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Toxocariasis and Ingestion of Raw Cow Liver in Patients with Eosinophilia

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Abstract: Ingestion of raw animal liver has been suggested as a possible mode of infection of human toxocariasis. We evaluated the relationship between toxocariasis and the ingestion of raw meat in patients with eosinophilia of unknown etiology. The study population consisted of 120 patients presenting with peripheral blood eosinophilia (> 500 cells/μl or > 10% of the white blood cell count). They were divided into 2 groups: 104 seropositive patients based on a *Toxocara* excretory-secretory IgG ELISA and 16 seronegative patients. While 25.0% of seronegative patients had a recent history of eating raw cow liver, 87.5% of seropositive patients had this history. Multivariate statistical analysis showed that a recent history of eating raw cow liver was related to an increased risk of toxocariasis. Collectively, it is proposed that raw cow liver is a significant infection source of toxocariasis in the patients with eosinophilia of unknown etiology.

Key words: *Toxocara canis*, toxocariasis, eosinophilia, raw cow liver

INTRODUCTION

Toxocara canis is a common round worm found in the small intestines of dogs; however, *T. canis* can also infect other animals. Infection of dogs as well as other animals takes place by ingestion of soil contaminated with eggs in dooryards and parks. The infected larvae reach the liver and are dormant in the liver parenchyme. They move slowly from place-to-place within the liver, or migrate to the lungs and other tissues, which is called as visceral larva migrans [1,2]. These encapsulated larvae in animal tissues do not grow into adult worms, but are capable of transmitting to other animals that eat the infected tissues harboring encapsulated larvae. This mode of transmission among carnivorous vertebrates has been established with experimental studies [1,3-5]. A large variety of non-canine animals can be infected with *T. canis*. Known paratenic hosts include mice, rats, chickens, pigeons, lambs, pigs, and cows. Animals are infected by ingestion of embryonated eggs in contaminated soil or of encapsulated larvae in the tissues of paratenic hosts.

Like animals, human infections may take place in 2 ways: 1) ingestion of embryonated eggs, and 2) transfer (ingestion) of encapsulated larvae of *T. canis* in the tissues of a paratenic host [2]. In certain ethnic groups, some adults tend to eat uncooked animal tissues which contain encapsulated infective larvae. After swallowing, the encapsulated larvae are liberated after hatching in the small intestine, penetrate the intestinal wall, get into the portal vein, and then reach the liver and lungs. They again become encapsulated and remain alive for a certain period. Uncooked livers of cow [3,6-8], pig [9], lamb [10], and chicken [11,12] have been reported as sources of human infections. However, epidemiologic data on the role of ingesting raw liver of animals in the transmission of *T. canis* from animals-to-humans is limited [8]. In order to evaluate the relationship between toxocariasis and the ingestion of raw meat, we conducted a prospective study.

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MATERIALS AND METHODS

Patients

Between March 2006 and April 2007, 146 patients registered in the allergic clinic in Samsung Medical Center, Sungkyunkwan University School of Medicine, for evaluation of eosinophilia of unknown etiology. Eosinophilia was defined as > 500 cells/μl in the peripheral blood or $\geq$ 10% of the total white blood cell count [13]. Among the 146 patients, 120 agreed to participate in this study. One interviewer gave the patients a questionnaire. We told the patients on the possibility of toxocariasis through ingestion of uncooked animal tissues or breeding dogs in the house or garden. The study protocol was approved by the In-

stitutional Review Board and we obtained an informed consent from each patient. There were 97 males and 23 females (age range, 21-76 yr; median age, 53 yr, mean age, 53.4 yr) enrolled in the study.

Questionnaire

One trained interviewer used a structured questionnaire to collect data regarding each patient's social characteristics, including a history of eating raw liver or meat of cows or other animals, raw blood of animals, and raw freshwater fish. The questionnaire contained the time and frequency, the number of occasions and the amount they ate, and the species of animals. The questionnaire also included a question whether patients had a recent history (within a year) of keeping dogs. The study coordinator and physicians made every effort to keep the interviewer blind to the clinical information of the patients. After a thorough review of the questionnaire filled up by the interviewer, an experienced physician without knowledge of any other information concerning the patient determined whether or not he or she had a significant history of eating raw tissues of animals or freshwater fish. The patient was considered to have a significant recent history of eating raw tissues if he or she met all of the following criteria: 1) one or more definite experiences of eating raw tissues of animals or fish, 2) the amount consumed was more than a single mouthful, and 3) the time of ingestion was within 1 yr.

Diagnosis of toxocariasis

ELISA kit (Bordier Affinity Products SA, Crissier, Switzerland) was used for the serologic diagnosis of human toxocariasis, which detects human IgG antibodies to *Toxocara* excretory-secretory (ES) antigens. This kit has been reported to have a 91% sensitivity and a 86% specificity [14]. The titers for positive results were variable, according to the daily reference control. Although some cross reactions may occur in other human helminthiases, such as trichinosis, fascioliasis, and strongyloidiasis, the titers in these helminthiases are lower than those in positive control sera in patients with toxocariasis [14]. All patients underwent ELISA for parasite infections not uncommon in Korea, i.e., *Clonorchis sinensis*, *Paragonimus westermani*, sparganosis, and cysticercosis.

Statistical analysis

We evaluated the relationships of patients with positive results in *Toxocara* ELISA and their recent histories of eating raw livers of cows or other animals, raw meat of animals, raw blood of animals, and a history of eating raw freshwater fish, a history of keeping dogs, and serologic results of other parasites with multivariate statistical analysis. Odd ratios (ORs) of results of *Toxocara* ELISA, together with their corresponding 95% confidence intervals (CIs), in relation to 7 variables were derived using a multiple logistic regression analysis. A P value of < 0.05 was considered a significant difference. Data analyses were performed with a commercially available software program (SPSS for Windows, version 11.0; SPSS, Chicago, Illinois, USA).

RESULTS

One hundred four (86.7%) of the 120 patients showed positive results in Toxocara ELISA tests. Among them, 92.3% were confidently diagnosed as toxocariasis because they had no other possible causes to increase the eosinophil count. Twenty-four patients were diagnosed as other parasitic infections, as they showed positive ELISA results for *C. sinensis* (n = 12), *P. westermani* (2), sparganosis (4), and cysticercosis (6). Among the seropositive patients for toxocariasis, 87.5% had a recent history of consuming raw cow liver, whereas only 25.0% of seronegative patients had such a history. In 28 patients who ate raw cow livers frequently (4 times or more per year), the seropositive rate was 96.4%. In 45 patients who ate raw cow livers within 6 months prior to the interview, the seropositive rate was 95.6%. Twenty-one patients ate raw livers of animals other than the cow, such as pig (n = 7), dog (4), goat (3), chicken (3), rabbit (2), duck (1), and goose (1). Among these patients, 95.2% had a history of eating raw cow liver. Nineteen patients drank raw blood of animals, such as deer (n = 16), goat (2), duck (2), cow (1), pig (1), or mud turtle (1).

Table 1 presents the distribution of seropositive and seronegative patients in *Toxocara* ELISA. According to multivariate analyses, a recent history of eating raw cow liver was related to an increased risk of toxocariasis. Recent histories of eating raw liver of other animals, raw meat of animals, raw blood of animals, and raw freshwater fish, keeping dogs, and serologic results for other parasites were not related to an increased risk of toxocariasis.

DISCUSSION

Chops of raw cow liver are one of the popular dishes in some restaurants or buffets in Korea. Chops of raw cow liver are usually served along with usual cooked or barbecued meat. Some people believe that raw liver and meat are good for health, par-

Table 1. Distribution of 104 seropositive and 16 seronegative patients for *Toxocara* ELISA

History	Positive rate (%) for *Toxocara* ELISA	Negative rate (%) for *Toxocara* ELISA	*P* value[a]	OR (95% CI)[b]
Ingesting raw cow liver				
Ever	87.5	25.0	< 0.001	34.861 (5.971-203.513)
Never	12.5	75.0		
Ingesting raw liver of other animals				
Ever	19.2	6.3	0.974	1.040 (0.098-11.002)
Never	80.8	93.8		
Ingesting raw meat of animals				
Ever	77.9	31.3	0.388	1.979 (0.419-9.340)
Never	22.1	68.8		
Ingesting raw blood of animals				
Ever	17.3	6.3	0.997	1.004 (0.087-11.597)
Never	82.7	93.8		
Ingesting raw freshwater fish				
Ever	28.8	12.5	0.489	2.023 (0.275-14.901)
Never	71.2	87.5		
Keeping a dog				
Ever	34.6	18.8	0.082	5.260 (0.811-34.115)
Never	65.4	81.3		
Serologic tests for other parasites				
Positive	21.2	12.5	0.054	7.281 (0.970-54.678)
Negative	78.8	87.5		

[a]Multivariate statistical results by using multiple logistic regression analysis.
[b]OR, odds ratio; 95% CI, 95% confidence interval.

ticularly for eyesight. In our study population, patients had a history of eating raw cow liver within 1 yr and some people ate chops of raw cow liver frequently whenever they go to meat restaurants. Not infrequently, some people eat raw liver of pigs, dogs, chickens, goat, duck, goose, or rabbits. Because of this eating habit, there are many patients with subclinical toxocariasis. Usually, they are checked by clinicians because of eosinophilia [8], or sometimes after small nodular lesions are incidentally found in the liver, lungs, or both on sonography or computed tomography [7].

The results of our study suggest that the ingestion of raw cow liver substantially increase the risk of toxocariasis. The seropositive rate in patients who ate raw cow liver was more than 3 times higher than in patients who did not eat raw cow liver. Patients who ate raw cow liver frequently or more recently showed very high seropositive rates. It appears that the seropositive rate is higher in people who had history of eating raw cow liver frequently and recently.

In spite of being seropositive for toxocariasis, some patients denied a history of ingestion of cow livers. Ingestion of raw livers of pigs, lambs, and chicken has been reported as route of human infections [9-12]. We attempted to establish a role of eating habit of raw animal livers other than cow livers in toxocariasis. There were 21 seropositive patients who had a history of eating raw livers of other animals, but they all had a history of eating cow livers as well. Therefore, we could not verify the relation between toxocariasis and ingestion of raw livers of other animals.

Several patients who denied a history of ingestion of cow livers were keeping dogs (3 in the house and the other 4 in gardens). Infection might take place by ingestion of eggs of *T. canis*, which were laid by their own dogs and then embryonated in their surroundings. In our study, however, the history of keeping dogs was not statistically significant in infection of *T. canis*. Among these 7 patients, 3 were not only keeping dogs but also ate raw meat of animals within 1 yr. In other 2 patients who were seropositive without history of raw cow liver ingestion, infection might have taken place by eating raw cow meat. They have eaten raw meat of animals without history of keeping dogs. There have been several case reports that toxocariasis probably took place by ingestion of raw meat of animals [15,16]. In animal experiments, *Toxocara* larvae were recovered in the lungs, liver, kidneys, brain, and also in muscles [3,17]. Tahira et al. [18] suggested the possibility of zoonotic risk of toxocariasis through eating animal meat. In our study, many adults who ate raw cow liver also ate

raw cow meat. We could not make a differentiation of the patients infected through ingestion of raw cow liver from those infected through ingestion of raw cow meat.

We did not determine the route of toxocariasis in 4 patients. We cannot exclude the possibility of toxocariasis by other *Toxocara* spp., such as *T. cati* and *T. leonina* [19]. There may be some cross reaction of human IgG antibodies to *Toxocara* ES antigens to other helminthiases, such as trichinosis, fascioliasis, and strongyloidiasis [20].

The toxocariasis seropositive rate in general population is variable depending on countries; specifically, 18% in rural areas in China [21], 20% in Malaysia [22], 26% in Iran [23], 6-36% in the Czech Republic [24], 2-5% and 14-37% in urban and rural areas in the Midi-Pyrenees area in France, respectively [25], 5% in Switzerland [26], and 5% in a rural area of Korea [27]. Because dogs and cats are popular pets, there is widespread contamination of environment with infective eggs, and therefore toxocariasis is a worldwide disease, irrespective of developed or underdeveloped countries. Higher rates of seroprevalence have been reported in Indonesia (68%) and Nepal (81%) [28,29]. It was suggested that a high seroprevalence among healthy adults of Taiwanese aboriginal populations (46%) was due to their habit of eating raw liver or meat [9]. The population enrolled in this study consisted of patients with eosinophilia of unknown etiology. Thus, they showed very high rates of seropositivity for toxocariasis and a history of eating raw cow liver. Further studies on the relationship between toxocariasis and ingestion of raw food in general population with lower seropositive rate are needed.

This study had some limitations. This study was cross-sectional and thus temporal associations cannot be inferred. A bias arising from recall data based on the patient's ability to recall past history of eating raw tissue of animals cannot be avoided. We first expected the ingestion of raw liver of other animals and raw meat of animals as possible risk factors. However, only the ingestion of raw cow liver increased the risk of toxocariasis in our multivariate statistics. The two ingestion histories could not be demonstrated as risk factors because of the small numbers of cases and substantial overlapping histories of ingesting raw cow livers. Another limitation is that we did not count the amount of animal tissues ingested in determining the seropositivity of the enrolled patients. Finally, the results of this study could be different from the general people. Only a minority of Koreans eat raw cow liver. When we designed this study, we worried about a very low toxocariasis seropositive rate in general population. Therefore, we selected patients with eosinophilia.

With the limitations of our study in mind, we suggest that ingestion of raw cow liver increase the risk of toxocariasis. Ingestion of uncooked livers of paratenic hosts may also be a potential source of human toxocariasis, at least in patients with eosinophilia.

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