

REVIEW

Cutaneous manifestations of human toxocariasis

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Human toxocariasis is a parasitic disease characterized by the presence of larvae of the genus *Toxocara* in human tissues. *T canis* and *T cati*, the adult roundworms of which are found in dog and cat intestines, respectively, are the most common causative agents of the disease. Toxocaral larvae usually cause two severe syndromes: visceral larva migrans and ocular larva migrans, depending on the location of the larvae. Two other syndromes, covert toxocariasis and common toxocariasis, which are less typical and not as severe, have also been described. During the last two decades, cutaneous manifestations such as chronic urticaria, chronic pruritus, and miscellaneous eczema, in patients with *Toxocara* antibodies, have been studied by different authors. In some cases, these cutaneous manifestations are the only signs indicating the presence of the disease, and they are cured after antihelminthic treatment when there is good patient compliance. In this review, we focus on these particular skin manifestations regarding their clinical description, diagnosis, and treatment. (J Am Acad Dermatol 10.1016/j.jaad.2008.06.031.)

Human toxocariasis is a widespread zoonotic parasitic disease caused by a nematode of the genus *Toxocara*. Dogs and cats play an essential role in the parasitic life cycle and act as reservoirs for the parasite. Reproductive adult roundworms of the parasite *T canis* and *T cati* are present in the intestinal tracts of dogs and cats, respectively. Human infestation by *Toxocara* is usually caused by ingestion of eggs from the environment. After egg ingestion, emerging infective second-stage (L2) larvae migrate through the liver and lungs to visceral tissues; they remain there for a long period, neither growing nor differentiating. Migration of the larvae in the host is usually associated with peripheral blood hypereosinophilia and induces eosinophilic infiltration into deeper organs such as the liver, lungs, brain, and muscles. *Toxocara* typically causes two severe syndromes called visceral larva migrans (VLM) and ocular larva migrans (OLM), depending on the location of the larvae in human host tissues,

Abbreviations used:

ABZ:	albendazole
DEC:	diethylcarbamazine
ELISA:	enzyme-linked immunosorbent assay
MBZ:	mebendazole
OLM:	ocular larva migrans
TES:	<i>Toxocara canis</i> excretory-secretory
VLM:	visceral larva migrans

and they usually require a specific anthelmintic treatment. During the last two decades, two other syndromes have been discovered: common toxocariasis and covert toxocariasis. These syndromes are not as severe, and are spontaneously cured in most cases.

Since the first clinical description of toxocariasis, with the help of more sensitive, specific diagnosis techniques that detect toxocaral antibodies directed against *T canis* excretory-secretory (TES) antigens using an enzyme-linked immunosorbent assay (ELISA) followed by a Western blot method, the clinical spectrum of toxocariasis has been enlarged. Many articles have reported cases of associated skin disorders, and among the most frequently mentioned is chronic urticaria. Other cutaneous manifestations associated with toxocariasis such as chronic pruritus, chronic prurigo, miscellaneous eczema, panniculitis, and vasculitis have also been observed.¹⁻⁵ In some cases, dermatologic symptoms were the only signs indicating the presence of the disease.^{6,7}

When dermatologists examine a patient with cutaneous lesions (regardless of the presence or absence of blood hypereosinophilia), that have been recurring for several months or years, and for which

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Table I. Symptomatology of the visceral larva migrans in children and in adults (Ehrhard and Kernbaum,¹³ 1979)

Clinical signs	Biological signs			
	Children	Adults		
Hepatomegaly	79%	47%	Hypereosinophilia > 400/mm ³	100%
Respiratory disorders	72%	42%	Hypereosinophilia > 5000/mm ³	76%
Fever	69%	71%	Leukocytosis	84%
Malnutrition	46%	36%	Hypergammaglobulinemia > 12 g/L	82%
Digestive disorders	44%	60%	Hypergammaglobulinemia > 30 g/L	74%
Asthenia	38%	63%	Positive <i>Toxocara</i> serology	68%
Neurologic disorders	36%	33%	Anemia	63%
Splenomegaly	35%	18%	Hypoalbuminemia < 40 g/L	62%
Anorexia	31%	30%	Presence of toxocaral larvae in the	37%
Pallor	29%	12%	hepatic biopsy specimen	
Cutaneous signs (rashes, urticaria, hypodermic nodules)	23%	29%		
Adenopathy	21%	19%		
Edema	13%	5%		

no origin has been found despite repeated clinical examinations and investigations, they should think of toxocariasis, given its high prevalence throughout the world. We will now review the dermatologic aspects of toxocariasis.

CLINICAL REMINDERS

A wide variety of clinical syndromes has been described for human toxocariasis, although most infections are probably subclinical. In 1950, Wilder⁸ reported 24 cases of OLM in children suspected of having retinoblastoma. Migration of the *T canis* larvae to the eye causes loss of vision. It has been reported that the presence of only one larva in the ocular cavity can cause irreversible blindness. In 2001, Dzbenksi et al⁹ injected rabbits via the carotid artery with the L2 larvae of the parasite to cause ocular toxocariasis. They observed the presence of toxocaral IgG antibodies and parasite antigens in the anterior chamber fluid samples.

Two years later, VLM was described by Beaver et al¹⁰ in 3 children with hepatomegaly and hyper-eosinophilia. VLM typically affects 2- to 7-year-old children with a history of geophagia, exposure to dogs at home, and living in poor socioeconomic conditions. Clinical signs are mainly hepatic and pulmonary. These symptoms include hepatomegaly, coughing, wheezing, abdominal pain, decreased appetite, restlessness, fever, and asthma. Biological findings are marked eosinophilia, leukocytosis, hypergammaglobulinemia, anemia, and hypoalbuminemia.^{11,12} In adults, the VLM symptomatology is slightly different. In a review of the literature in 1979, Ehrhard and Kernbaum et al¹³ reported 350 VLM cases. The disease mainly occurred in children (82%)

and was more frequent in boys and men (60%). Cutaneous manifestations, including transient rash, urticaria, and hypodermic nodules, were observed in 23% of the pediatric cases and 29% of the adult cases. Table I lists the clinical and biological symptoms and their frequency in pediatric patients versus their frequency in adult patients.

Other less typical and less severe forms of toxocariasis occur in industrialized countries and are called common toxocariasis and covert toxocariasis.

The term "common toxocariasis" was introduced by Magnaval et al¹⁴ in 1994. However, the disease was first described in 1987 by Glickman et al¹⁵ in 37 French adults. Common toxocariasis typically affects adult patients living in rural areas of the Midi-Pyrénées region of France, and presenting with chronic asthenia associated with digestive disorders and allergic manifestations (moderate hypereosinophilia and increased total serum IgE). Skin symptoms such as pruritus, eczema, and urticaria are sometimes present. Table II summarizes the common toxocariasis symptomatology. The diagnosis of this syndrome was made as a result of improved techniques that were more sensitive and specific. Detection of serum IgG directed against *T canis* was performed using an ELISA test. Diagnosis was then confirmed by a Western blot procedure.

The spectrum of covert toxocariasis was identified for the first time in 1987 in a case-control study carried out in 14 Irish children presenting with increased serum toxocaral ELISA antibody levels. Only half of these patients had hypereosinophilia. In all, 37% of them displayed a normal blood eosinophil count despite high titers of anti-*Toxocara* antibodies. Comparison of this seropositive pediatric population

Table II. Symptomatology of the toxocariasis in adults living in the Midi-Pyrénées region of France (Magnaval et al,¹⁴ 1994)

Clinical signs					
Early clinical signs		Late clinical signs		Biological signs	
Asthenia	30.4%	Chronic asthenia	77%	Positive <i>Toxocara</i> Western blot	100%
Abdominal pains	13%	Pruritus	41%	Total IgE > 150 kIU/L	79.7%
Urticaria	7.2%	Abdominal pains	37%	Presence of specific IgE	79.7%
Asthma	6.5%	Rhinitis	29%	Hypereosinophilia > 600/mm ³	74%
Vertigo	5.1%	Chronic cough	27%		
Pruritus	4.4%	Urticaria	26%		
Diarrhea	3.6%	Headache	23%		
Eczema	3.6%	Conjunctivitis	20%		
Edema	2.9	Myalgia	20%		
Epigastralgia	2.9%	Edema	15%		
Bronchitis	2.2%	Asthma	14%		
Adenopathy	1.5%	Weight loss	14%		
Löffler infiltrate	1.5%	Arthralgia	10%		
Myalgia	1.5%	Eczema	8%		
Weight loss	1.5%	Hepatomegaly	2%		

with a seronegative pediatric population revealed a significant association between the positive *Toxocara* serology and the existence of at least one of the following clinical symptoms: cough, abdominal pains, headache, sleep disorders, vomiting, or hepatomegaly.¹⁶ In addition, the combination of 3 specific clinical features (headache, abdominal pain, and cough) was more significantly associated with a higher antibody titer ($P < .05$) than was each separately studied, individual symptom. In this study, no cutaneous manifestations were mentioned. However, 1 year later, another study published by the same authors revealed the presence of rashes in 7% of the pediatric cases of covert toxocariasis presenting with high toxocaral antibody levels.¹⁷

MAIN CUTANEOUS CLINICAL MANIFESTATIONS STRONGLY ASSOCIATED WITH TOXOCARIASIS

Chronic pruritus

Numerous cases of chronic pruritus associated with a large variety of helminthiasis have been reported.^{18,19} In 1964, Areal¹⁹ noted the frequency with which pruritus and prurigo accompanied toxocariasis. Then, in 1972, Rook and Staughton²⁰ reported the case of a man with severe pruritus that was initially localized on palmoplantar surfaces, and then on the thoracic region. In a preliminary study carried out in our department, 27.5% (13 of 47) of patients with positive *Toxocara* serology results presented with generalized chronic pruritus associated with itching lesions or nodular prurigo (Fig 1). Eleven of these patients had high toxocaral antibody

**Fig 1.** Chronic prurigo associated with toxocariasis.

titers, suggesting evolving toxocariasis, whereas two of them showed moderate antibody levels connected with cicatricial toxocariasis (unpublished data).

In a case-control study, Humbert et al⁵ found that 38.1% of patients with chronic prurigo had positive *T canis* ELISA serology result (Table III). Correlation between chronic prurigo and positive toxocariasis serology was statistically significant ($P < .01$). On the other hand, no significant relationship between chronic pruritus and positive *Toxocara* serology was found (Table III). However, results indicated that toxocariasis was involved in 21.5% (8/38) of cases with sine materia pruritus.²¹

Table III. Cutaneous lesions associated with positive *Toxocara* serology: Case-control studies

Skin symptoms	Case-control studies	Serologic test	OR	95% CI	P	References
Chronic prurigo	38.1% Positive serology in prurigo group (n = 21) vs 12.7% in dermatologic control population (n = 236)	TES-ELISA	4.10*	1.51-11.16	<.01 [‡]	Humbert et al, ⁵ 2000
Chronic pruritus	15.4% Positive serology in pruritus group (n = 52) vs 12.7% in dermatologic control population (n = 236)	TES-ELISA	1.04*	0.43-2.49	>.05	Humbert et al, ⁵ 2000
Chronic urticaria	65% Positive serology in chronic urticaria group (n = 51) vs 21% in dermatologic control population (n = 81)	TES-ELISA Western blot	6.90 [†]	2.90-16.3	<.0001 [‡]	Wolfrom et al, ²⁷ 1995 Wolfrom et al, ¹ 1996
	19.5% Positive serology in urticaria group (n = 128) (chronic urticaria [n = 111], acute urticaria, Quincke edema, cold urticaria, or pressure urticaria) vs 12.7% in dermatologic control population (n = 236)	TES-ELISA	2.23*	1.19-4.19	<.02 [‡]	Humbert et al, ⁵ 2000
	29% Positive serology in chronic urticaria group	TES-ELISA	ND	ND	<.05 [‡]	Demirci et al, ⁴ 2003
	27.7% Positive serology in chronic urticaria group (n = 65) vs 13.3% in dermatologic control population (n = 30)	TES-ELISA	ND	ND	<.05 [‡]	Ismail and Khalafallah, ³⁴ 2005
Miscellaneous eczema	18.6% Positive serology in eczema group (n = 72) vs 12.7% in dermatologic control population (n = 236)	TES-ELISA	1.30*	0.63-2.71	>.05	Humbert et al, ⁵ 2000

CI, Confidence interval; ELISA, enzyme-linked immunosorbent assay; ND, not determined; OR, odds ratio; TES, *Toxocara canis* excretory-secretory.

*OR adjusted for age and sex with their 95% CI.

[†]Crude OR with their 95% CI. Patients and control subjects were similar for their distribution of age, dwelling in rural areas, and contact with pets.

[‡]Statistically significant difference ($P < .05$) between patients and control subjects.

Several physiopathological hypotheses have been presented regarding the relationship between the parasite *Toxocara* and the occurrence of pruritus or

prurigo. Toxocariasis is usually characterized by blood hypereosinophilia, and both pruritus and prurigo are classic clinical manifestations in hypereosinophilic

syndromes.^{22,23} In these types of syndromes, cutaneous chemotactic factors that attract blood eosinophil cells are released and may explain the dermatologic manifestations.²⁴ Another possibility is that toxocaral larvae have a pruriginous effect. Hinck and Ivey²⁵ demonstrated the proteinase activity of larval excretory-secretory antigens from another helminth species, *Ascaris suum*. In another study, bacterial exogenous proteases, such as streptokinase, were shown to first produce histamine-releasing activity and then a potential pruriginous effect.²⁶

Chronic urticaria

The association of toxocariasis with urticaria is now recognized by a number of authors and urticarial manifestations have been reported among patients with a positive serology for toxocariasis (Fig 2).^{1,4,5,27}

In a study carried out in a dermatologic population, Wolfrom et al^{1,27} found that 65% of patients with chronic urticaria had anti-*Toxocara* antibodies (Table III). This association was highly significant ($P < .0001$).

In another case-control study, 19.5% of patients presenting with different forms of urticaria had positive TES-ELISA serology.⁵ None of the patients in the acute urticaria group had positive serology results. The risk of a positive result to *T canis* serology was significantly higher ($P < .02$) in the chronic urticaria group than in the control group (Table III). Because urticaria was commonly observed in patients with VLM or covert toxocariasis,^{14,28,29} and because a possible relationship between allergic diseases and infection by some parasites was previously suggested,^{30,31} the authors proposed a possible relationship between *Toxocara* infection and chronic urticaria. Moreover, half of the patients with urticaria associated with a positive TES-ELISA result were cured after anthelmintic treatment (unpublished data). In a study carried out in 1379 Dutch elementary schoolchildren, the authors found that 8% of them had serum toxocaral antibodies. Allergic manifestations (ie, allergic asthma and recurrent bronchitis) occurred in 7% of the children. This variable was associated with *Toxocara* seroprevalence.³² In a recently published article on an adult Spanish population, it was demonstrated that *Toxocara* exposure was also associated with allergic sensitization, especially to mites.³³

In a case-control study carried out in 65 Egyptian patients with dermatologic conditions and chronic urticaria lasting for at least 3 years, the authors found a strong association between toxocariasis seropositivity and chronic urticaria (Table III).³⁴ Diagnosis of toxocariasis was based on an indirect ELISA procedure using TES antigens. Patients with urticaria were divided into two groups: one with 27 patients with



Fig 2. Urticaria associated with toxocariasis.

good anti-histamine antagonist (H1) therapeutic responses, and the other with 38 patients with recurrent exacerbations and unsatisfactory responses to anti-H1 treatment. In the first group, only 11.1% of the patients were seropositive ($P > .05$). In contrast, 39.5% of the second group were seropositive for toxocariasis ($P < .01$). The authors suggested that the exposure to *T canis* may account for the severe cases of chronic urticaria and the resistance to anti-H1 treatment. They recommended testing patients with chronic urticaria for toxocariasis, especially those with an increased risk of environmental exposure to the parasite such as poor socioeconomic status, rural origin, contact with pets and/or farming, or a combination of these.

According Byers and Kimura,³⁵ immune reactions against the human tissues may occur even after the death of the toxocaral L2 larvae in deeper organs. Although nothing specific has been reported about a possible relationship between the persistence of dead larvae in deeper organs and serum total IgE levels and blood hypereosinophilia, there is a recent study that has characterized the effect of *T canis* infection on the lungs in BALB/c mice. The authors concluded that the persistent pulmonary inflammation, airway hyperreactivity, eosinophilia, and increased IgE production could be caused by the presence of *T canis* larvae in the lungs at 60 days postinfection.³⁶

Miscellaneous eczema

There are very few reports of different forms of eczema associated with *Toxocara* infection in the medical literature.



Fig 3. Acquired disseminated eczema associated with toxocariasis.

In a recent case-control study carried out on 72 patients consulting for eczema (70% had miscellaneous eczema including atopic dermatitis [Fig 3] and 30% had dyshidrosis [Fig 4]), 18.6% had positive *Toxocara* serology results (Table III).⁵ However, no statistically significant association between positive *Toxocara* serology and all these forms of eczema was found. Nevertheless, because some of chronic miscellaneous eczema disappeared after albendazole (ABZ) therapy in these patients, the search for *T canis* infection is systematically performed, especially in patients owning pets.

UNUSUAL SKIN MANIFESTATIONS OF TOXOCARIASIS

Hypodermatitis

In 1964, Brain and Allan³⁷ described the case of a 32-year-old British woman presenting with recurrent subcutaneous granulomatous lesions of the trunk and the right lower extremity, associated with focal epilepsy, and with moderate blood eosinophilia (600 blood eosinophil cells/mm³). Subcutaneous lesions were excised; they resembled granuloma containing lymphocytes, fibroblasts, plasma cells, and eosinophils. Even after careful examination of each specimen, no *Toxocara* larvae were found. The diagnosis of toxocariasis was suggested because of a positive *T canis* skin test result. Specific antihelminthic treatment with diethylcarbamazine (DEC) (3 mg/kg) was given 3 times daily for 3 weeks. Clinical status of the patient was re-evaluated 3 months later; she did not present any additional subcutaneous lesions (Table IV).

Almost 10 years after this case report, Rook and Staughton²⁰ described the case of a 72-year-old British man who developed migratory panniculitis



Fig 4. Dyshidrosis associated with toxocariasis.

of VLM (Table IV). This patient was a gardener. He lived in a country village, and he had never left Britain. A few months before, the patient reported a history of severe pruritus on his hands, face, and soles of the feet, lasting for 3 months. When seen by dermatologists, the man had generalized erythema with very marked dermal edema spreading predominantly over the lower aspect of his abdomen and thighs. Superficial excoriations over all areas except the face were also noted. There was discrete axillary adenopathy, but no splenomegaly. After the visit to the dermatologist, the patient developed elongated subcutaneous nodules that rapidly (over 3 or 4 days) spread into the deeper tissues. There were 13 nodules in all, and the largest covered the biceps on the left arm. No suppuration was observed. The nodules spontaneously disappeared in 2 to 3 weeks. During the fourth week, the man developed a transient erythematous macular rash over the lower aspect of his chest and upper aspect of his abdomen. Nodules continued to develop and the skin concomitantly became edematous and pruritic. Biological investigations revealed the presence of eosinophilia (3500 eosinophil blood cells/mm³). Results of an immunofluorescent serum antibody test to toxocariasis were positive. Nodule biopsy specimen showed acute panniculitis with some fat-laden macrophages, and many eosinophils in the subcutaneous tissue infiltrate. However, no larvae were found. A 3-week course of DEC (250 mg twice daily) was prescribed as specific treatment. The patient recovered completely as evidenced by a normal eosinophil count and a negative *Toxocara* fluorescent antibody test result.

Vasculitis

Few cases of Henoch-Schönlein purpura associated with *T canis* ELISA serology have been reported (Table IV).^{38,39}

In the case report published by Hamidou et al,³⁸ a male adolescent was hospitalized because of a clinical spectrum of abdominal pain, fever, and arthritis

Table IV. Case reports of cutaneous lesions associated with positive *Toxocara* serology

Skin symptoms	Case reports	Positive <i>Toxocara</i> serologic test	Biopsy	Anthelmintic treatment	Clinical course	References
Hypodermitis	A case of recurrent subcutaneous granulomatous lesions of trunk and right lower extremity associated with focal epilepsy in 32-year-old woman	Skin test	No <i>Toxocara</i> larvae	DEC 3 mg/kg 3 times/d for 3 wk	Recovery	Brain and Allan, ³⁷ 1964
Vasculitis	A case of migratory panniculitis (subcutaneous nodules) in 72-year-old man	Immunofluorescent test	No <i>Toxocara</i> larvae	DEC 250 mg twice/d for 3 wk	Recovery	Rook and Staughton, ²⁰ 1972
	A case of systemic granulomatous vasculitis in 2-year-old child (transient edema of face)	None	L2 <i>Toxocara</i> larvae detected	None	Death	Brill et al, ⁴⁰ 1953
	A case of Henoch-Schönlein purpura in 17-year-old boy (purpuric rash on lower limbs)	TES-ELISA Western blot	No <i>Toxocara</i> larvae	None	Recovery	Hamidou et al, ³⁸ 1999
Reiter syndrome	A case of Reiter syndrome	TES-ELISA	None	None	Recovery	Our unpublished data
Wells syndrome	Two cases of Wells syndrome	TES-ELISA	None	Albendazole 400 mg/d for 10 d	Recovery	Hurni et al, ⁴² 1997
Eosinophilic folliculitis	Eosinophilic folliculitis in 51-year-old Caucasian woman	TES-ELISA	ND	Albendazole 400 mg twice/d for 5 d	Recovery	Gesierich et al, ⁴³ 2006

DEC, Diethylcarbamazine; ND, not determined.

affecting wrists, elbows, shoulders, and ankles; all signs appeared within 1 week. He also had a purpuric rash on the lower limbs. Biological investigations performed to find a specific cause all produced negative findings except for the *T canis* ELISA serology, which was positive both for IgG and IgE. A complete pattern showing 7 fractions was obtained by a Western blot method and confirmed the positive ELISA result. The patient also had blood eosinophilia (1500 eosinophil blood cells/mm³). No toxocaral larvae were observed on skin biopsy specimen. Henoch-Schönlein purpura spontaneously improved in 2 weeks. In this case report, the physicians did not prescribe any specific anthelmintic drug because they wanted to avoid a possible acceleration of the immune vasculitis process, caused by larval lysis.

In 1953, a case of systemic granulomatous vasculitis associated with evolving toxocariasis was also reported by Brill et al⁴⁰ (Table IV). The patient was a 2-year-old child who presented with fever, abdominal pain, hepatomegaly, and neurologic disorders, which led to coma and death. The patient also presented with transient edema of the face. Blood hypereosinophilia suggested a possible involvement of *Toxocara*. Autopsy showed the existence of many necrotic and granulomatous sources in the liver, kidneys, heart, and lungs, and confirmed the diagnosis of toxocariasis. Granulomas were composed of histiocytes, giant cells, and many eosinophils in the center of which was a necrotic vein. L2 toxocaral larva was detected in one of these lesions. Granulomatous reaction was probably related to an exacerbation of the cellular response to toxocaral larvae.

Reiter syndrome

The role of *Toxocara* has been suggested in some cases of Reiter syndrome.⁴¹ In our department, only one case of Reiter syndrome associated with toxocariasis has been observed (Table IV) (unpublished data). The patient presented with chronic erythematous squamous balanitis and recurrent sternocostal arthralgia. Investigations revealed blood hypereosinophilia and the presence of the antigen HLA B5. *T canis* serology revealed positive findings. The patient was treated with a tetracycline regimen; no specific antihelmintic drug was prescribed.

Wells syndrome

Wells syndrome has been reported in association with *Ascaris lumbricoides* and *Onchocerca volvulus* infection. In 1997, two cases of Wells syndrome associated with positive *T canis* serology results were reported (Table IV).⁴²

In the first case, the eosinophil count at 520 eosinophil cells/mm³ was high, whereas the total IgE level was normal. Diagnosis of *Toxocara* infection was suggested by a positive serology result showing a moderate increase in specific IgG antibodies. The cutaneous lesions disappeared 2 weeks after treatment by oral ABZ (400 mg/d for 10 days) associated with topical corticosteroids. Four months later, both toxocaral serology and eosinophilia findings were normal.

The second case was a 47-year-old man with itchy, erythematous lesions that appeared within 2 weeks. Skin biopsy specimen showed typical eosinophilic infiltration of the edematous dermis. Investigations revealed the presence of blood hypereosinophilia (720 eosinophil cells/mm³) and a positive TES-ELISA serology result with a titer of *Toxocara* IgG antibodies of 11 AE/mL (normal < 1 AE/mL). After treatment by ABZ (400 mg/d for 10 days) associated with oral prednisolone (50 mg/d for 4 days) and topical corticosteroids, the patient was symptom free 2 weeks later. *Toxocara* antibodies and blood eosinophils returned to normal levels within 3 months.

For these two cases, the authors concluded that *T canis* may play a causative role in the outbreak of Wells syndrome. In contrast, in a third patient with eczematoid skin lesions, blood eosinophilia, and high levels of anti-*Toxocara* antibodies, no relationship was found between toxocariasis and eosinophilic cellulitis. After ABZ treatment, no clinical improvement was observed for this patient despite serologic normalization. He was classified as having idiopathic hypereosinophilic syndrome.

Eosinophilic folliculitis

Gesierich et al⁴³ described a case of eosinophilic folliculitis associated with toxocariasis in a 51-year-old Caucasian woman (Table IV). High levels of toxocaral IgG antibodies directed against TES antigen were detected by ELISA serology. In addition, the patient presented with low blood hypereosinophilia (700 eosinophil cells/mm³; normal range: 40-360/mm³). Biopsy specimens of the upper aspect of the back and a cheek revealed prominent pustular folliculitis. The authors did not mention the presence or absence of *Toxocara* larva. Topical tacrolimus treatment (twice daily for 3 weeks) was first initiated because tacrolimus reduces the functioning and viability of eosinophil cells. Even though this treatment eradicated the facial and truncal lesions, the cutaneous eruptions reappeared 3 weeks after termination of the treatment. Given the possibility of infestation by *Toxocara* as suggested by the positive serology result, and given

the fact that the woman had a dog as a pet, specific antihelmintic treatment with ABZ was prescribed (400 mg twice daily for 5 days) in combination with oral methylprednisolone for 4 days and then indomethacin. With this regimen, cure was rapid and complete; only a discreet residual erythema could be seen on the patient's face. Blood eosinophil count and *Toxocara* antibody levels decreased significantly. The woman showed no signs of recurrence of the disease 10 months later.

Very little is known about the origin and pathogenesis of eosinophilic folliculitis. Three cases of eosinophilic folliculitis associated with parasitological infection have been described in the medical literature. Two of them occurred with cutaneous larva migrans, and one with scabies. In each case, the cutaneous lesions disappeared after a specific antihelmintic regimen.

DIAGNOSIS OF CUTANEOUS MANIFESTATIONS OF TOXOCARIASIS

Toxocara infection is the main cause of unknown peripheral blood hypereosinophilia with an eosinophil cell count up to 500/mm³ or up to 10% of white blood cell count.⁴⁴ However, blood eosinophilia is usually normal in chronic cutaneous manifestations of toxocariasis. If this is the case, and the patient is at risk for infection by the parasite (ie, owns pets), investigations for the disease should be undertaken.

In suspected clinical cases of VLM, OLM, and covert and common toxocariasis, the definitive diagnosis is based on histopathologic examination and morphologic identification of L2 larvae in tissue samples. Methods such as polymerase chain reaction and restriction fragment length polymorphism or sequencing of *Toxocara* nuclear ribosomal DNA, mitochondrial DNA, or repetitive DNA extracted from human tissues are rarely performed because acquisition of biopsy material containing larvae is too unpredictable. The most effective method for confirming toxocariasis in clinically suspected cases is serology based, ie, detection of the IgG antibodies directed against the excretory-secretory antigens of *Toxocara* (TES) with an ELISA called TES-ELISA, which is then confirmed by a Western blot method. In mice infected with *T canis* by oral administration of embryonated eggs of the parasite, specific toxocaral IgG and IgM antibodies were detected in the sera collected at the fourth week of infection.⁴⁵ The TES-ELISA technique is also used to detect specific IgA and/or IgE antibodies. In a serologic follow-up study carried out on 27 1- to 12-year-old children with VLM, OLM, or both in Sao Paulo, Brazil, the sensitivity for IgE, IgA, and IgG ELISA was 78.3%, 47.8%, and 100%, respectively. Specific IgE antibody

titers decreased significantly during the first year after treatment with thiabendazole, IgA titers decreased in the second year, and IgG titers decreased only from the fourth year. Single or multiple parasitosis did not appear to affect the anti-*Toxocara* immune response. One year after treatment, the level of eosinophil leukocytes decreased significantly, suggesting that IgE antibody plus eosinophil counts are helpful parameters for patient follow-up after chemotherapy.⁴⁶ In another study, the authors concluded that after antihelmintic treatment, the return of IgG antibodies to their normal level is a very slow process. Positive IgG serology results were found in 57% of 168 children treated for toxocariasis even after 4 to 7 years, and the decrease of the mean titer of antibodies did not exceed 45%.⁴⁷ Because testing for IgG antibody levels does not provide a satisfactory indication of the positive effect of the treatment and because blood hypereosinophilia is often nonexistent in patients with positive toxocariasis serology, Magnaval et al⁴⁸ studied eosinophilic cationic protein assessment and demonstrated that it could be useful for distinguishing between active and past toxocaral disease. A sharp increase in eosinophil cationic protein levels suggests that viable *Toxocara* larvae are still present in the human host tissues, and that the patient should be treated with an appropriate antihelmintic regimen.

In cases of OLM, some authors use a modification of the standard ELISA test (dot ELISA) to confirm ocular disease in aqueous or vitreous fluid samples.⁴⁹

With the commercially available TES-ELISA kits, positivity thresholds were defined using a pool of sera collected from patients with VLM (ie, who had very high *Toxocara* antibody levels). For some patients with toxocariasis cutaneous lesions (especially chronic urticaria, chronic pruritus, and prurigo), we observed lower optical densities than the threshold recommended by the manufacturer when performing the TES-ELISA test, despite a positive *Toxocara* Western blot serology result. This could indicate that these patients with dermatologic conditions had lower antibody levels than those with standard VLM. In our opinion, the Western blot method is more suitable for the diagnosis of toxocariasis in patients with chronic skin lesions such as chronic urticaria, chronic pruritus, or prurigo.

CUTANEOUS MANIFESTATIONS OF TOXOCARIASIS AND PATIENT CARE

Human toxocariasis is a widespread parasitosis. Its seroprevalence is estimated at 92.8% in La Réunion, France; 81% in Kathmandu, Nepal; 39% in La Plata, Buenos Aires, Argentina; 27.4% in the

Slovak Republic; and 15% in Southwestern France.⁵⁰⁻⁵⁴ The disease is usually asymptomatic. Even if they have blood hypereosinophilia, spontaneous cures occur with patients with common toxocariasis or covert toxocariasis, and a prophylactic approach is recommended to prevent reinfection.⁵⁵ In cases of symptomatic patients with patent VLM or OLM, specific antihelminthic treatment in association with prophylaxis is systematically required because of the severity of the symptoms.

With cutaneous manifestations associated with positive serology for toxocariasis, patients are usually treated. In one study by Humbert et al,⁵ appropriate antihelminthic treatment of patients with prurigo and toxocariasis cured 80% of cases. Of patients with chronic urticaria associated with toxocariasis, 50% were cured after antihelminthic treatment.⁵ When treating patients with chronic skin manifestations associated with toxocariasis, dermatologists usually use oral ABZ (800 mg/d over 5 days), thiabendazole, or DEC (6 mg/kg b/w daily divided into 3 doses for 7-10 days) associated with an antihistaminic compound such as cetirizine.^{56,57}

For the treatment of toxocariasis, DEC, usually indicated in therapy for filariasis, is probably more effective than ABZ. However, DEC sometimes has neurologic side effects (headache, dizziness) and causes Mazzotti-like reactions (hypersensitivity reaction caused by larva lysis) and it must be gradually administered to reduce allergic side effects. In addition, DEC is not available in all countries. Mebendazole (MBZ), a benzimidazole derivative drug, is available worldwide. MBZ is almost as effective as DEC for treating toxocariasis, and its side effects are not as severe as those of DEC.⁵⁸ If neurologic side effects occur with DEC, MBZ could be a good alternative. ABZ, because it has proved to be safe and is available worldwide, is the most commonly used drug for the treatment of toxocariasis. In a comparative study carried out on 34 patients with VLM or OLM between 1986 and 1988, no significant difference in treatment efficacy between thiabendazole and ABZ was observed.⁵⁹ Because it is better tolerated, the authors recommended ABZ for the treatment of VLM and OLM, with a minimum dose of 10 mg/kg daily for 5 days. Treatment may have to be repeated, depending on the biological and clinical response. Usually ABZ is combined with corticosteroids for the treatment of ocular and neurologic manifestations.⁵⁹ In an open study of a dozen cases of VLM caused by *T canis* or *T cati*, ivermectin, a drug that is usually indicated in the treatment of onchocerciasis and strongyloidiasis, showed no significant efficacy. After a single oral 12-mg-dose ivermectin intake, clinical signs for two of the 15 symptomatic patients (13%) disappeared, but

hypereosinophilia levels did not change. Four patients (27%) showed clinical improvement, and the remaining 9 (60%) showed no clinical or serologic improvement. No significant difference was observed between pretreatment and posttreatment mean values of eosinophilia. No significant correlation was observed between the rate of ivermectin absorbed or the posttreatment time gap on the one hand and the effect on clinical symptoms or the posttreatment mean eosinophil count on the other hand. These results contrast with those for DEC and MBZ, both of which elicited significant decreases in clinical signs and blood eosinophilia, on average 4 weeks after the treatment ended.⁶⁰

In all cases of symptomatic or asymptomatic toxocariasis, and for cutaneous manifestations, prophylactic measures must be taken; they can prevent reinfection and must be explained carefully to patients. For example, dogs and cats must be treated by a veterinarian; risk behaviors such as geophagia and poor personal hygiene must be avoided; and dogs must be banned from public playgrounds so that children cannot be infected or reinfected by ingestion of toxocaral eggs from contaminated sand.

Conclusion

This review of the dermatologic literature shows that cutaneous symptoms are relatively frequent in cases of *Toxocara* infection, especially in VLM and common toxocariasis cases. Skin symptoms can be the only suggestive signs of an underlying toxocaral infection. The most commonly encountered skin manifestations associated with toxocariasis are chronic pruritus or prurigo, different forms of eczema, and chronic urticaria. Because of the long course of these diseases and the difficulty in establishing an origin and, thus, a specific treatment, dermatologists need to investigate for possible toxocaral infection in high-risk patients presenting with the above-described cutaneous lesions. Toxocaral investigations should be undertaken especially, but not exclusively, in the presence of blood hypereosinophilia and/or increased total IgE, and/or if the patient has risk factors for infection by the parasite such as frequent contacts with dogs at home. In addition, physicians have to keep in mind that toxocaral antibody levels are usually low in cases of chronic cutaneous manifestations of toxocariasis and, when using a standard TES-ELISA test for their detection, the optical density is lower than the thresholds recommended by manufacturers. In our opinion, Western blotting procedure, a much more sensitive technique than the ELISA method, is more suitable for the serologic diagnosis of toxocariasis in patients with these dermatologic manifestations. In

these cases, an atypical, incomplete blot pattern with only two or 3 low-intensity, specific low-weight molecular fractions, is usually obtained.

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