Larval toxocariasis and its clinical manifestation in childhood in the Slovak Republic

J. Kinčeková*, K. Reiterová and P. Dubinský

Parasitological Institute of the Slovak Academy of Sciences,
Hlinkova 3, 040 01 Košice, Slovak Republic

Abstract

Results are presented of 90 children aged 1–15 years hospitalized with toxocariasis. Blood count analysis and laboratory examination were done by routine clinical laboratory methods. Anti-*Toxocara* antibodies were detected in the serum of patients using an ELISA method. Demographic analysis of the children's families exposed to the risk of disease allowed estimation of age-specific rates for clinical toxocariasis. The probability of toxocaral infection and the intensity of its clinical manifestations in children are determined by the epidemiology of this zoonosis and by the risk factors in the family. The presence of high titres of specific IgG antibodies in all age categories correlates with the clinical manifestations of toxocariasis. The highest admission rate is in the age categories of 3–5 years (43.3%) and 6–10 years (36.7%). Laboratory findings show that the most conspicuous changes occur in the age category 1–5 years. The high percentage of seropositive dog-keeping and puppy-breeding families and the possibility of infection with repeated doses of larvae stimulate eosinophilia, which prevails in children under the age of five years. We present the percentage of patients whose parameters showed deviations from the reference values for a particular age category. Analyses of laboratory indices and of clinical manifestations will contribute to the accuracy of diagnosis and effectiveness of treatment of this disease.

Introduction

The understanding of the larval toxocariasis epidemiology is a key to the diagnosis, therapy and prevention of this disease, since children are infected in the environment contaminated with *Toxocara* eggs. The eggs make their way into the environment in faeces of definitive hosts, namely dogs (*Toxocara canis*) and cats (*T. cati*). Most cases of severe visceral larva migrans are reported in children aged 18 months to 3–4 years (Preiss, 1982; Schantz, 1989). In these children, the disease is clinically manifested especially after infection with a large number of eggs. Older children and adults, with good hygiene, when exposed to the same environment either avoid the infection or ingest a lower dose of eggs and more frequently develop ocular toxocariasis and moderate symptoms of visceral larva migrans (Glickman & Schantz, 1981).

The clinical form of toxocariasis in childhood is associated with a long-term repeated contact with the environment and with habits such as geophagy and pica. The main risk factors in a family include the keeping of dogs or cats or breeding of puppies (Schantz, 1989; Kinčeková *et al*., 1996). Persistent antibodies after primary infections may also be the cause of a high seroprevalence in older children (Kimmig *et al*., 1991). Data of several authors (Schantz, 1989; Logar *et al*., 1993; Gillespie *et al*., 1993) suggest that the most frequent systemic symptoms include:

1. Respiratory system disorders, which range in incidence between 20 and 40% and include cough, rhonchus, dyspnoea, asthmatic bronchitis and pneumonia. Also, cytological examinations of bronchoalveolar lavage showed oesinophilia up to 64% (Roig *et al*., 1992).

* Fax: 421 95 63 31414
E-mail: pausav@saske.sk

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2. Gastrointestinal tract disorders, which are characterized by up to 87% hepatomegaly, while the levels of transaminases are moderately increased (Ishibashi *et al*., 1992). Even with no increase in transaminases, the alkaline phosphatase activity was elevated in 13% with cholesterol and creatinine levels in up to 30% of the hospitalized children. The clinical picture very often showed abdominal pains (72.1%), although hepatomegaly was recorded in only 11.6% of patients (Kinčeková *et al*., 1996).

Children above six years of age are more frequently diagnosed with the ocular form of infection, while other symptoms (Ellis *et al*., 1986) are usually absent. Lesions are unilateral in almost every case, with bilateral lesions being reported in only 3% of patients (Kerr-Muir, 1994).

This paper reports on the epidemiological and laboratory findings in 90 children of different ages hospitalized with larval toxocariasis in Košice, Slovak Republic.

Materials and methods

We studied 90 children aged 1–15 years, admitted to the Children's Hospital in Košice, East Slovakia region, with larval toxocariasis that was confirmed serologically. Patients were allocated into four categories, according to their reference values. Their haematological, biochemical and immunological parameters, together with their clinical symptoms were studied during the hospitalization period of 10–14 days.

Blood count analyses and laboratory examinations of hospitalized patients were done by routine clinical laboratory methods. Normal results were considered those not exceeding the values given for children of the age category under 5 and under 15 years (Sakalova & Lipšic, 1995).

Anti-*Toxocara* antibodies were determined in the serum of patients using an ELISA procedure as previously described by Mančal (1987). Microtitre plates were coated overnight at 4°C with *Toxocara canis* excretory-secretory larval antigen containing $1\,\mu g\,ml^{-1}$ protein diluted with carbonate buffer pH 9.6. The antigen was prepared by the method of de Savigny (1975).

Results

The median age of the group of 90 patients was 5.86 years. The children originated largely from villages and

Table 1. Epidemiological characteristics of children hospitalized with clinical toxocariasis.

		Age in years									
		1–2		3–5		6–10		11–15		Total	
Variable	Group	n	%	n	%	n	%	n	%	n	%
No. patients examined		9	10	39	43.3	33	36.7	9	10	90	100
Sex	Males	7	77.8	23	58.9	16	48.5	2	22.2	48	53.3
	Females	2	22.2	16	41.0	17	51.5	7	77.8	42	46.7
Location	Village	8	88.9	31	79.5	28	84.8	8	88.9	75	83.3
	Town	1	11.1	8	20.5	5	15.2	1	11.1	15	16.7
Dog, cat in the family		7	77.8	30	76.9	26	78.8	8	88.9	71	78.9
Puppy breeding		2	22.2	13	33.3	6	18.2	4	44.4	25	27.8
Geophagy		7	77.8	24	61.5	10	30.3	1	11.1	42	46.7

n = number examined.

Table 2. Haematological parameters in children with clinical toxocariasis.

Age group (years)	Variable	Erythrocytes^{+}	Haemoglobin^{++}	Leucocytes†	Eosinophils‡	ESR$^{\#}$
1–2	No. examined	9	9	9	9	9
	Increased, suppressed*	3*	5*	5	8	5
	%	33.3*	55.5*	55.5	88.8	55.5
	Mean values ± S.D.	2.84 ± 0.11*	100.2 ± 9.8*	16.72 ± 6.06	2.15 ± 2.15	19 ± 8
3–5	No. examined	39	39	39	39	37
	Increased, suppressed*	6*	16*	19	36	30
	%	15.4*	41.0*	48.7	92.3	81.1
	Mean values ± S.D.	3.23 ± 0.21*	111.4 ± 8.7*	12.71 ± 1.23	1.36 ± 1.34	23 ± 15
6–10	No. examined	33	33	33	33	29
	Increased, suppressed*	0	11*	7	20	17
	%	0	33.3*	21.2	60.6	58.6
	Mean values ± S.D.	–	113.1 ± 6.4*	12.1 ± 1.76	0.55 ± 0.19	20 ± 12
11–15	No. examined	9	9	9	9	9
	Increased, suppressed*	0	0	2	5	4
	%	0	0	22.2	55.5	44.4
	Mean values ± S.D.	–	–	11.35	0.819 ± 0.262	21 ± 11

SI Reference intervals and units: $^{+}3.5–4.5\times10^{12}\,l^{-1}$ for age category 1–5; $4.5–5.5\times10^{12}\,l^{-1}$ for age category 6–15; $^{++}120–140\,g\,l^{-1}$ for age category 1–5; $140–180\,g\,l^{-1}$ for age category 6–15; †$4–10\times10^{9}\,l^{-1}$; ‡$0.1–2.5\times10^{9}\,l^{-1}$; $^{\#}0–10\,mm\,h^{-1}$. ESR, erythrocyte sedimentation rate.

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Table 3. Clinical symptoms of toxocariasis in hospitalized children.

	Age in years							
	1–2		3–5		6–10		11–15	
Symptoms	n=9	%	n=39	%	n=33	%	n=9	%
Fever	5	55.5	25	64.1	12	36.4	2	22.2
Abdominal pain	8	88.9	31	79.5	23	69.7	4	44.4
Bronchitis	6	66.7	17	43.6	21	63.6	5	55.5
Pharyngitis	5	55.5	8	20.5	8	24.2	3	33.3
Lymphadenopathy	4	44.4	10	25.6	11	33.3	3	33.3
Hepatosplenomegaly	0	–	6	15.6	8	24.2	1	11.1
Pericarditis	0	–	6	15.6	5	15.1	0	–
Arthritis	0	–	3	7.7	0	–	0	–
Iridocyclitis	0	–	0	–	11	33.3	4	44.4
Amblyopia	0	–	0	–	2	6.1	2	22.2
Macular lesion	0	–	0	–	2	6.1	0	–

n=number examined.

from dog- or cat-keeping families or puppy-breeding families. Geophagy was most frequently recorded in the 1–2 years old group (table 1).

Distinct haematological values were most frequently observed in the 1–2 years age group (table 2) where the most common clinical symptoms (table 3) were abdominal pain, bronchitis, pharyngitis and lymphadenopathy. Values of IgE were elevated in all children and IgM values also increased in up to 50% of children (fig. 1). Very high titres (1:3200) of specific IgG antibodies predominated (fig. 2).

As in all patients with larval toxocariasis, eosinophilia was also most frequent in the 3–5 years old group of children (table 2). Characteristic clinical symptoms included abdominal pain often accompanied by anorexia, vomiting and hepatosplenomegaly. These patients also showed symptoms of the locomotor and cardiovascular systems, manifested by systolic and diastolic murmurs, which were absent in younger children. Pericarditis was accompanied by increased levels of cholesterol (table 4). High values of total IgE were recorded in this group (fig. 1). Elevated values of total IgM were observed, which indicates that this disease was diagnosed at its early stage and very high titres of specific IgG antibodies were recorded (fig. 2).

Eosinophilia and increased erythrocyte sedimentation rate were frequent in the 6–10 years old group (table 2) with the most common clinical symptoms being abdominal pains and bronchitis. Less frequent were fever and pharyngitis. For the first time this age category exhibited symptoms of ocular disorders, such as iridocyclitis: amblyopia and deteriorated vision and, as in younger children, the total IgE and IgM values had increased. High titres of IgG anti-*Toxocara* antibodies predominated.

The clinical symptoms elicited by larval toxocariasis in the 11–15 years old group of patients were similar to those in the 6–10 years old group. Ocular symptoms were most common and granulomata of posterior pole with calcifications in four cases was also confirmed by X-ray and computer tomography (CT) examinations.

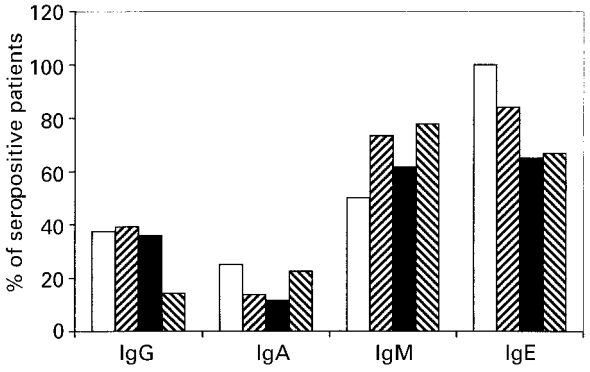

Fig. 1. Comparison of patients with toxocariasis, showing increased values of total immunoglobulins. Age categories (in years): □, 1–2; ▨, 3–5; ■, 6–10; ▧, 11–15.

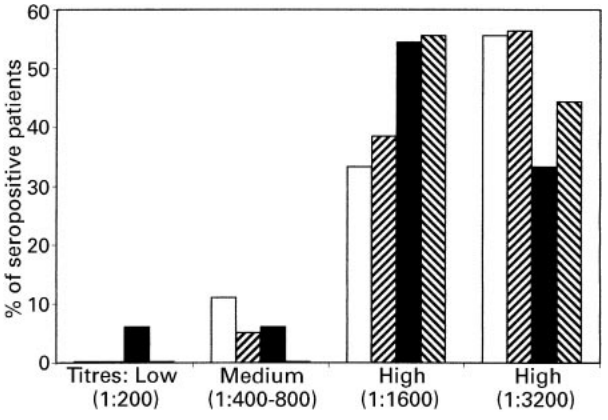

Fig. 2. Titres of anti-*Toxocara* IgG antibodies in children with clinical toxocariasis. Age categories (in years): □, 1–2; ▨, 3–5; ■, 6–10; ▧, 11–15.

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Table 4. Biochemical values in the blood sera of children with clinical toxocariasis.

Age group (years)	Variable	Cholesterol*	Urea**	Creatinine^{+}	C-reactive protein^{++}	AST‡	ALT†	ALP$^{\#}$
1–2	No. examined	8	9	6	8	8	8	9
	Increased values	2	1	0	2	0	0	0
	%	25	11.1	0	25	0	0	0
	Mean values ± S.D.	5.8	–	–	21.5	–	–	–
3–5	No. examined	37	37	37	31	38	38	31
	Increased values	4	4	3	2	3	1	4
	%	10.8	10.8	8.1	6.4	7.9	2.6	12.9
	Mean values ± S.D.	5.85 ± 0.5	6.8 ± 1.3	97.37 ± 2.1	51.3	0.9 ± 0.05	–	8.88 ± 2.29
6–10	No. examined	31	30	29	30	31	31	27
	Increased values	4	0	2	0	0	0	0
	%	12.9	0	6.9	0	0	0	0
	Mean values ± S.D.	6.61 ± 1.12	–	99.6	–	–	–	–
11–15	No. examined	7	7	7	7	7	7	6
	Increased values	0	0	0	0	0	0	1
	%	0	0	0	0	0	0	16.7
	Mean values ± S.D.	–	–	–	–	–	–	–

SI reference intervals and units: *2.6–5.8 mmol l^{-1}; **0–7 mmol l^{-1}; $^{+}$21–97 μmol l^{-1}; $^{++}$0–10 mg l^{-1}; ‡0.16–0.83 μkat l^{-1}; †0.15–0.72 μkat l^{-1}; $^{\#}$1.2–6.3 μkat l^{-1}.
AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase.

Discussion

Most cases of human toxocaral infection take a latent course. This course is often asymptomatic and patients either have no objective or subjective symptoms or symptoms are non-specific and often attributed to other illnesses. In any case, antibodies to *Toxocara* are being produced. An analogy is reported to exist between toxocaral infections and poliomyelitis (Ellis *et al*., 1986), although only a small portion of seropositive individuals develop a severe form of the disease.

Clinical diagnosis, based only on the presence of clinical symptoms in the group of 1–2-year-old patients, is not reliable enough. All infected children showed the predominance of non-specific symptoms and frequent disorders of the respiratory system, which may result in the narrowing of the spectrum in the differential diagnosis of respiratory infections. Acute bronchitis in fact occurs in 70–90%, primarily of viral aetiology (Karalus *et al*., 1995; Kinčeková *et al*., 1996). Data of Schantz (1989), Logar *et al.* (1993) and Kimmig *et al.* (1991) suggest that the most frequent symptoms are those of the respiratory tract, with incidence values of between 20 and 40% being recorded, including cough, hoarseness, rale, dyspnoea, asthmatic bronchitis and pneumonia. X-rays usually confirm the presence of lung infiltrates. The lung changes may be temporary in the sense of Löffler's infiltrates but may persist for months. Buijs *et al.* (1994), suggested that toxocariasis in pre-school children, in addition to other environmental factors, may contribute to the manifestation of allergic asthma and eczema in allergy-predisposed children. In lower respiratory tract infections and pneumonia, almost all groups of pathogens are equally present, whilst in the aetiology of the acute exacerbations of chronic bronchitis, bacterial pathogens predominate (de Vliegera *et al*., 1992; Notario *et al*., 1994). A suitable algorithm for a correct diagnosis of toxocariasis is a laboratory examination of haematological parameters, with special emphasis on the examination of eosinophils, sedimentation and levels of total immunoglobulins. Changes in these parameters are generally observed in children with acute infections or with frequent protracted infections (Taylor *et al*., 1988). The spectrum of clinical symptoms in children under 5 years is characterized by infections of the gastrointestinal tract. Typical symptoms include abdominal pain, vomiting and anorexia. Hepatomegaly can be detected in up to 87% of cases based on the presence of eosinophilic granulomata in samples taken by ultrasonographic controlled aspiration biopsies (Ishibashi *et al*., 1992). Biochemical and haematological changes are important in children under 5 years, while in older patients these changes are minimal.

Symptoms in the locomotor system of patients with toxocariasis have been reported by several authors, including Van Linthout *et al.* (1990), who described coxarthropathy in a young girl, whereas Le Luyer *et al.* (1990) found the joints to be affected. Sensitivity and specificity of diagnostic methods vary within a relatively wide range, largely depending on the localization of the *Toxocara* larvae.

Ocular symptoms are due to damage of tissues by *Toxocara* larvae or by the immune response to the presence of larvae and their products in the eye. Olson (1976) showed that in experimental infections in mice, larvae are attracted to the eye region and a single larva is sufficient to trigger severe ocular symptoms. Eosinophilia was absent in mice despite the presence of 2–3 larvae in the eye (Ghafoor *et al*., 1984). Infections with lower doses of *Toxocara* are likely to result in ocular toxocariasis (Glickman & Schantz, 1981), especially in children aged 6–8 years and in adults. Other organ symptoms are generally lacking (Ellis *et al*., 1986), and lesions are unilateral in almost every case. Ocular infections in children take a more severe course than those in adults, which can be attributed to a less well developed immune system and higher levels of infection, resulting in

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endophthalmitis, as larvae are free to migrate and elicit heavy infections (Végh & Danka, 1987). These authors also report a close relationship between the characteristics of *Toxocara*-induced ocular disorders and host age, namely diffuse endophthalmitis occurs mostly in the age category 2–9 years, retinal granuloma in the 6–14 years old category and pars planitis in the 6–40 years old category. The most common symptoms include deterioration of vision, strabismus and amblyopia (Gillespie *et al*., 1993). A frequent symptom detected by opthalmologists is leucorrhea, i.e. a white mass observable through the pupil (Buijs *et al*., 1994). CT and X-ray examinations showed the presence of calcifications (Schönherr & Bialasiewicz, 1990). The ocular form of toxocariasis in a CT image is imitated as diffuse endopthalmitis or pseudoglioma (Edwards & Pordell, 1985). The absence of eosinophilia, however, does not rule out the presence of toxocariasis. Eosinophilia also occurs in only 5–10% of cases with ocular toxocariasis (Gillespie *et al*., 1993). Other methodologies such as ultrasonography and magnetic nuclear resonance may well contribute to the diagnosis of toxocariasis (Rüttinger & Hadaidi, 1991). Differential diagnosis may also employ a serological examination of endopthalmic fluid for the presence of specific antibodies to *Toxocara* (Petithory *et al*., 1993), although eosinophilia was absent.

From an analysis of the parameters used in the present study, clinicians should be able to more accurately diagnose toxocariasis and make its therapy more effective.

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