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Mini-Review

Toxoplasmosis in Immunocompetent Children: A Narrative Mini-Review

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Abstract

Toxoplasmosis is a zoonotic infection caused by the parasite *Toxoplasma gondii*. *T. gondii* is found worldwide, with the possible exception of Antarctica. The parasite is capable of invading and replicating within almost all mammalian cells. It is estimated that approximately 25 to 35% of the world's human population is infected with *Toxoplasma*. There are different clinical presentations depending on the immune status of the host. Infection with *T. gondii* in immunocompetent persons is generally asymptomatic. Acute infection is usually benign and self-limiting, and symptoms resolve within a few weeks to months without the need for anti-parasitic medication. However, *T. gondii* is an intracellular parasite that has successfully developed strategies to evade or manipulate the host's immune response, forming tissue cysts in almost any tissue, although most commonly in the central nervous system, retina, myocardium, and muscle. As a result, *T. gondii* can survive throughout the host's life as a latent long-term infection and potentially reactivate, usually in the brain or eye, if the host becomes immunocompromised. This is a narrative literature review of the clinical findings on acute, latent, and chronic *T. gondii* infections in immunocompetent children, with a particular focus on cases of disease associated with acquired infection.

Keywords: *Toxoplasma Gondii, Toxoplasmosis, Zoonosis, Parasites.*

Introduction

Toxoplasma gondii was first described in 1908 by Nicolle and Manceaux, who found the parasite in the North African rodent *Ctenodactylus gundi* during a study conducted in Tunis[1]. Just three months later, Splendore reported the parasite in rabbits in Brazil. Subsequent studies have demonstrated its presence in almost all continents and its ability to infect mammals. The definitive hosts for the zoonotic parasite *T. gondii* are members of the family *Felidae*, including domestic cats. Other mammals serve as intermediate hosts.

Domestic and wild cats become infected with *T. gondii* through ingestion of oocysts in the soil or cysts in meat from infected animals, such as mice. The parasite colonizes the intestine, and oocysts are later excreted in fecal matter[2]. The oocysts are highly resistant to environmental factors. Transmission to humans occurs through ingestion of tissue cysts in undercooked meat or in contaminated food or water. It is estimated that one third of the world's human population is infected with *T. gondii*[3].

Studies with human semen in immunocompetent and latently infected human volunteers support the possibility of sexual transmission, as intact *T. gondii* cysts were found in thin smears of the semen of those volunteers[4].

T. gondii rarely causes clinically significant disease in immunocompetent people. However, there are cases of immunocompetent people who developed clinically significant disease with an acquired *T. gondii* infection. Patients, including children, who have an acquired latent infection and then become immunocompromised due to various causes, including chemotherapy or organ transplantation, can develop reactivation of toxoplasmosis, which causes disease. Toxoplasmosis is also a rare but highly lethal opportunistic infection after allogeneic hematopoietic cell transplantation[5].

The aim of this narrative literature review is to identify diseases associated with acquired *T. gondii* infection in immunocompetent children.

A review of the available scientific evidence from 2005 to 2025 was conducted in the electronic databases PubMed, Medline, and supplementary references. The following MeSH terms were used: ^Toxoplasmosis^ OR ^etiology^ OR ^T.gondii^

Acquired toxoplasmosis

Following the ingestion of undercooked meat containing tissue cysts, or water or food contaminated with cat feces containing oocysts, the outer wall of the *T. gondii* oocyst is proteolyzed by gastric acid in the digestive tract. Uncoated sporozoites and bradyzoites invade intestinal epithelial cells and transform into the rapidly multiplying tachyzoite stage. Tachyzoites can penetrate any nucleated cell in the body, including dendritic cells, monocytes, and neutrophils, allowing them to spread widely.

Through various molecular mechanisms, *T. gondii* can effectively block both cell-intrinsic (mitochondrial) and extrinsic (death receptor-mediated) pathways of apoptosis in the cells it has invaded. This may help the parasite to preserve its intracellular niche, replicate, and avoid clearance by humoral immunity[6]. It then transforms into the slowly dividing bradyzoite stage. Bradyzoites have thick cyst walls and form tissue cysts[7]. These cysts can form in any tissue, but are typically found in the central nervous system, retina, myocardium, and muscle. *T. gondii* can survive throughout the host's life as a latent long-term infection. Clinical progression depends on the immune status of the host.

In summary, *T. gondii* infects infiltrating immune cells and uses them to spread systematically, reaching distant organs such as the brain, eyes, heart, and kidneys. Its ability to persist allows it to become a latent or chronic parasitic infection in these organs.

Toxoplasmosis and neurological diseases

T. gondii is a neurotropic parasite that infects the central nervous system, causing illness in individuals with an impaired immune system, such as fetuses with congenital toxoplasmosis or patients with human immunodeficiency virus (HIV).

As of 2024, 18 cases of immunocompetent patients with isolated toxoplasmosis of the nervous system have been reported in the literature[8 9 10]. Two of these were children and are described below.

An Indian study reports a 14-year-old adolescent boy with upper motor neuron palsy of the right facial nerve, with involvement of the IX and X cranial nerves. MRI brain showed a hypo- intense lesion in the pons extending into the medulla. The lesion was heterogeneously enhancing with contrast. Several tachyzoite forms of *T. gondii* were seen in the lesion on immunohistochemistry[11].

Another Indian study reports the case of a 5-year-old boy who presented with cervical lymphadenopathy because of acquired toxoplasmosis accompanied with unilateral facial nerve paralysis. *T. gondii* DNA detection in blood by polymerase chain reaction, as well as elevated specific immunoglobulin M antibodies against it, established the diagnosis. Characteristic brain lesions on magnetic resonance imaging were absent[12].

Toxoplasmosis and polyradiculoneuritis

A few cases of acute polyradiculoneuritis have been reported in immunocompetent patients with increasing levels of immunoglobulin G and IgM antibodies directed against *T. gondii*. One case study of a 21-year-old even mentions the ingestion of undercooked warthog and doe meat as a possible mechanism of infection with *T. gondii*[13]. In pediatric patients, one case report describes an immunocompetent 3-year-old boy with Guillain-Barré syndrome associated with acute toxoplasmosis[14].

Toxoplasmosis and epilepsy

A 2015 meta-analysis identified six published studies that analyzed the association between *T. gondii* infection and epilepsy [15]. This possible association was also described in a meta-analysis by Sadeghi et al. in 2018, where subgroup analyses according to age showed a significant positive association in children, supporting the association between *T. gondii* infection and epilepsy[16].

The epileptogenic mechanisms of toxoplasmosis are probably multifactorial. The brain is one of the primary targets for the formation of *T. gondii* cysts. Their wall may eventually rupture in immunocompetent hosts, liberating numerous bradyzoites that are capable of infecting new cells and inducing localized inflammation. This process may produce microglial scars (glial nodules). It has been suggested that scar tissue formation is one of the main causes of epilepsy in toxoplasmosis patients[17].

Toxoplasmosis and psychiatric disorders

Epidemiological studies have shown a link between autism and positive *T. gondii* serology. The Finnish Prenatal Study of Autism (FIPS-A) assayed the maternal sera of almost all offspring diagnosed with autism in Finland for *T. gondii* IgM and IgG antibodies. The findings suggest that low *T. gondii*-specific IgM levels in pregnant women may be related to an increase in offspring odds of autism[18]. It has been reported that *T. gondii* infection significantly affects brain development, becoming symptomatic in early childhood up until school age[19]. The results of a study of 50 autistic and 50 normal children between 3 and 12 years old showed that autistic children had a higher rate of infection by *T. gondii* than normal children, and that children infected with *T. gondii* were more aggressive than the non-infected group[20].

The potential link between latent *T. gondii* infection and various neuropsychiatric and behavioral disorders is based on research showing neurochemical changes in the central nervous system of animals infected with *T. gondii*. These animals show increased levels of dopamine or dopamine metabolites, which may explain the mental and motor abnormalities that accompany or follow toxoplasmosis in rodents. This has been described in studies with rodents, though another group was unable to confirm these changes. One explanation for these contradictory findings is that each group used different mouse strains, which can affect the immune response to *T. gondii*[21].

A recent study by a research group in Sweden examined the possible link between chronic or latent *T. gondii* infection and schizophrenia or the bipolar spectrum. The group evaluated patients with *T. gondii* immunoglobulin G (IgG) seropositivity, reflecting previous infection and current latency. These patients had increased circulating neuron-specific enolase (NSE), a marker of brain damage, and interleukin-18 (IL-18), an innate immune marker. The two markers were more frequent in patients diagnosed with schizophrenia and bipolar disorder with positive serology for *T. gondii*[22].

Another study demonstrated that some antipsychotic and mood-stabilizing agents, such as haloperidol and valproic acid, have the ability to inhibit *T. gondii* proliferation in cell culture[23].

Acquired toxoplasmosis associated with immune thrombocytopenia in children

Stogiannis et al. describes the case of a previously healthy 2.5-year-old boy who developed acute immune thrombocytopenia with a life-threatening platelet count a few days after a *T. gondii* infection. The boy underwent 3 intravenous immunoglobulin treatments within a trimester. He only began to recover after the third treatment, which was administered in conjunction with an antibiotic medication for the *T. gondii* infection[24].

Toxoplasmosis and hematological malignancies

Most cases of toxoplasmosis after allogeneic hematopoietic stem cell transplantation result from reactivation of a latent *T. gondii* infection, in patients who were seropositive for *T. gondii* before they underwent transplantation[25]. Osthoff et al. describe a patient who developed primary disseminated toxoplasmosis following hematopoietic stem cell transplantation[26]. Hematological guidelines propose weekly blood screening by use of quantitative PCR to identify infection early as a pre-emptive strategy[27].

Ocular toxoplasmosis

Ocular toxoplasmosis is the most common cause of posterior uveitis worldwide, with an estimated incidence of 8.4%[28]. Ocular toxoplasmosis in adults was perceived as a recurrence of congenital infection, but recent evidence suggests that most cases with ocular involvement are most probably postnatal acquired infections[29].

Toxoplasmosis and myocarditis

This clinical presentation of acute acquired toxoplasmosis has been described in adults[31] [32] [33], but no pediatric cases were found in the literature.

However, some pediatric cardiology associations mention it as a possible etiology[34] [35].

Pulmonary toxoplasmosis

In animal models, the earliest change following intravenous injection of infective tachyzoites is an interstitial pneumonitis with focal infiltrates of neutrophils, eosinophils, and mononuclear cells. As the interstitial infiltrate spreads, the exudation of fibrin along with neutrophils and macrophages into alveolar spaces can occur. This can finally evolve into a pattern of diffuse alveolar damage with pneumocyte proliferation and focal necrosis[36].

Vasantham et al. describe a case of a child with pulmonary tuberculosis who underwent bronchoalveolar lavage. The Ziehl-Neelsen stain for acid-fast bacilli was positive, and the Giemsa-stained cytosmears also showed clusters of tachyzoites in a background of lymphocytes[37].

Toxoplasmosis and kidney disease

Nephrotic syndrome has been described as one of the manifestations of congenital toxoplasmosis[38]. One proposed pathological mechanism is that *T. gondii* antigen-containing immune complexes cause glomerular damage, and this can also occur in acquired toxoplasmosis[39].

In one paper, seven cases of children aged between 11 months and 7 years with concomitant nephrotic syndrome and asymptomatic acute *T. gondii* infection are reported. In one of those patients, only the administration of anti-*Toxoplasma* therapy was enough to control the clinical and laboratory manifestations of the disease[40].

A rare source of *T. gondii* infection

In a group of children with β-thalassemia major who regularly received blood transfusions, the seroprevalence of *Toxoplasma* infection was 23.2% and 53.6% for IgM and IgG anti- *Toxoplasma* antibodies, respectively. From the positive IgG samples, 65.5% had low avidity, indicating recent infection, while 38.73% had high avidity, indicating past infection. In the control group, the prevalence was 5% and 18% for IgM and IgG anti-*Toxoplasma* antibodies, respectively[41].

Conclusion

We have found evidence that acquired *T. gondii* infection can cause disease in immunocompetent children. The different clinical presentations can be explained by the ability of the parasite to invade different organs via immune cells, such as monocytes and neutrophils.

The literature includes cases of epilepsy, facial paralysis, polyradiculoneuritis, and nephrotic syndrome that are usually reported as idiopathic because the *Toxoplasma* infection is not actively sought. It is therefore possible that *T. gondii* infection and toxoplasmosis, understood as the disease associated with acute or latent acquired infection, are underdiagnosed. Fortunately, guidelines now recommend testing for the infection before classifying an illness as idiopathic.

Given these cases of clinically significant disease in immunocompetent children, it is important to establish guidelines for anti-parasitic treatment. Failing to treat *T. gondii* infection in immunocompetent individuals can lead to long-term consequences, including the potential development of mental illnesses due to the physiochemical changes caused by the parasite's lifelong presence in the body.

Conflict of Interest

The author declares no conflict of interest.

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