, evasion of the host's cellular immunity, and generation of nitric oxide and oxygen oxidative radicals. In contrast, carcinogenesis can be influenced by several physiologic, exogenous, environmental, genotypic, and phenotypic factors. These malignancies included basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and lymphoma. Although some parasitic infections have been very strongly associated with specific cancers, the available reported data have potentially linked leishmaniasis infection with the development of malignancy in humans and in animals.[36]

The potential associations between leishmaniasis and malignancy included the following: (1) leishmaniasis mimicking malignancy; (2) leishmaniasis coexisting with malignancy; (3) malignancy developing in patients with leishmaniasis; and (4) leishmaniasis developing in patients with malignancy. Numerous studies have reported a well-established relationship between Leishmania spp. and the pathogenesis of malignant lesions, including BCC, SCC, lymphoma, leukemia, and hemangiosarcoma. Amastigotes have been identified in infiltrating macrophages and within the cytoplasm of neoplastic cells from tumors with different histogenesis variants. In addition, prolonged antigenic stimulation and chronic immunosuppression, typical of leishmaniasis, might play a crucial role in the etiopathogenesis of certain cancers, such as T-cell lymphoma. Possible causal association between leishmaniasis infection and the subsequent appearance of skin or mucous membrane malignancy reported that BCC, SCC, or hepatocellular carcinoma had developed at the site of healed leishmanial scars or within a few months after the first symptoms. The chronic irritation hypothesis remains a widely supported mechanism for carcinogenesis by infectious agents. This is because many cancers arise from sites of infection.[36]

Recent data have expanded the concept that chronic inflammation is a critical component of the neoplastic process, fostering proliferation, survival, and migration of cancer cells. The chronic inflammation process due to prolonged persistence of Leishmania spp. in the host leads to repeated cycles of cell damage (caused by the host's immune response to the infection rather than by the infecting organism itself) and compensatory cell proliferation, thus orchestrating a tumor microenvironment. Host tissue damage during parasite

development, along with the active wound healing, has been recognized as a carcinogenic mechanism. The presence of Leishmania amastigotes has been documented in the cytoplasm of neoplastic cells from tumors of different histogenesis. The transfer of genetic material from the Leishmania parasite to the host can cause DNA damage and directly interfere with cell transformation.[37][38]

Prolonged immunosuppression and chronic leishmanial antigenic stimulation have been shown to play a crucial role in the etiopathogenesis of T-cell lymphoma.

The development of malignant lesions, in particular, BCC and SCC, at the sites of previous dermal scars is a well-recognized phenomenon. Almost all such cases develop in exposed areas.

Thus, it has been hypothesized that the accompanying atrophy and decreased vascularity and adnexal structures in areas of scarring might render the affected tissues more susceptible to the effects of environmental factors, such as ultraviolet radiation.[39]

2- Toxoplasmosis

Chronic *Toxoplasma gondii* infection is one of the most prevalent parasitic infections in humans worldwide. *T gondii* transforms into fast replicating tachyzoites and infects various organs of the body including the central nervous system (CNS).[40] To evade host immune response, some of the tachyzoites differentiate in to bradyzoites, which are slow growing and form tissue cysts in the brain. During chronic infection, *T.gondii* tissue-cysts persist for lifetime of the host without provoking any host immune attack.[41] Detection of parasitic proteins with kinase and phosphatase domains in the host nucleus suggests that the parasite modulates the host cell signaling and gene expression. *Toxoplasma* is an important non-viral pathogen shown to be associated with the occurrence of brain tumors. Antibody positivity to *Toxoplasma* is associated with meningioma. Incidences of adult brain cancers and *Toxoplasma* infected people associated a nearly two-fold increase in the risk of brain cancers across the range of prevalence in Toxoplasma infection. These studies, though correlational, suggest that *Toxoplasma* should be investigated further as a possible oncogenic pathogen in humans.[42] A recent work conducted in France showed that mortality rates due to brain cancer correlated positively with the local sero-prevalence of *Toxoplasma.* Hypothesis that Toxoplasma infection may have the ability to modulate the host miRNAs and could potentially promote the development of brain cancer. During intracellular infections, the host

cell responds by initiating apoptotic response which reduces survival and proliferation of the parasites and makes the parasites susceptible to immune attack.[43][44] However, Toxoplasma has established several strategies to neutralize the extrinsic and intrinsic cellular suicide programs of the infected cells. Invasion of Toxoplasma turns host cells resistant to multiple inducers of apoptosis, including Fas-dependent and Fas-independent CTL-mediated cytotoxicity, IL-2 deprivation, gamma irradiation, UV irradiation, and calcium ionophorebeauvericin. *Toxoplasma* infection has been shown to specifically increase levels of mature miR-17-92 derived miRNAs in primary human foreskin fibroblasts. *Toxoplasma* dependent up-regulation of the miR-17-92 promoter is at least partly responsible for this increase.[45] High throughput microarray technology will be used to identify miRNA signatures associated with *Toxoplasma* infected brain cancer cells. Brains of the animals chronically infected with Toxoplasma will be monitored *in vivo* for malignant transformation and tumor growth using neuroimaging techniques.

3- Amebiasis

The major clinical manifestation of *Entameba histolytica* infestation is liver abscess[46] amebiasis cause tender hepatomegaly during the acute phase (amebic hepatitis) which is more common in chronic carriers, and an amebic abscess may develop.[47] Hepatic amebiasis is the commonest extraintestinal complication. Patients may also present with picture of obstructive jaundice. Ameboma can stimulate malignancy in barium enemas but the diagnosis is made by endoscopic biopsies.[48][49]

4- Hydatid Cyst

Echinococcus granulosis is the most common form of hydatid disease in humans. Cysts caused by *E. granulosis* grow slowly and develop over many years. There are recent developments diagnosis of hydatid disease as in serological tests (using ELISA technique) and in radiological using ultrasound classification. A liver cyst may rupture into the biliary tree causing obstructive jaundice and a lung cyst may rupture into pleural cavity presenting with a pleural effusion.[50] Hydatid cysts of the liver are usually single but can be multiple. They may be large and cause pressure effect on the liver or may rupture into the biliary tree leading to biliary obstruction by daughter cysts.[51]

A case of large cell carcinoma of the lung mimicking pulmonary hydatid cyst is reported herein. History of slowly progressive breathlessness and painful swelling over the left chest wall. Computed tomography of the chest showed a well defined cystic lesion in the left upper

lobe with outward extension through the left 2nd–3rd intercostal space in the absence of bony destruction. The patient was found to have positive serological test for *Echinococcus granulosus* and therefore the preoperative diagnosis was that of complicated pulmonary hydatid cyst. Intra-operative findings included presence of a large cavity filled with necrotic material and "daughter cysts". Dense adhesions between the cavity wall and the thoracic cage prevented complete surgical resection. Histopathological evaluation of the excised specimen showed large cell carcinoma. The case highlights the fact that a lung carcinoma may rarely have clinical, radiological, and serological features similar to those of a pulmonary hydatid cyst. Evaluates the antitumor immune response induced by human hydatic cyst fluid (HCF) in an animal model of colon carcinoma.[52] Edgardo Berriel et al., 2013 found in his study the evaluate the antitumor immune response induced by human hydatic cyst fluid (HCF) in an animal model of colon carcinoma. They found that anti-HCF antibodies were able to identify cell surface and intracellular antigens in CT26 colon cancer cells. In prophylactic tumor challenge experiments, HCF vaccination was found to be protective against tumor formation for 40% of the mice.[53]

This vaccination generated memory immune responses that protected surviving mice from tumor rechallenge, implicating the development of an adaptive immune response in this process. They performed a proteomic analysis of CT26 antigens recognized by anti-HCF antibodies to analyze the immune cross-reactivity between *E. granulosus* (HCF) and CT26 colon cancer cells. they identified two proteins: mortalin and creatine kinase M-type. Interestingly, CT26 mortalin displays 60% homology with *E. granulosus* hsp70.

5- Fasciola

After ingestion, *Fasciola* metacercariae excyst in the duodenum. In contrast to other liver flukes (*Clonorchis* and *Opisthorchis*) that migrate through the ampulla of Vater and ascend the biliary tree, *Fasciola* metacercariae penetrate the duodenal wall, migrate through the peritoneal cavity, and enter the liver. A liver ultrasound demonstrated an 8 cm hypoechoic, heterogenous mass in segment 5/6. Her serology for hepatitis B and C was negative, and a range of tumor markers (alpha fetoprotein, carcinoembryonic antigen, cancer antigen 19.9, cancer antigen 125) was normal. At laparoscopy, adjacent to the mass in segment 5/6, the diaphragmatic surface of the liver appeared nodular, and there were several adhesions. Biopsies from the liver mass demonstrated necrotizing lesions, with a mixed inflammatory infiltrate consisting of lymphocytes, plasma cells, and numerous eosinophils. Scattered

Charcot-Leyden crystals were noted. The biopsy from the nodular peritoneum also demonstrated abundant eosinophils and Charcot-Leyden crystals.[54]

CONCLUSION

Parasitic pathogens and infection associated malignancy may be blood flukes, liver flukes, plasmodia species, *strongyloides stercoralis*, *trypanosome curizi* and sometime intracellular protozoan parasites like *leishmania* and *toxoplasma gondii*.

Although there are some parasites itself is not classified carcinogenic, but their risk more than the cancers as leishmaniasis, toxoplasmosis, amebiasis, hydatid cysts and *fasciola hepatica*.

List of abbreviation

UGS: Urogenital schistosomiasis

CEQ: Catechol estrogen quinones

SEA: Soluble egg antigen

CCC: Cholangiocarcinoma

CDC: The Centers for Disease Control and Prevention

HTLV-1: human T-cell lymphotopic virus type 1

EBV: Epstein-Barr virus

HIV: human immunodeficiency virus

AIDS: Activation-induced cytidine deaminase

Ig: Immunoglobulin

PfEMP1: *P. falciparum* erythrocyte membrane protein 1

TLR: Toll-like receptor

CD: Chagas disease

ADCC: Antibody-dependent cellular cytotoxicity

VL: Visceral leishmaniasis

CL: Cutaneous leishmaniasis

BCC: basal cell carcinoma

SCC : Squamous cell carcinoma

CNS : Central nervous system

HCF: Hydatic cyst fluid

Declarations

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The author agree to use data and materials with refer to the reference.

Authors' contributions

I am participated in preparing and treating of the experiments and writing of the manuscript. Author read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable

Consent for publication

The author is consent for publication this manuscript in the NRC bulletin.

Competing interests

The author declare that they have no competing interests.

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