Risk Factors for Toxocaral Ocular Larva Migrans: A Case-Control Study

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Abstract: Twenty-four patients with serologically confirmed toxocaral ocular larva migrans (OLM) and 24 age- and sex-matched controls were the subjects of an epidemiologic study. Information on the exposure to dogs and other factors possibly associated with transmission of toxocariasis was obtained by contacting the parents of the subjects. The odds of having had a dog present in the household within the year previous to onset of illness were 3 to 1 for cases vs controls. An association of pups (<3 months) in the households of OLM patients within one year of onset was statistically significant ($P < .05$). Twenty-three of 24 OLM patients had had dogs in their homes some time before their illness, and the twenty-fourth patient had a history of geophagia, a behavioral pattern previously identified as a risk factor for toxocariasis. Exposure to cats and other animals in or outside the home did not differ for patients and controls. Infected dogs, especially pups, in the patients' homes were the most probable sources of infection for this group of OLM patients. (*Am J Public Health* 1980; 70:1269-1272.)

Introduction

Ocular larva migrans (OLM) is one of the clinical manifestations of human toxocariasis and is characterized by damage to the retina at the point of larval penetration that leads to total or partial loss of vision in the affected eye.[1, 2] Hundreds of cases have been reported from numerous countries,[3] and the disease probably occurs wherever *Toxocara canis* is present in dogs, i.e., throughout temperate and tropical areas. Although we do not know what proportion of human toxocaral infections involve ocular invasion, at least in the southern United States, OLM is not uncommon. For example, in a single group practice of ophthalmology in Georgia, 41 seropositive cases of OLM were diagnosed in an 18-month period.[4] That number represented 37 per cent of all retinal disease diagnoses in the pediatric portion of that practice.

An earlier study in the southern United States showed a statistically significant association with dogs, especially pups, in the home within one year before onset of the ocular illness.[5] This finding was considered preliminary, however, because the mean age of the patients was considerably lower than that of the controls. Pet ownership appears related to the age structure of the family, thereby introducing potential bias into the comparison of dog ownership for groups of different ages. We report here on a retrospective study of OLM patients and age- and sex-matched controls to determine the type of pet exposure and other risk factors associated with infection.

Materials and Methods

Patients and controls were selected from persons examined in a single group practice of ophthalmology in Atlanta, Georgia. The clinical characteristics and serologic results for these patients have been reported.[4] For the epidemiologic study, we selected 24 persons with clinically diagnosed OLM who had fundus lesions typical of those described as caused by *T. canis* invasion[4] and serum toxocaral enzyme-linked immunosorbent assay (ELISA) titers of $\geq 1:16$. An additional criterion for inclusion was that their first observed onset of ocular illness was within one year of examination. Controls were selected from a group of patients who had surgery for ocular conditions not caused by *Toxocara*[4] and whose serum ELISA titers were $\leq 1:4$. The age of each control was matched to that of an OLM patient as closely as possible. Age matching was possible within one year in 20 instances, within two years in three instances, and within four years for the oldest OLM patient (age 17 years).

The cooperation of the patients' parents in providing more complete medical histories was requested at the time of clinical examination. They were later contacted by telephone and asked a series of questions about medical history and exposure to animals and other environmental factors that might be associated with the risk of acquiring toxocariasis.

The toxocaral ELISAs were performed at the Parasitology Serology Laboratory, Center for Disease Control,

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according to the method described by Cypress *et al*,[6] and modified by Glickman *et al.*[7]

Statistical testing to determine factors associated with OLM was done by matched pair analysis of data obtained from patients and controls.[8]

Results

The patients and controls were closely matched for age, sex, race, and socioeconomic characteristics, with no statistically significant differences ($P > .05$ in every test) as shown in Table 1.

Twenty-three OLM patients had ocular lesions with no other current or previously reported signs of illness likely to have been associated with toxocaral infections. One patient and one control had been hospitalized with at least some signs compatible with the various manifestations of the toxocaral visceral larva migrans syndrome,[1, 2, 9] although in neither case had this condition been diagnosed, and both patients recovered completely.

According to the patients' parents, nine (38 per cent) OLM patients and two (8 per cent) controls were reported as having pica behavior (defined to the parent as the compulsive eating of nonfood items) before their current illnesses ($P > .05$).

Some measurements of dog exposure before onset of illness are shown in Table 2. Dogs had been present in 96 per cent of the homes of the OLM patients and in 54 per cent of the homes of controls at some time during the patients' lifetimes. Using cross product ratios, the odds of having a dog present in the household within the year previous to onset were 3 to 1 for cases vs controls. Dogs were present in the household within one year before illness in 92 per cent of the homes of the OLM patients and 33 percent of homes of the controls. When we considered only household exposure to pups (defined as ≤3 months of age) within one year of illness, 58 per cent of OLM patients but only 8 per cent of controls had such exposure. The odds of having had pups or a litter in the household within the previous year were 4.2 to 1 for cases vs controls. For the three situations—pet dogs in home before onset of ocular illness, pet dogs of any age in home within one year of onset, and pup in home within one year of onset—there were no pairs with "no" for cases and "yes" for controls, but 10, 14, and 12 pairs, respectively, with "yes" for cases and "no" for controls.

Among dog-owning families of both OLM patients and controls, there were no statistically significant differences ($P > .05$) in where the dogs were kept (outside or inside the house, or both). Nineteen (79 per cent) of OLM patients' families who owned dogs indicated that they consulted a veterinarian regularly for their pet's health care, as did nine (75 per cent) of the dog-owning control families. The other families who owned dogs either took their pets to a veterinarian for vaccinations only or not at all. Nine and six parents from the patient and control families, respectively, said that they were aware (before their child's illness) that some worm infections of dogs or cats could be transmitted to humans. Two parents from each group said that they learned this fact from their veterinarians, and the others said that they read about it in a newspaper or popular magazine.

TABLE 1—Comparison of Some Characteristics of 24 Toxocaral Ocular Larva Migrans Patients and Their Controls

Characteristics		Patients	Controls
Age at Examination	Mean	8.9 years	8.6 years
	Range	4–17 years	4–20 years
Sex	Male	16	16
	Female	8	8
Race	White	17	18
	Black	2	3
	Not determined	5	3
Residence location	Urban	15	12
	Rural	9	12
Hollingshead Index	Mean	47.1	45.2
	Range	18–77	11–70
Number of Members of Household	Mean	4.9	4.3
	Range	2–9	2–7

Cats were present in the homes of 11 (46 per cent) of the OLM patients and in 10 (42 per cent) of the homes of controls ($P > .05$). Exposure to various other types of animals was reported for 10 of the OLM patients and 10 of the controls.

Discussion

The results of this study confirm and strengthen the association of household dogs as a risk factor for human toxocariasis that was noted in a study in a different part of the southeastern United States.[5] Twenty-three of 24 OLM patients had had dogs in their homes before becoming ill. When only the presence of a pup (<3 months old) in the household within one year before illness was considered, the statistical association was also significant. The birth of a litter of pups or introduction of a pup into a household theoretically provides a greater risk for acquiring toxocariasis than exposure to older dogs because pups have a much higher infection rate than do older dogs.[10] Because of the efficiency of prenatal and neonatal transfer of larvae from infected bitches to pups, most if not all dogs are infected early in life.[11, 12] These worms start laying eggs and contaminating the environment by the time the pups are three weeks old. Dogs over six months of age are less likely to have patent intestinal infections.[10]

These results cannot be interpreted to mean that our patients' infections were first acquired the year before they began having ocular symptoms. It is not known whether larval invasion of the eye occurs immediately after infective eggs are ingested or after periods of months or even years.[9] The fact that most persons diagnosed as having OLM are older than those diagnosed as having the more common toxocaral visceral larva migrans (approximately eight years of age vs three years) and the lack of systemic signs of acute inflammation in OLM patients[2, 9] support the latter concept of pathogenesis. If many of our patients had a delayed ocular

TABLE 2—Comparison of Pet Dog Exposure of 24 Toxocaral Ocular Larva Migrans Patients and Their Controls

Exposure	Cases	Controls		Total	McNemar's Chi Square	P value
		Yes	No			
Pet dogs in home sometime before onset of ocular illness	Yes	13	10	23		
	No	0	1	1	8.10	.004
	TOTAL	13	11	24		
Pet dogs of any age in home within one year of onset	Yes	8	14	22		
	No	0	2	2	12.07	<.001
	TOTAL	8	16	24		
Pup in home within one year of onset	Yes	2	12	14		
	No	0	10	10	10.08	.002
	TOTAL	2	22	24		
Patient exposed to dogs other than in home	Yes	13	8	21		
	No	1	2	3	4.00	.045
	TOTAL	14	10	24		

invasion, recent histories of familial dog exposure may simply reflect continuation of previous pet-owning practices. In fact, all of the OLM patients in our series who owned dogs within a year before becoming ill had also owned other dogs before that time.

The only OLM patient in this series who had not had household exposure to dogs had a history of eating dirt. Studies in several parts of the United States have shown that 10 per cent to 32 per cent of soil samples collected from parks, playgrounds, and other public places are contaminated with *Toxocara* eggs;[13-15] and the child with geophagia is particularly prone to ingestion of eggs from any source.

The strong association between pet dogs and toxocaral infection demonstrated in this and another study in the southeastern United States [5] contrasts markedly with findings in London, England where less than 50 per cent of patients had a history of household or other close exposure to dogs. Woodruff suspected that most of these persons were exposed to *Toxocara* eggs in the soil in parks and other public places.[16]

The frequency of exposure to pet cats and miscellaneous animals (excluding dogs) did not differ significantly for patients and controls. Although *T. cati* transmitted from cats is believed to be capable of causing larva migrans for humans,[17] it has rarely been associated with human cases, and fewer of its eggs than those of *T. canis* are found in soil samples.[13]

As far as could be determined from our interviews, relatively few (31 per cent) of the parents of OLM patients and controls knew about the public health hazards posed by toxocariasis or other helminth infections of pet dogs and cats. Without such knowledge, pet owners are unprepared to take the measures necessary to minimize the risk of infection for family members. We believe that practicing veterinarians should warn pet owners of potential zoonotic risks and provide the necessary advice and chemotherapeutic intervention to minimize them.[10]

An important consideration in epidemiologic studies to determine risk factors is the availability of diagnostic methods to confirm that patients have the disease and to rule out the possibility that controls do. This is particularly true for infections such as human toxocariasis, which are thought to be often inapparent.[2, 9] Confirming the presence of larvae in specimens taken at biopsy is still the only basis for a definitive diagnosis; however, recently developed ELISA for toxocariasis[6] is a useful tool for epidemiologic studies. In tests of specimens from patients with clinical symptoms of toxocariasis, the diagnostic sensitivity of the assay ranged from 78 per cent and 90 per cent, and the specificity was about 90 per cent.[4, 7] The low level percentage of positive titers in the asymptomatic controls probably reflects the prevalence of subclinical infections. The ELISA involves larval stage antigens that do not cross react with antibodies stimulated by other helminth infections.[18, 19]

REFERENCES

1. Zinkham WH: Visceral larva migrans: A review and reassessment indicating two forms of clinical expression: Visceral and ocular. Am J Dis Child 1978; 132:627-633.
2. Glickman LT, Schantz PM, Cypess RH: Canine and human toxocariasis; Review of transmission, pathogenesis, and clinical disease. J Am Vet Med Assoc 1979; 175:1265-1269.
3. Brown DH: The geography of ocular *Toxocara canis*. Ann Ophthalmol 1974; 6:343-344.
4. Pollard ZF, Jarrett WH, Hagler WS, *et al:* ELISA for diagnosis of ocular toxocariasis. Ophthalmology 1979; 86:743-749.
5. Schantz PM, Meyer D, Glickman LT: Clinical, serologic, and epidemiologic characteristics of ocular toxocariasis. Am J Trop Med Hyg 1979; 28:24-28.
6. Cypess RH, Karol MH, Zidian JL, *et al:* Larva-specific antibodies in patients with visceral larva migrans. J Infect Dis 1977; 135:633-640.
7. Glickman LT, Schantz PM, Dombroske RL, *et al:* Evaluation of serodiagnostic tests for visceral larva migrans. Am J Trop Med Hyg 1978; 27:492-298.
8. Fleiss JL: Statistical methods for rates and proportions. New York: John Wiley and Sons, 1973, pp 73-77.
9. Schantz PM, Glickman LT: Toxocaral visceral larva migrans. N Engl J Med 1978; 298:436-439.
10. Schantz PM, Glickman LT: Canine and human toxocariasis: The public health problem and the veterinarian's role in prevention. J Am Vet Med Assoc 1979; 175:1270-1273.
11. Sprent JFA, English PB: The large roundworms of dogs and cats—A public health problem. Aust Vet J 1958; 41:161-171.
12. Stone WM, Giardeau MH: Transmammary passage of infective-stage nematode larvae. Vet Med 1967; 62:252-253.
13. Headlee WH: The epidemiology of human ascariasis in the met-

ropolitan area of New Orleans, Louisiana. Am J Hyg 1936; 24:479-487.
14. Dubin S, Segall S, Martindale J: Contamination of soil in two city parks with canine nematode ova including *Toxocara canis:* A preliminary study. Am J Public Health 1975; 65:1242-1245.
15. Dada BJO, Lindquist WD: Studies on flotation techniques for the recovery of helminth eggs from soil and the prevalence of eggs of *Toxocara* spp in some Kansas public places. J Am Vet Med Assoc 1979; 174:1208-1210.
16. Woodruff AW: *Toxocara canis* and other nematodes transmitted from dogs to man. Br Vet J 1975; 131:627-632.
17. Beaver PC: Zoonoses, with particular reference to parasites of veterinary importance, IN: Soulsby EJL (ed): Biology of Parasites. New York: Academic Press, 1966, pp 215-227.
18. Schantz PM, Glickman LT: Toxocariasis, IN: Immunoserology of Parasitic Diseases. Walls KW (ed). New York: Marcel Decker, Inc., (in press) 1980.
19. DeSavigny DH, Tizard IR: Toxocaral larva migrans: the use of larval secretory antigens in hemagglutination and soluble antigen fluorescent antibody tests. Trans Royal Soc Trop Med Hyg 1977; 71:501-507.

Infant Drugs Addicts: Report of a Case (Circa 1915)

"Textbooks teach us that the opiates are excreted through mother's milk. This is a fact long known, and in reading or studying this fact we have . . . retained it in our memory as a matter of course, just as we have done with many other facts that we have studied or read about. . . .

"The infant born of addicted parents is an unfortunate victim. . . .

"Another case of infantile addiction was treated at the Wills Mountain Sanatorium in Maryland. This child was sixteen months of age and had also become addicted through the mother's milk. In my case the child was not emaciated, but was pale and flabby looking. Its lips were almost colorless. The pupils upon the day of admission were pin point in size, and did not react to light. The child slept all afternoon and night. The next day it was doubled up in cramps and sweated profusely. It cried often and had to be laid on its abdomen to quiet it. I was forced to give it paregoric. The treatment was begun by allowing the mother to nurse the child but once a day, preferably at night. During the day the child was given the bottle. A mixture containing one minim of tincture of nux vomica and five minims of camphorated tincture of opium to the dram was administered to the baby three times a day. The child was under my treatment for four days. At the end of that time the child seemed more cheerful and suffered no more cramps. Castor oil, drams two, was also administered on the first and third nights. . . .

"These cases should sound a severe warning to mothers and to female addicts . . . . the public must be taught the evil effects of drug addiction. It is the duty of every physician to warn all addicts coming under his care of the serious effects that addiction may have upon their future and upon future generations."

—Lichtenstein, PM: Infant drug addicts. New York Medical Journal, 102: 906, 1915. [Dr. Lichtenstein worked in forensic medicine and with inmates of the city prison.] (Contributed by Jean Pakter, MD, Director, Bureau of Maternity Services and Family Planning, New York City; and Marvin Blumberg, MD, Director of Pediatrics, Jamaica Hospital, Queens, NY.)