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# The influence of age on a clinical presentation of *Toxocara spp.* infection in children

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## Abstract

Toxocariasis is a helminthozoonosis due to the infestation of humans by roundworms, *Toxocara spp.* Actual informations indicate it the most common worm infection in many countries, typically connected with rural areas. The authors analyzed the documentation of 84 children with positive serology to this worm. An individual record was made and following data were restricted: anamnesis data, clinical symptoms, epidemiological data, eosinophils number, level of immunoglobulins G and E. The highest *Toxocara spp*. seropositivity frequency was found in the schoolchildren aged 7-10. The most frequent clinical findings in children infected *Toxocara spp*. were lymphadenopathy, hepatomegaly, arthralgia and arthritis. 15.5% of seropositive patients presented non-specific symptoms originating from the central nervous system: headaches, sleep and behavioural disorders, and hyperactivity. The mean eosinophilia in the peripheral blood was detected in the youngest children: 4,023 cell/µl, which is 15.55 times more than the limit value. Hyperimmunoglobulinemia E was detected in all age groups, and the youngest children presented a serum concentration of IgE that was 16.47 times higher than the limit value.

**Conclusions**: 1. *Toxocara spp*. infection is detected in children at every age, but the most specific age group are schoolchildren, representing 38% of positive individuals. 2. The clinical spectrum of toxocariasis reflects various manifestations depending on the internal organs infected by the migrating worms and the intensity of infection. 3. Eosinophilia seems to be a good marker of infection in young children who have a more symptomatic course of the disease. 4. Hyperimmunoglobulinemia IgE can be the important element which distinguishes between current and past *Toxocara* infection, but its meaning is not connected with the age of infected children

## Key words

*Toxocara*, children, clinical presentation

**The influence of age on a clinical presentation of *Toxocara sp.* infection in children.** Human toxocariasis is a helminthozoonosis due to infestation of humans by the roundworms *Toxocara (T.) canis* and *T. cati* [1]. The disease was first described in the 1950s and for many years was regarded as uncommon in childhood. Current data indicate that toxocariasis is the most common worm infection in many countries and that its global importance may be greatly underestimated. Seroprevalence surveys in Western countries varied from 2-5% of healthy adults in urban areas to 14 or 20-37% in rural areas. In tropical countries, the seroprevalence of *Toxocara sp*. was higher (e.g. 86% in India) [2].

Human infection occurs through accidental ingestion of embryonated eggs of the parasite found in contaminated soil. The eggs hatch in the stomach and infective larvae migrate to a wide variety of tissues, causing a local inflammatory and allergic reaction in different organs (eyes, lungs, liver, and brain) [3].

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Toxocariasis occurs in 5 forms: systemic (visceral larvae migrans syndrome – VLM), ocular (ocular larvae migrans syndrome – OLM), neurological (NLM – neurological larvae migrans syndrome), covert, and asymptomatic. Classic VLM is characterized by hepatosplenomegaly, lung involvement, high eosinophilia and hyperimmunoglobulinemia IgE. OLM is a localized eye infection which may cause severe inflammation and progressive ocular damage, leading to retinal detachment, cataract formation, endophthalmitis, strabismus and blindness [4]. The NLM form is usually asymptomatic, although there may be symptoms ranging from minor neurological deficiencies to eosinophilic menigoencephalitis [5]. The covert form is connected with non-specific symptoms produced by the stimulation of a parasite antigen on the human immune system. These symptoms are: lymphadenopathy, dermatological disorders, arthralgia, and asthma. The asymptomatic form occurs when eosinophilia and *Toxocara* antibodies are accidentally detected in the patient without typical symptoms [6].

Children are the main infected group. Behaviours such as geophagia, poor personal hygiene and lack of parental supervision, as well as close contact with young dogs, increases the risk of infection [7]. The form of infection depends on the intensity of the infestation, the larva's'

localization, reinfestation, and the efficiency of the host's immune system. The goal of this study was to determine the connection between age and the clinical presentation of toxocariasis.

## MATERIAL AND METHODS

The study was carried out from August 2009 - April 2011 among children hospitalized in the Department of Infectious Diseases and Child Neurology at the University of Medical Sciences in Poznań. The children were 1-18 years old (mean 8.04). For the analysis, the patients were divided into 4 groups according to the typical, paediatric classification of age developmental periods made by Krawczyński [8]. For the statistical analysis, the group of school-age boys and girls was divided into 2 subgroup: 1) patients aged 7-10 years; 2) teenagers 11-15 years old.

Individual records were made for each child, **tracing the following data was registered:** anamnesis data, clinical symptoms (bronchospasm, recurrent bronchitis, hepato- and splenomegaly, abdominal pain, strabismus, visual loss, convulsions, headaches, and other signs of central nervous system involvement, urticaria, arthralgia), epidemiological data (age, gender), eosinophils number, level of immunoglobulin's G (IgG) and E (IgE). All children were examined by a paediatrician to detect the physical symptoms of infection. Ophthalmoscopies were performed for all patients.

For haematological and immunological tests, blood was collected in special tubes with and without EDTA, and stored at -20 °C until analyzed. The analysis was carried out using the Sysmex XT2000i. Automated Haematology Systems used fluorescent flow cytometry and hydrodynamic focusing technologies. The haemogram included: a leukocytes count and leukocyte differential formula. Eosinophilia was defined as an absolute eosinophils count of more that 600 cell/μL for children aged 0-15, and 500 cell/μL for children aged 16-18 [6].

The level of G class immunoglobulin was measured using the immunofelometric technique. Based on information provided by the producer, the upper limits for each age group were: 1,360 mg/dL for children aged 0-3 years, 1,410 mg/dL for children aged 4-6, 1,510 mg/dL for 7-15, and 1,610 mg/dL for those aged 16-18.

Total immunoglobulin E class concentration was measured using the immunoenzymatic method. The age limits for each group were: 40 μg/mL for 0-3 year-old-patients; 60μg/mL for children 4-6 years old; 70μg/mL for 7-15 and 63.6μg/mL for 16-18.

Anti-*Toxocara* IgG antibodies were detected by the ELISA –IgG test using a excretory/secretory (E/S) antigen derived from second-stage larvae. The cut off was 11 IU/mL.

## RESULTS

A total of 84 children were positive for *Toxocara sp.*: 37 girls and 47 boys. The number of children in each age category is shown in the first diagram. The highest seropositivity frequency was found in the 7-10 year-old group, representing 29% of positive children. This was followed by those aged 0-3 and 4-6 years old, with 21% and 23%, respectively. The lowest seropositivity was observed in the children older than 10 years (Fig. 1).

The most frequent clinical findings in children infected with *Toxocara sp.* were lymphadenopathy (37%), hepatomegaly (18%), arthalgia and arthritis (17%). 15.5% of the seropositive patients presented non-specific symptoms originating from the central nervous system: headaches, sleep and behavioural disorders, and hyperactivity. Ocular infection with retinal granulomatous lesions were only detected in 3.6%, similarlto pulmonary involvement (4.89%) (Fig. 2).

**Table 1.** Eosinophila in the age subgroups of children infected by *Toxocara spp.*

| Age subgroup (years) | Absolute eosinophils count (cell/μL) | Mean eosinophilia (cell/μL) | Mean eosinophilia as a factor of the absolute eosinophils count |
|---|---|---|---|
| **0-3** | 600 | 4023 | 6.70 |
| **4-6** | 600 | 596 | 0.99 |
| **7-10** | 600 | 534 | 0.89 |
| **11-15** | 600 | 294 | 0.49 |
| **16-18** | 400 | 263 | 0.65 |

Analysis of the connection between the frequency of clinical symptoms and the age of patients was not statistically significant (Fig. 3).

Average eosinophilia in peripheral blood was detected in the youngest children aged 0-3: 4,023 cell/μL, which was 6.7 times more than the limit value. In patients more than 3 years old, the number of mean peripheral blood eosinophils was estimated at 596 cell/μL (0.99 times) in children aged 4-6 years, and 477 cells/μL (0.76 times) in the 7-15 years old subgroups. Teenagers aged 16-18 also did not show peripheral blood eosinophilia (Table 1). The relation between the number of eosinophils and seropositivity frequencies was statistically significant (Fig. 4).

Hyperimmunoglobulinemia IgE was detected in all age groups of children with *Toxocara spp.* In children 0-3 years old, the mean serum concentration of IgE was 659 μg/dL (16.47 times higher than the limit value). In patients aged 4-6 years, it was 543μg/dL (9.05 times), and in those aged 7-15 years – 606 μg/dL (8.65 times%). However, in the teenagers group, 16-18 years old, the mean level of IgE was 150 μg/dL (2.36 times) (Table 2). The connection between the mean concentration of IgE and the children's age was not statistically significant (Fig. 5).

Hyperimmunoglobulinemia IgG was not detected in any subgroup of children infected by *Toxocara spp.* In children aged 0-3 years, the mean serum concentration of IgG was 1,151 μg/dL (0.85 of the limit value). In patients aged 4-6

**Table 2.** Mean immunoglobulin E class concentration in the children with *Toxocara spp.* infection

| Age subgroup (years) | Immunoglobulin E class concentration –cut off point (ug/L) | Mean immunoglobulin E class concentration (μg/mL) | Mean hyperimmuno-globulinemia as a factor of the limit value |
|---|---|---|---|
| **0-3** | 40 | 659 | 16.47 |
| **4-6** | 60 | 543 | 9.05 |
| **7-10** | 90 | 732 | 8.13 |
| **11-15** | 90 | 199 | 2.21 |
| **16-18** | 63.6 | 150 | 2.36 |

years, it was 1,083 μg/dL (0.77 of the limit), and in those aged 7-10 – 1,180 μg/dL (0.78). In the group of teenagers aged 16-18, the mean IgG level was 1,131 μg/dL (0.71), and in patients aged 11-15 years – 1,116 μg/dL (0.73) (Table 3). The connection between the mean concentration of IgG and age of the observed children was not statistically significant (Fig. 6).

**Table 3.** Mean immunoglobulin G class concentration in children with *Toxocara spp.* infection

| Age subgroup (years) | Immunoglobulin G class concentration –cut off point (ug/mL) | Mean immunoglobulin G class concentration (μg/mL) | Mean immunoglobulin G concentration as a factor of the limit value |
|---|---|---|---|
| **0-3** | 1360 | 1151 | 0.85 |
| **4-6** | 1410 | 1083 | 0.77 |
| **7-10** | 1510 | 1180 | 0.78 |
| **11-15** | 1510 | 1116 | 0.73 |
| **16-18** | 1600 | 1131 | 0.71 |

## DISCUSSION

In 1952, Beaver identified the *T. canis* larva in the liver of one of his patients and subsequently was able to reproduce the infection in an experimental animal. He introduced the term 'visceral larva migrans syndrome' to describe the clinical manifestations of larval migration in a human body. The syndrome was characterized by eosinophilia, leukocytosis, hepatomegaly, respiratory symptoms, and pulmonary infiltration in young patients with geophagia [9].

In actual fact, toxocariasis is considered a zoonosis of wide geographic distribution occurring in developed and undeveloped countries. In Poland, the number of new diagnosed infections has also increases successively. A nonohomogenous clinical picture leads to many difficulties in diagnostic procedure, and often induces doctors to continue searching for other pathologies, despite a positive serological test.

In many countries, the diagnosis of *Toxocara spp.* infection is based on serological surveys with banked sera that detect specific antibodies. The enzyme immunoassay (EIA) using *Toxocara* excretory-secretory antigen from infective-stage larvae is the most useful test. Commercial methods detect total anti-*Toxocara* immunoglobulin class G. The assay detects infections caused by both *T. canis and T. cati* [2, 10]. The sensivity and specificity of the *Toxocara* EIA are estimated at 78% and 92%, respectively, at a titer of 1:32 [10]. EIA sensivity is lowered by the stadia specificity and antygens' variability. Anti-*Toxocara* antibodies detected in the host can be an indirect marker of parasites presence. Their high levels can be found in the blood for 2-3 years after their elimination.

*Toxocara spp.* infection is detected in children at every age, but many studies indicate schoolchildren as the most typical age group [13]. The presented analysis confirms this observation: the highest seropositivity frequency was found in the 7-15 year-old subgroup, representing 38% of positive individuals. This was followed by individuals aged 4-6 years and 0-3 years, with 23% and 21% seropositivity, respectively. [12].

The association between gender and positive serology for *Toxocara* indicates that the male children might be at greater risk for toxocariasis. Several studies have shown a higher frequency of *Toxocara* infection in boys, which may derive from differences in play and social behaviour [1].

The presence of signs and symptoms associated with positive serology indicates a *Toxocara* infection in paediatric patients, as reported by many authors [1, 3]. In the presented study, the most frequent symptoms were lymphadenopathy, hepatomegaly and arthritis, although their frequency was not significant. Many authors have observed that the evidences of clinical signs or symptoms suggestive of *Toxocara* infection in different child populations are not specific. The clinical spectrum of toxocariasis reflects various manifestations, depending on which internal organs are infected by the migrating worms, and on the intensity of infection [11, 12]

Toxocariasis is one of the causes of eosinophilia in peripheral blood and causes eosinophilic infiltration in internal organs. The eosinophilia measured in peripheral blood is proportional to tissue eosinophilia, where there is local reaction to the *Toxocara* larva, or the antigens remain in the tissue following the larval migration. Positive cases evidence both the activity of the infection and the antibody response. Extended studies on the prevalence and clinical characteristics of toxocariasis are rare [13]. In the presented study, severe eosinophilia was detected in children aged 0-3; the subgroups of children aged 4-19 did not present an increased number of eosinophils. Eosinophilia seems to be a good marker of infection in young children, who have a more symptomatic course of the disease. Older children presented 'covert' toxocariasis with an unspecified mean number of eosinophils [1, 14].

In the serum an increase in the concentration of total IgE can be found in patients with atopic diseases, parasite infections, and congenital immunodeficiency. Induced by the parasite, hyperimmunoglobulinemia IgE is the effect of lymphocyte B polyclonal stimulation and has a protective function [15]. This parameter seems to have the most significant association between signs/symptoms and positive *Toxocara* serology. Similar to peripheral blood eosinophilia, hyperimmunoglobulinemia IgE is more visible in young children than in teenagers [16].

The level of immunoglobulin IgG was not significant for *Toxocara* infection in the presented analysis [17].

Toxocariasis is a cosmopolitan zoonosis and reliable, highly sensitive and specific assays for diagnosis and therapeutic evaluation are required in public health programs. The clinical symptoms vary as a consequence of larvae migration, ranging from asymptomatic forms to those with severe organ injuries. In the absence of parasitological evidence of infection, biochemical methods play a relevant role in the diagnosis of toxocariasis. In the presented study it was found that an elevated concentration of IgE is the most indicative of active toxocariasis. Therefore, immunologic testing should be accompanied by the determination of serum total IgE.

Clinical findings which reveal hyperimmunoglobulinemia IgE can be an important element which distinguishes between current and past *Toxocara* infection. The significance of IgE is not related to the age of infected children.

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