Immunohistochemical Findings in Eyes of Cats Serologically Positive for Feline Immunodeficiency Virus (FIV)

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With 3 figures and 1 table

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Summary

In this study the eyes of 15 cats in the terminal stage of FIV infection were examined. The findings were compared to those in cats, which were euthanized because of other infectious diseases or for non-infectious reasons. Thirteen FIV-infected cats showed an anterior uveitis by means of light microscopy. No accumulation of retinal lesions were found in FIV-infected cats compared to the other cats examined. Additionally, there were no indications of lesions caused by opportunistic infections. In the posterior segments of the eyes, immunohistochemical examinations proved the plasma proteins C3 and IgG to be predominantly intravascular. The eyes of 11 serologically FIV-positive cats were available for immunohistochemical examination. In all 11 cats at least one of the plasma proteins C3 or IgG could be detected in the extravascular tissue of the anterior uvea. The extravascular presence of plasma proteins within the tissue seemed to be caused by an increased permeability of the vessels due to inflammation. Furthermore, the similar extravascular distribution pattern of IgG and complement component C3 in four cases indicated that immune complexes may play a role in the anterior uveitis of FIV-infected cats.

Introduction

In 1987 PEDERSEN et al. found a new lentivirus in cats which was named feline immunodeficiency virus (FIV). Compared to the human immunodeficiency virus (HIV) infection in humans many similarities in the clinical staging have been found (ISHIDA and TOMODA, 1990).

In HIV infection ocular symptoms occur in 70-100% of the patients in the AIDS-stage of the disease. Apart from the cytomegalovirus retinitis the main ocular findings in humans are cotton-wool spots and retinal haemorrhages which are both symptoms of a microangiopathy syndrome (FREEMAN et al., 1984; JABS et al., 1989). The cotton-wool spots are found on the fundus of the eye and are thought to be caused by a focal ischaemia in the nerve fibre layer (NEWSOME et al. 1984). As there are many
similarities between the two infections the possibility of there being comparable symptoms like cotton-wool spots in the eyes of cats at an advanced stage of FIV infection, was investigated (GEIER et al., 1994).

A few possible reasons for the microangiopathy syndrome in HIV infection are the direct toxic effect of the viral agent, the deposition of immune complexes and disseminated coagulopathy and rheological phenomena (FREEMAN et al., 1984; NEWSOME et al., 1984; PEPSE et al., 1985). In relation to FIV infection in cats conjunctivitis has often been described as part of the systemic mucocutaneous alterations in patients (PEDERSEN et al., 1987; ISHIDA et al., 1988, 1990; NEU, 1989; YAMAMOTO et al., 1989; HOPPER et al., 1989; SHELTON et al., 1990; HUTSON et al., 1991). ENGLISH et al. (1990) found an iridocyclitis in several FIV-infected cats.

The aim of this study was to examine the eyes of serologically FIV-positive cats to find out whether their eyes are affected by FIV infection and whether any changes are similar to those in HIV-infected humans.

Materials and Methods

The eyes of 38 cats were examined. The cats were patients of the Small Animal Clinic in the School of Veterinary Medicine, Hannover. The cats were divided into three groups. Group 1 included all cats which were serologically positive for FIV, group 2 included cats with other infectious diseases and group 3 included cats without infectious diseases. All animals were euthanized because of poor prognosis. The eyes were fixed in 5% neutral-buffered formalin or 3% glutaraldehyde.

Fifteen cats were serologically positive for FIV and in the terminal stage of the disease. All 15 cats were male or male castrated and 11 were older than 4.5 years. So, these cats showed the typical age and sex distribution for FIV-infection (YAMAMOTO et al., 1989). The serological tests were carried out by means of a commercial ELISA (Cite-Combo®, Idexx Corp., Portland, USA). A Western blot was performed additionally by Dr. Egerink. In the FIV-group two cats were also serologically positive for feline leukemia virus (FeLV) antigen (Cite-Combo®, Idexx Corp.). one cat suffered from upper respiratory tract disease and another one from feline infectious peritonitis (FIP). The FIP was diagnosed clinically by the effusion pathognomonic for this disease and by histopathological examination.

The eyes of 13 cats with other infectious diseases were also examined, five of these cats being older than 5 years. Within group 2 seven cats suffered from feline infectious peritonitis, three cats from feline leukemia virus infection, two cats from upper respiratory tract disease and one from both feline infectious peritonitis and feline leukemia virus infection.

Furthermore, the eyes of 10 cats which were euthanized for non-infectious reasons, mostly because of trauma, were examined. In group 3 the age of the cats was almost identical to those of the FIV-infected cats. Eight cats out of 10 were older than 5 years. All of the cats with the exception of four from groups 2 and 3 were European short hairs.

The eyes of all 38 cats were examined by light microscopy. Due to the fixative used the eyes from 26 cats were available for immunohistochemistry. The avidin-biotin-complex (ABC) method was performed by using polyclonal antisera against feline IgG (rabbit anti-cat, Nordic Immunology, Tilburg, the Netherlands) and complement component C3 (rabbit anti-cat, Institute of Virology, University of Utrecht, the Netherlands). In order to interpret the findings it was necessary to compare the reactions for IgG and C3 within the same locations. Therefore, serial sections were stained for IgG and C3.

Results

Light microscopic findings

Degenerative alterations of the retina were found in all groups. The most common alteration was a cystoid atrophy. An infiltration of inflammatory cells in the retina could only be found in one case of FIP. In an unclear case of a chronically ill cat a retinal vasculitis was observed. In the FIV-infected cats no infiltration of inflammatory cells in the retina was seen. Lymphosarcoma were found in the chorioidea of two FeLV-infected cats, one of them being FIV-infected as well. Inflammation of the
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Fig. 1. Diffuse infiltration of mononuclear cells in a ciliary body. Magnification: x 175

Table 1. Extravascular reaction for IgG and C3 in the anterior segment (iris/ciliary body)

<table>
<thead>
<tr>
<th>Positive extravascular reaction for</th>
<th>FIV-infected cats (n=11)</th>
<th>Cats with other infectious diseases (n = 7)</th>
<th>Cats without infectious diseases (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C3</td>
<td>10</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>IgG</td>
<td>9</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

anterior uvea was found in three cats of group 2 and in one cat of group 3. In the FIV-infected cats inflammation of the anterior uvea was more common than in the other cats and was diagnosed in 13 out of 15 FIV-infected cats. In most cases a diffuse infiltration of both lymphocytes and plasma cells was observed (Fig. 1). A perivascular accumulation only occurred in some eyes.

**Immunohistochemical findings**

The eyes of 26 cats were available for immunohistochemical examination, 11 of
these cats being FIV-infected. IgG or C3 was detected in the extravascular tissue of the posterior segment in only two cases. In one cat with FIP the retina and chorioidea were affected. The other cat was FIV-infected and the extravascular presence of C3 and IgG in the retina was caused by retinal bleeding. In the anterior segment the extravascular presence of the plasma proteins was more common (Table 1).

Positive extravascular reactions for the plasma proteins in the iris and ciliary body were mainly located around vessels and in the processes of the ciliary body. The extravascular reactions were more often found in the ciliary body than in the iris. Different distribution patterns and degrees of reaction were seen. In the iris depositions of IgG and C3 were found predominantly perivascularly whereas the surrounding tissue hardly showed any reaction for the plasma proteins (Fig. 2). In the ciliary body a more diffuse kind of distribution pattern was seen (Fig. 3) and different degrees of deposition were observed.

Discussion

Light microscopic findings

In the posterior segment only a few signs of inflammation could be found. The predominant findings in the retina were degenerative alterations, especially cystoid degeneration. These alterations are found in old cats (SCHAFFER, 1992). Due to the fact that even an 8-month-old cat showed degeneration, changes other than those which are age-related had to be considered. There were no indications for physical or toxic influences in any case. Furthermore, there were no signs of a nutritional lack of taurin. One possible reason for the degenerative changes may be alterations in the intraocular pressure. Glaucoma is a common reason for secondary atrophies of the retina (SCHAFFER, 1992), but there were no indications of glaucoma in the clinical examination by means of applanation tonometry (tonopen®, Mentor O. & O. Inc., Norwell, USA). Signs of acute inflammation were rarely seen in any group. One case
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Fig. 3. Diffuse deposition of C3 in a ciliary body. Magnification: x 350

of severe chorioretinitis was caused by FIP. The reason for one case of retinal vasculitis in a chronically ill cat remained unclear. Involvement of the retina in a generalized disease of unknown aetiology was suspected.

Lymphosarcoma occurred in the chorioidea of two FeLV-infected cats. It was very likely that these tumours were induced by the FeLV infection.

The findings in the anterior segment were different in the three groups. Thirteen out of 15 FIV-infected cats showed an iridocyclitis. In most cases both lymphocytes and plasma cells were observed. Due to these findings an association between FIV infection and anterior uveitis seems to be very likely. Such an association was also noted by English et al. (1990). Nevertheless, the number of cats examined was not large enough to make any statistically significant comparisons between the three groups. Perivascular aggregations of lymphoid cells were interpreted as accessory lymphatic tissue, as described by Peiffer (1980). It was not possible to identify the antigen causing the infiltration. After a primary disturbance of the blood-eye barrier, lymphocytes not specific for the causative antigen can reach the eye (Blisner et al., 1979). The uveitis observed in most cases seemed to be the typical recurrent kind of inflammation, as described in many species (Streilein, 1990; Swanston, 1990). It was not possible to determine the causative agent, but its occurrence in most FIV-infected cats suggests a relation to this infection. It remained unclear whether FIV is directly involved or whether indirect mechanisms like secondary infections or alterations in the immune system caused the uveitis.

Within the other groups inflammation was not that common. All three cats with iridocyclitis in group 2 suffered from FIP, which is well described for this disease (Doherty, 1971; Campbell and Reed, 1975; Pedersen and Boyle, 1980; Pedersen, 1988; Kellner and Litschi, 1989).

Immunohistochemical findings

In all groups the immunohistochemical examinations proved the plasma proteins C3 and IgG to be predominantly intravascular in the retina and chorioidea. At least
one of the plasma proteins C3 or IgG could be detected in the extravascular tissue of
the anterior uvea in all 11 FIV-infected cats. The presence of plasma proteins in the
tissue seemed to be caused by an increased vascular permeability due to inflammation.
Furthermore, the similar extravascular distribution pattern of IgG and complement
component C3 accompanied by a moderate degree of reactivity indicated a deposition
of immune complexes in four of the 11 FIV-infected cats. It seemed to be possible that
these immune complexes had increased or even caused the inflammations. In the other
FIV-infected cats the extravascular reaction for plasma proteins was interpreted as an
extravasation of plasma only. In the 15 serologically FIV-negative cats the plasma
proteins were found in the extravascular tissue to a much lesser extent. Nevertheless,
the most prominent deposits of C3 and IgG were found in two cats suffering from
feline infectious peritonitis. Depositions of immune complexes are known to be
involved in the pathogenesis of this disease (JACOBSE-GEELS et al., 1980, 1982;
PEDE RSEN and BOYLE, 1980; WEISS et al., 1980; PEDE RSEN, 1988).

Both FIV infection and HIV infection lead to changes as far as the eyes are
concerned. There were, however, differences between the eye alterations in cats and
those described for HIV-infected humans in the terminal stage of the disease. In
humans the most common findings are cotton-wool spots and retinal haemorrhages
caused by a microangiopathy syndrome. Furthermore, opportunistic infections,
especially the cytomegalovirus infection, cause characteristic lesions. In this study no
accumulation of retinal lesions could be found in FIV-infected cats compared to other
cats examined. It remains unclear whether FIV is directly involved in the inflammatory
alterations of the anterior uvea and the suspected deposition of immune complexes or
whether secondary effects are responsible. At least, inflammations of the iris and ciliary
body were more common in FIV-infected than in the other cats. One similarity
between the ocular changes in FIV and HIV infection may be an involvement of
immune complexes, which is suggested in the literature to be related to a micro-
angiopathy syndrome in AIDS.

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