EXPERIMENTAL OCULAR LARVA MIGRANS INFECTION IN MICE

INFECCIÓN EXPERIMENTAL EN RATONES CON LARVA MIGRANS OCULAR

STANGOGIANNIS DE, MARVAL H, MORENO DE MM, MARTÍNEZ M, STANGOGIANNIS DC

ABSTRACT

Objective: To characterize the histologic alterations in the ocular globe of mice infected with eggs of Toxocara canis, during both the acute and chronic stages of the infection.

Method: Performance of an experimental, prospective study in vivo, with right and left ocular globes [using 5 groups of 4 mice in each study; 2 white (A/J) and 2 black (C57/BL)], infected by the intravenous injection of 1000 embrionated Toxocara canis eggs. The mice were sacrificed sequentially post infection (3-180 days), the eyes evaluated by conventional microscopic techniques and the histopathology findings recorded.

Results: All the mice revealed some degree of ocular damage in one or both eyes. The retina was the most affected layer with edema, hemorrhage and severe degenerative changes seen. Other alterations included inflammation of the cornea, and obliteration of the anterior chamber with fibrinoid material. We also demonstrated changes in the normal histology of the uvea and lens. In only two eyes were segments of larva found in the retina, and in each instance there was no evidence of an inflammatory reaction around them.

Conclusion: Most of the changes seen were not related to the presence of larval forms, suggesting they were due to the effect of excretion-secretion.

RESUMEN

Objetivo: Caracterizar las posibles alteraciones histológicas en el globo ocular de ratones infectados masivamente con Toxocara canis, durante los estadíos agudos y crónicos de la infección.

Método: Se realizó un estudio experimental, prospectivo in vivo, con globos oculares derechos e izquierdos correspondientes a cinco grupos de cuatro ratones cada uno (dos blancos (A/J) y dos negros (C57/BL) infectados por vía endovenosa con 1.000 huevos embrionados de Toxocara canis. Los ratones fueron sacrificados de forma secuencial post infección (3-180 días), se realizó microscopía convencional e histopatología fotografiadas.

Resultados: Todos los ratones mostraron algún grado de daño ocular en uno o ambos ojos. La retina era la capa más afectada con edema, hemorragia y cambios degenerativos severos. Otras alteraciones incluyeron reacción inflamatoria de la córnea, obliteración de la cámara anterior con material fibrinoid de, asimismo, se evidenció cambios en la histología normal de la uvea y del cristalino. En dos ojos de ratones se encontraron segmentos de larva en la retina, sin reacción inflamatoria alrededor de ellos.

Conclusión: La mayoría de las alteraciones no se relacionó a la presencia de formas larvarias, sugi-
INTRODUCTION

There is a group of diseases with certain peculiar characteristics which predominate in tropical zones, and are generally known as tropical diseases (1).

Toxocariasis is a helminth infection common in dogs, but it also affects other mammals including humans, where the parasites exhibit a special behavior giving rise to a different nosological organization, well known as intestinal larva migrans (2,3).

The clinical manifestations of this syndrome appear as persistent and intense blood hypereosinophilia, maintained for over a year and without concomitant symptoms. In addition, it is associated to the formation of granuloma in the posterior pole giving rise to an early state of retinoblastoma inducing the total or partial loss of vision in one or both eyes. It has also been associated to granuloma in the peripheral retina, pars planitis, endophthalmitis and uveitis. Less common expressions include hypopyon, vitreous abscess, optical neuritis, keratitis or secondary strabismus (4).

Many studies have been made in experimental animals with the aim of establishing an animal model to understand the presence of larva migrans, which occurs with increasing frequency (1-5). Nevertheless, this was not the case with experimental ocular toxocariasis. For this reason, at the present time many aspects of this infection are not known such as clear pathogeny, diagnosis and treatment. By way of continuation of the CI-2-0000220/84-96 project, titled «toxocariasis: histopathology and treatment» we set out to study this pathology from the experimental viewpoint to characterize the possible histological alterations in the ocular globe of mice massively infected with Toxocara canis, during the acute and chronic stages of the infection.

SUBJECTS, MATERIAL AND METHODS

The general scheme followed to fulfill the objectives placed the present study within the following categories: Experimental, Prospective in vivo.

RESULTS

Figure 1 corresponds to the image of the ocular structures of a normal mouse. As of the seventh day post-infection, in all the infected animals (white and black mice) we observed histological alterations, mainly in the posterior pole, which intensified as the time of infection increased. The retina was the most affected ocular structure, with the following initial pathological characteristics being observed: edema, vascular congestion, disintegr-
tion of the layers and atypical cellular organizations, particularly in the form of rosettes, in the external and internal nuclear layers (fig. 2). In the animals with infections exceeding two months, the retina displayed intense subretinal and retrolental hemorrhage (fig. 3), folding (fig. 4) and in many cases loss of the constituent layers thereof (fig. 3).

In the black mice (C57/BL) the uveal layer was seriously affected. We observed a cellular pleomorphism of the pigmentary epithelium (fig 5) and the presence of great amounts of extracellular pigments (fig 6) which in some cases were accompanied by a slight inflammatory reaction, mainly polymorphonuclear, i.e., eosinophiles (fig 6). We also found vacuolization of the non-pigmentary epithelium of the ciliary processes (fig 6). However, in the white mice (A/J) the only expression observed in the uveal layer was increased cellularity in the iris and ciliary processes.

In a single case, in addition to the serious injuries of the retina, we found deep changes in the anterior pole which exhibited intense edema in the layer of the cornea, with large spaces between the collagen strands and inflammatory infiltration. In addition, this animal exhibited a fiber hyaline pink material which totally obliterated the anterior chamber with a granulomatous inflammatory response made up mainly by eosinophiles.

The lens was another ocular structure that exhibited evident alterations in its normal morphology such as: vacuolization and in some cases atrophy of the anterior epithelium. In spite of the alterations derived from the Toxocara canis infection, only two mice (one white, one black) exhibited segments of larvae without any inflammatory process around them.
In none of the studied animals we observed peripheral granuloma in the posterior pole or retro-lental hyaline membranes.

**DISCUSSION**

The infection with *Toxocara canis* in A/J and C57/BL mice caused important histological alterations in the cellular structures of the eye, which became evident from the seventh day post-infection and were predominantly located at the level of the posterior pole.

The retina was the most affected ocular structure, the first expression being an edematization which advanced as the time of the infection extended, until its layers finally disintegrated after the cellular elements became disorganized. These alterations were accompanied by a congestion of the retina vessels and extensive hemorrhage, mainly at the level of the subretinal and retro-lental space. These results match the findings of those who affirm that the retina is the site of impact of *Toxocara canis* infection (6-8). At the same time, Watzke RC et al found retinal alterations similar to those obtained in our study, jointly accompanied by perivasculitis, retinal nodules and uveitis (8).

Similarly, our study matched those which indicated that the alterations by *Toxocara canis* affect not only the retina but other structures of the posterior pole (19). On the other hand, the anterior pole is also affected such as those observed in the cornea, the lens and the anterior chamber where we noticed histological alterations of its normal cytological architecture accompanied by intense edema and granulomatous inflammatory response. It is important to emphasize the observed changes in the lens, which is not very often involved in the alterations caused by *Toxocara canis* infection. In our case, the lens was seriously affected, finding vacuolization of the anterior epithelium, with disintegration of fibers of its central core, an occurrence which is not described in the literature. Probably these alterations are due to the opacity of the lens (1). Another important aspect of this ocular pathology involving the lens was its atrophy, observed only in a single case and not described either in the reviewed literature (1).

The difficulty involved in diagnosing ocular larva migrans lies mainly in the visualization of the larva of *Toxocara canis* in the ocular tissue. However, after the infection of C57/BL mice with *Toxocara canis* eggs in a study made by Ghafoor et al, 26 larvae were found in the retina and the retinal vessels (7). In our investigation, only in two cases we observed larvae located in the retina, specifically in the layer of rods and cones, without inflammatory reaction in the periphery. This last finding agrees with other experiments in which where post-inoculation was observed after nine months, apparently viable larvae, without inflammatory reaction in the retina; also the larvae were surrounded by acute inflammatory granulomas or chronic fibrotic granulomas without necrotic appearance (8). These results suggest that the larvae of *Toxocara canis* apparently move through tissue at any stage of the infection, with some being trapped. This migratory capacity of the larvae was discussed in studies made in rodent brains (10).

The presence of such severe histological alterations and the absence of larvae suggest that this is the consequence of a tissue response involving the

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**Fig. 5: Pleomorphism of pigmentary epithelium.**

**Fig. 6: Vacuolization in the ciliary processes.**
immunological defense mechanisms in the presence of the infection, as occurs in other cases of visceral larva migrans.

It must be emphasized that all the alterations demonstrated in our study were observed generally in both ocular globes but with greater intensity in one. This finding contradicts the observations of those who consider the unilaterality of injuries caused by Toxocara canis infection as the norm, with bilateral infection being the exception (9,11,12).

REFERENCES