THE SPECTRUM OF OCULAR TOXOCARIASIS

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SUMMARY

Ocular toxocariasis is rare and therefore the spectrum of clinical disease is difficult to establish. We present a review of the clinical features and laboratory findings in a group of patients with positive *Toxocara* serology and ocular toxocariasis. The clinical spectrum was diverse and milder disease was commoner than might be supposed from reviews of the literature. Eosinophilia was unusual, but featured in two cases of unilateral pars planitis.

Toxocara canis is an ascarid parasite of canids and produces disease in humans due to the migration of second stage larvae (L2) throughout the body. This migration continues for months or years because the parasite is unable to complete its life cycle in humans.

Two syndromes have been described: visceral larva migrans and ocular disease. The former is characterised by fever, bronchospasm, cough, anaemia, hepatosplenomegaly, eosinophilia and positive *Toxocara* serology.[1] Characterisation of the latter is the subject of this study.

Wilder was the first to describe the syndrome of nematode infection of the eye.[2] She reported the pathological findings in 47 eyes enucleated for suspected retinoblastoma, but in which there was microscopic evidence of nematode infection. All of these patients presented with leucocoria. Retinal granuloma was the predominant pathological finding. In 24 of the eyes either the larva or a residual hyaline capsule was seen. Nichols later identified the nematode as *Toxocara* sp.[3]

Subsequently, different clinical features and pathology have been described, mostly in small series or literature reviews.[4–6] Because individual practitioners see only a few cases, the clinical spectrum of ocular toxocariasis has been difficult to establish. Moreover, many of these cases were reported before the development of reliable serological techniques. The purpose of this study was to review the clinical features, treatment and laboratory findings in a group of patients with positive *Toxocara* serology and ocular toxocariasis.

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PATIENTS AND METHODS

All clinicians throughout the British Isles who had referred specimens to the London School of Hygiene and Tropical Medicine during 1987–8 were sent a questionnaire requesting clinical details of all patients with positive *Toxocara* serology. The presence of serum antibodies to *Toxocara canis* excretory–secretory (ES) antigen was determined by enzyme-linked immunosorbent assay (ELISA) as previously described.[7] A positive result was defined as an optical density (OD) reading of greater than 0.25. Anti-*Toxoplasma* antibodies were also sought by latex agglutination and IgM capture ELISA.

RESULTS

Thirty-six questionnaires provided enough information to make an ocular diagnosis. In 3 of them a specific diagnosis other than toxocariasis was deemed likely and these were excluded from this study. Of the remaining 33 patients, 22 were males and 11 females. The mean age was 15.9 years. The serology of all patients was positive with a mean OD for *Toxocara canis* ES antibody of 0.61. This compared with 0.83 for a group of patients with visceral larva migrans diagnosed at this laboratory.

Of the 33 patients, 26 complained of visual loss and 8 complained of eye pain. A retinal abnormality was present in 17 patients, uveitis in 20 and endophthalmitis in 9. Active retinal granulomatous lesions dominated the clinical picture in 9 cases. The findings in these 9 cases are summarised in Table I. Endophthalmitis was present or was an associated feature in 9 cases. In 2 of these the major feature was a papillitis which was associated with retinal oedema and vitreous exudates. Chorioretinitis was present in 2 cases and endophthalmitis associated with a retrolental mass in 1 case. In 5 cases seropositivity was found without evidence of active ocular disease. The clinical findings are set out in Table II, although the presence of these ocular findings and seropositivity may be incidental. Two patients had pars planitis, the details of which are given in Table III.

Table I. Clinical features of patients in whom active retinal mass lesions were the main finding

Patient no.	Age (yr)	Sex	OD	Description
1	14	M	0.4	Subretinal inflammatory lesion upper temporal quadrant; vitreoretinal traction and dense cellular infiltration of the vitreous
2	7	M	0.71	Macular mass; vitritis
3	21	M	0.46	Peripapillary granuloma with macular oedema and vitreous detachment
4	14	M	0.38	Retinal mass inferiorly associated with fibrous traction band
5	10	M	0.47	Peripheral retinal mass with vitreous traction band to disc
6	5	F	0.56	Peripheral chorioretinal scar with tunnel-shaped vitreous condensation
7	8	M	0.67	Peripheral mass; panuveitis; hypopyon
8	27	M	0.23	Central retinal granuloma; posterior uveitis
9	8	M	0.72	Central retinal mass; posterior uveitis; posterior synechiae

M, male; F, female; OD, optical density.

Table II. Ocular findings in patients without active disease

Patient no.	Age (yr)	Sex	OD	Description
1	6	F	0.34	Detached retina (right eye)
2	11	M	0.33	Peripheral fibrous mass extending from the optic disc; evidence of old vitritis
3	18	M	1.02	Macular scarring consistent with previous uveitis
4	10	M	0.38	Depigmented area right of optic disc
5	3	F	0.71	Macular scar

The only clinical finding in 1 patient was of anterior uveitis. This 33-year-old presented 3 years after a febrile illness with features of visceral larva migrans and an associated scleritis. Clinical evidence of associated visceral and ocular disease was found in this patient and in 2 others: a boy of 11 with bronchospasm and cough and an 18-year-old man with cough, bronchospasm and convulsions.

Severe visual loss was reported in 12 patients and the pathological causes are summarised in Table IV.

An eosinophil count of greater than 0.5×10^9/l was uncommon. Of 16 cases in which the eosinophil count was recorded, only 3 had an absolute eosinophilia. Despite this there was a significant positive correlation between the eosinophil count and anti-ES antibody level ($r = 0.56$, $p = 0.02$) (Fig. 1).

Full details of therapy were reported in 15 patients: 2 were treated with topical steroids, systemic steroid therapy was used in 7 (5 of these in combination with anti-helminthic agents) and 3 received no treatment since the disease was inactive. In all, 7 patients received anti-helminthic treatment: thiabendazole in 5 cases, albendazole in 1, and diethylcarbamazine in 1.

It is of note that in 3 cases the ocular lesions were discovered as the result of a school medical examination.

DISCUSSION

The spectrum of ocular toxocariasis has been established by reviews of the medical literature.[4–6] This study was performed prospectively and therefore provides the opportunity to study those cases which were less severe or considered not sufficiently unusual to merit publication. The range of clinical features reported here may not even be complete as ocular disease in the absence of antibodies in the serum has been reported.[8]

Toxocara seroprevalence varies in different communities. A survey of blood donors in London indicated a seroprevalence of 2.6%[7] and a study in children in Bedfordshire has reported 14.6%.[9] In countries where environmental conditions favour survival of *Toxocara* eggs and there is close contact between man and dogs seroprevalence in children may rise to 84%.[10]

The incidence of ocular toxocariasis is more difficult to assess. One study reported that of those specimens containing antibodies approximately 100 were from patients with ocular disease.[11] In the authors' own survey of 1182 specimens submitted in one 6-month period to the London School of Hygiene and Tropical Medicine one third of the 150 patients with positive serology had ocular symptoms or signs recorded by the referring clinician (unpublished observation).

The demographic characteristics of this patient group are in accord with previous surveys of case reports and short series in that the patients are predominantly male (2:1 ratio) and are children, albeit with a mean age higher than that of patients with both positive *Toxocara* serology and symptoms of visceral larva migrans.[4] It should be noted that all of our patients with ocular toxocariasis had positive serology, although mean antibody levels were lower than in visceral larva migrans.

The cases reported in this study help to establish the clinical spectrum of ocular toxocariasis. We found that the characteristic lesion was a retinal granuloma which could

Table III. Pars planitis and toxocariasis

Patient no.	Age (yr)	Sex	OD	Description
1	3	M	1.65	White mass involving peripheral retina; anterior and posterior uveitis; eosinophils 24%
2	9	M	0.38	Severe inflammation of the left eye; exudate on the inferior peripheral retina; vitreous opacities and anterior uveitis; eosinophils 11%

Table IV. Causes of severe visual loss

Cause	No. of patients
Fibrous traction band	4
Endophthalmitis	2
Macular lesion	2
Retinal detachment	1
Pars planitis	2
Papillitis	1

be central or peripheral and associated with a varying degree of inflammation in the structures of the eye. The most serious consequence of this inflammatory process is fibrosis and retinal traction bands leading to retinal detachment. In this study, many of the patients had peripheral granulomas. This contrasts with a review in 1970, in which posterior pole granulomas were the commonest single finding.[4]

Other reviews support our results. One study reported that 17 of 40 patients had a peripheral inflammatory mass.[12] Molk suggested that invasion of the eye by second stage larvae of *T. canis* commonly produced a reaction of endophthalmitis, posterior pole granuloma or peripheral granuloma.[5] He also noted individual cases of pars planitis, vitreous abscess, optic neuritis, keratitis, uveitis, hypopyon or motile larvae in the vitreous cavity.[5] More recently, Shields also reviewed the diverse spectrum of clinical findings, including posterior retinochoroiditis, peripheral retinochoroiditis, optic papillitis, endophthalmitis and motile chorioretinal nematode.[6]

In our study, 'pars planitis' was used to describe the clinical features of 2 patients. The aetiology of this condition is usually unknown and the inflammatory process is bilateral in more than 90% of patients. Molk refers to a single case report of unilateral pars planitis in which the diagnosis was confirmed histopathologically when the child died of other causes.[5] Pars planitis was also reported by Wilkinson as part of the differential diagnosis of toxocariasis.[14] Both of the cases described in this study had an associated eosinophilia, although peripheral eosinophilia is uncommon in ocular toxocariasis and other reports of peripheral granulomas.[1,8,9,12,14]

Ocular disease is caused by the immune response to the presence of *Toxocara* lavae and their products in the eye. In the mouse model, only two or three larvae were found in the eye, so a peripheral eosinophilia might not be expected.[15] From other animal experiments it appears that a history of previous *Toxocara* infection predisposes towards an accelerated inflammatory response to larvae in the eye.[16,17] The mechanism is unclear but it may have a local immunological basis. Because ocular toxocariasis may occur in the absence of eosinophilia, we suggest that *Toxocara* serology is indicated in all cases of unilateral pars planitis.

Despite the often severe inflammatory process in the eye, only a few of the patients reported ocular pain. Three patients were diagnosed after vision had fallen to counting fingers or had been discovered upon routine medical examination. Ocular toxocariasis may result in significant unilateral loss of vision with minimal symptoms. As many of the patients are children permanent visual loss may go unnoticed and undiagnosed. This emphasises the importance of screening by general practitioners and clinical medical officers in schools.

The many different therapeutic regimens reflect the diversity of opinion among clinicians reporting cases. Steroids are of value in controlling the acute inflammatory process in ocular infection, but the role of anti-helminthic agents is less clear.[18] Theoretical objections to the use of anti-helminthic agents in ocular disease have been based on the fear that the death of the parasite will result in increased release of parasite antigens and consequent inflammatory damage. Studies of a mouse model indicate that much of the inflammatory response is directed against deposited *Toxocara* ES antigen rather than the larva itself.[16] This removes one of the objections to the use of anti-helminthic agents, but it is difficult to achieve adequate concentrations in the eye. There is no evidence from controlled trials to support the use of any particular agent, but early intervention with steroids and anti-helminthics may improve the final result in some cases.[18] Ocular surgery may be necessary[19] where retinal traction bands have caused detachment, and laser coagulation has been used with reported success.[6]

In conclusion, ocular toxocariasis is an important, preventable cause of severe unilateral visual loss. However, our survey shows that a milder disease is more common than reviews of the literature might suggest. It also shows that the second stage larvae of *Toxocara* sp. are capable of causing diseases in most of the structures of the eye and thus the clinical spectrum is diverse. It includes retinal granulomas either by the posterior pole or situated peripherally. These may be associated with varying degrees of inflammation and endophthalmitis.

Ocular toxocariasis may present with a clinical syndrome similar to uniocular pars planitis and other syndromes such as retrolental mass and anterior uveitis; keratitis may also occur. In many cases the course is

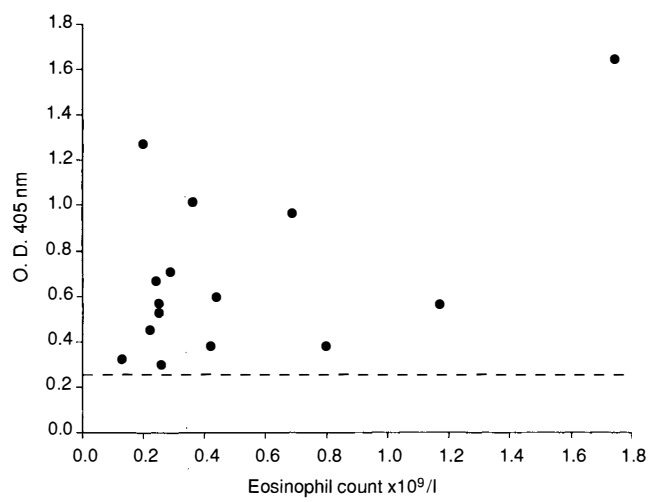

Fig. 1. *Plot of optical density against eosinophil count in 15 patients with ocular disease and serological evidence of toxocariasis. The dotted line represents the ELISA positive threshold.*

benign or discovered as an incidental finding on routine medical examination. Thus, toxocariasis may cause visual loss which goes undiagnosed and may therefore be more common than is recognised. Although we showed that the absolute eosinophil count correlates with anti-ES antibody concentration, eosinophilia $>0.5 \times 10^9$/l is very uncommon in patients with ocular toxocariasis and, if this diagnosis is suspected, serum should be sent for laboratory determination of the presence of anti-*Toxocara* ES antibodies.

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Key words: Pars planitis, Retinal granuloma, *Toxacara canis* infection, Uveitis, Zoonoses.

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