

CHILD TOXOPLASMOSIS AND LIMPHADENOPATHY - CASE REPORT

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Abstract: The purpose of this paper is to increase awareness of medical doctors to consider toxoplasmosis as one of the possible causes of lymphadenopathy in older children. Toxoplasmosis is one of the most common and widespread parasitic diseases in the world, even 22.5% of children over 12 years old are infected with Toxoplasmosis. The disease is caused by the parasite *Toxoplasma gondii*. The disease is transmitted through the feces of infected cats that are carriers of the parasite. We report the case of a 13-year-old child who appears to be a healthy and immunocompetent child and who clinically presents with enlargement of 2 lymph nodes in the left neck region that are unpainful on palpation, one of which measures 4/5 cm and the other with dimensions of 1/2 cm. The child is in good general condition without significant health disorders. The epidemiological survey is positive for frequent contact with a domestic cat. The performed serological tests show strongly positive values for the presence of IgM and especially for IgG antibodies for Toxoplasmosis. Surgical extirpation of the one bigger lymph node because of diagnostic dilemmas was carried out. Pathohistological analysis confirms diagnosis of Toxoplasmosis and malignancy was excluded. From the results obtained from the Enzyme Immune Test for the age of IgG antibodies (avidity), a low avidity of IgG antibodies was determined. Additional research is needed whether excessive exposure to the parasite *Toxoplasma gondii* can be associated with a more severe clinical picture of the disease.

Keywords: Toxoplasmosis, Children, Lymphadenopathy

Field: Medical sciences and Health

1. INTRODUCTION

Toxoplasmosis is one of the most widespread parasitic diseases in the world, caused by the parasite *Toxoplasma gondii*. The definitive hosts of the parasite are cats (Felidae), while birds and many mammals act as intermediate hosts (Dubey, 1996). Infection occurs through the ingestion of food or water contaminated with oocysts or live microorganisms. The infection can also be transmitted to humans through contaminated hands or by ingesting food and water contaminated with cat feces (Arranz-Solís & Saeij, 2022). Pregnant women can transmit the infection trans placentally to the fetus, which may result in congenital malformations (Sharifi et al., 2019). Infestation most commonly occurs through the consumption of undercooked meat, unwashed vegetables and fruits, or by working in contaminated soil (Ayoade & Chandranesan, 2022).

When *Toxoplasma gondii* enters the body, it invades through the intestinal epithelium and spreads to the tissues where it reproduces (Dubey, 1996). In cats, the parasite reproduces sexually in the intestinal epithelium, producing oocysts that are excreted with the host's feces (Arranz-Solís & Saeij, 2022). Immunocompetent hosts generally mount a strong immune response that controls the infection within weeks or months, leading to immunity that prevents reinfection (Ayoade & Chandranesan, 2022). In these hosts, the tissue cysts remain inactive and may persist without causing symptoms throughout their lives (Dunay et al., 2018).

However, in immunocompromised individuals, the disease may manifest with various clinical symptoms, including myocarditis, pneumonitis, and central nervous system (CNS) involvement (Dunay et al., 2018). Transplacental transmission may result in congenital toxoplasmosis, which can affect vision or cause other malformations (Sharifi et al., 2019). In immunocompetent individuals, toxoplasmosis is often asymptomatic, though 10-20% may develop lymphadenopathy or flu-like symptoms (Khawar Tariq & Shahid, 2022). Severe cases involving the CNS are rare but possible in otherwise healthy individuals (Khawar Tariq & Shahid, 2022).

A certain number of immunocompetent patients with acute infection may experience fever, myalgia, rash, splenomegaly, headache, pharyngitis, and painless lymphadenopathy, which may last for weeks (Kaparos et al., 2014). Diagnosis of toxoplasmosis is primarily based on serological testing, identifying *Toxoplasma gondii* IgM and IgG antibodies (Sharifi et al., 2019). Molecular methods like PCR can also detect the parasite's DNA in blood or other fluids (Madireddy et al., 2024). For tissue cyst identification, biopsies may provide a definitive diagnosis (Mercadante & Tadi, 2024).

Once diagnosed, treatment typically involves a combination of pyrimethamine and sulfadiazine for

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6 weeks, particularly for immunocompromised patients, alongside folic acid supplementation (Dunay et al., 2018). Prophylaxis may also be necessary for these patients to prevent reactivation of latent infection (Khawar Tariq & Shahid, 2022). Differential diagnosis in children can include cytomegalovirus (CMV), bacterial or viral infections, and malignancies of other etiologies (Madireddy et al., 2024). Some studies suggest that both toxoplasmosis and CMV may play a role in the etiology of autism (Hassan et al., 2023). While toxoplasmosis is generally self-limiting in immunocompetent patients with a favorable prognosis, the risk of reactivation remains due to latent infection (Khawar Tariq & Shahid, 2022). Preventative measures include thoroughly cooking food, washing hands, fruits, and vegetables, avoiding unpasteurized milk, and limiting contact between children and cats (Mirza Alizadeh et al., 2018).

2. MATERIALS AND METHODS

A 13-year-old male child comes to the examination. He is conscious, oriented in time and space, afebrile, with the presence of enlarged painless lymph nodes in the left anterior neck region that have increased without the presence of other symptoms in the last 4 weeks ago. The parents did not consider it seriously. After 2 weeks, one lymph node becomes enlarged, which is why the child's father visits the doctor for an examination. The child lives in the village and has a positive history of contact with a domestic cat. During the physical examination, there are no significant deviations, except during palpation of the lymph nodes in the front left neck region, two painless lymph nodes are palpated, one of which is 4/5 cm, and the other is 1/2 cm. Due to the enlargement of one lymph node, the child was referred for further investigation. A serological analysis was performed to determine infection with *Toxoplasma* by identifying IgM and IgG antibodies and an enzyme immunological test was performed for the age of the IgG antibodies (avidity). Other serological analysis was done to exclude CMV, EBV, and HIV infections. Biochemical analysis was also done to rule out hepatic involvement and other diseases. To rule out malignancy, surgical extirpation of the enlarged lymph gland was performed and submitted for histopathological analysis. The results obtained from the analysis show Toxoplasmosis infection and chronic inflammation of the lymph node, and the existence of a malignant process is excluded. Informed Consent: Written informed consent was obtained from the patient's guardian.

3. RESULTS

Table 1 – Serological analysis

	Referent value/ml U/ml	Results- First	Results/Second
CMV IgG	>6 positive	+226.5	
CMV IgM	>1.0 positive	0 (negative)	
EBV IgG	>1.0 positive	0	
EBV IgM	>1.0 positive	0	
The Architect <u>Toxo</u> IgG immunoassay	>3.0 positive	139.0	146
The Architect <u>Toxo</u> IgM immunoassay	>1. positive	7.44	8.68
ELISA HIV		negative	

Source: Institute for Public Health of the Republic of North Macedonia-Skopje; 50th Division Skopje Diagnostic laboratory-Laboratory for Cytology and Histology; Street. 1738 no. 20/1 1000 Skopje Republic of North Macedonia

An enzyme immunological test for the age of the IgG antibodies (avidity) for *Toxoplasma* was also performed. Avidity of IgG antibodies for *Toxoplasma*: 0.082 and indicated a low avidity and an infection that occurred in an interval of less than 3 months, which excludes the existence of congenital toxoplasmosis.

Analysis of blood count was in normal range, CRP-1 (normal), ASO=939 (0-200 normal), Analyses of liver function: ALT =11, AST= 19 (normal range), glucose 5.8 mmol/2-normal range.

Microscopic Examination of the sections from the extirpated lymph node showed Preserved Architectonics with Hyperplastic Lymphoid Follicles: The overall structure of the lymph node was maintained. There were many mature lymphocytes in the cortex with hyperplastic (enlarged) lymphoid follicles and prominent germinal centers. Presence of Macrophages with Tangible Bodies: Numerous macrophages containing phagocytized debris, indicative of active immune response, were seen in the germinal centers. Dilated Sinuses in the Medulla with Hyperplastic Sinus Macrophages: The medullary sinuses were expanded and filled with numerous macrophages, suggesting increased immune activity.

Preserved Capsule and Peripheral Collagen Tissue: The capsule of the lymph node and surrounding collagen tissue were intact, indicating no invasion or destruction typical of cancer.

Immunohistochemical Analysis: CD-20 and CD-79 Positive (+++): These are markers for B-cells, indicated a significant presence of B-cells, which are part of the immune response. CD-3 Positive (++): This is a marker for T-cells, showed that T-cells were also present and active. Bcl-2 Negative in Germinal Centers: Bcl-2 was a marker that inhibited apoptosis (cell death). Its absence in germinal centers suggested normal cell turnover and not a neoplastic process. Ki-67 was weakly positive only in germinal centers (+): Ki-67 is a marker for cell proliferation. Weak positivity indicated some cell proliferation, which is normal in an immune response. CD 15 was negative and CD 30 positive in activated hyperplastic lymphocytes: CD 15 negativity and CD 30 positivity in immunoblasts (activated lymphocytes) further supported a reactive process rather than a neoplastic one.

Correlation with Toxoplasmosis: Therefore, the immunohistochemical analysis confirms that the lymphadenopathy observed in this case is due to a reactive immune response to *Toxoplasma gondii* infection, rather than a neoplastic process. This supports the clinical findings and serological tests, further validating toxoplasmosis as the cause of lymphadenopathy in this patient.

4. DISCUSSION

Toxoplasmosis is a parasitic infection caused by *Toxoplasma gondii*, which can manifest in various clinical forms, ranging from asymptomatic to severe, especially in immunocompromised individuals. Serological analysis, histopathological examination, and immunohistochemical testing of excised lymph nodes can provide valuable insights into the lymphadenopathy observed in infected patients (Sharifi et al., 2019). In this case, the lymph node analysis revealed several features consistent with a reactive process due to toxoplasmosis. The lymph node maintained its structural integrity, which is typical of reactive conditions, as opposed to malignant processes that often disrupt normal architecture (Obiorah & Okoro, 2014). Additionally, the intact capsule and peripheral collagen tissue suggest a non-neoplastic process, unlike cancerous conditions that tend to show invasive characteristics (Obiorah & Okoro, 2014).

Immunohistochemical analysis further complemented the histopathological findings by identifying specific cell markers, indicating that the immune response involves a strong humoral component (Mercadante & Tadi, 2024). T-cell marker expression demonstrated that T-cells actively participated in the immune response. The absence of Bcl-2 in the germinal centers, indicating normal apoptotic processes, contrasted with neoplastic conditions, where Bcl-2 is frequently overexpressed to inhibit apoptosis (Qian et al., 2022). The weak positivity for Ki-67, a proliferation marker, suggested moderate cell proliferation, which is characteristic of reactive lymph nodes responding to infection. Furthermore, the immunohistochemical negativity for CD15 and positivity for CD30 in activated hyperplastic lymphocytes supported a reactive rather than neoplastic process (Obiorah & Okoro, 2014).

In some cases, such as this one, surgical extirpation of the lymph node may be necessary to exclude malignancy, especially when there are concerns from parents regarding the potential future risk of cancer (Obiorah & Okoro, 2014).

5. CONCLUSION

In conclusion, this paper underscores the importance for medical professionals to consider toxoplasmosis as a potential cause of lymphadenopathy in older children. The presented case of a 13-year-old child with painless lymph node enlargement and positive serological tests for toxoplasmosis highlights the clinical relevance of this parasitic infection. Pathohistological analysis confirmed the diagnosis, excluding malignancy, and identified a recent infection based on low IgG antibody avidity. The findings emphasize the need for heightened awareness and consideration of toxoplasmosis in differential diagnoses, especially in children with frequent exposure to domestic cats. Further research is warranted to explore the implications of prolonged exposure to *Toxoplasma gondii* on the severity of the disease.

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