Ocular surface health and tear film dynamics in normal cats and those infected with feline herpesvirus

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Introduction

Feline herpesvirus type 1 (FHV-1) is a leading cause of disease in domestic cats, with approximately 90% of cats being exposed to the virus. Following primary infection, viral reservoirs are formed in the ganglia of sensory nerves, specifically the trigeminal ganglion (TG), which is responsible for sensory input from the face in general, and the eyes in particular. In experimental mouse models, human herpesvirus infection induces loss of astrocytes and demyelination of axons at the trigeminal root entry zone (TREZ) of the pons. Diagnosis and treatment of herpetic disease in cats is difficult, and the disease can only be managed, not cured. Therefore, further research assessing the pathophysiologic mechanisms by which FHV-1 causes disease is critical.

Dry eye is a common disease characterized by decreased quantity or quality of the tear film, which leads to ocular surface disease. It is well understood in many species, especially in humans where decreased tear production has been documented in patients with herpes simplex virus infection. By contrast, dry eye is poorly understood in cats, and relationships between dry eye and herpesviral infection have not yet been investigated. If experimentally shown to be connected, this would be a major cause of increased morbidity in cats with herpetic disease and would result from a currently unrecognized mechanism not addressed with standard antiviral therapy.

Hypothesis

Feline herpesvirus-infected cats will have altered tear dynamics due to neural dysfunction in the lacrimal unit (cornea, conjunctiva and lacrimal glands).

Table 1. Results from antemortem clinical tests and ex-vivo confocal microscopy in FHV-1-naive (specific-pathogen free) cats. Data from cats naturally infected with FHV-1 to follow.

<table>
<thead>
<tr>
<th>Test</th>
<th>Mean</th>
<th>Standard deviation</th>
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<tbody>
<tr>
<td>Spontaneous blink rate (blinks/min)</td>
<td>14</td>
<td>7</td>
</tr>
<tr>
<td>Basal Schirmer tear test (mm/min)</td>
<td>21</td>
<td>3</td>
</tr>
<tr>
<td>Stimulated Schirmer tear test (mm/min)</td>
<td>23</td>
<td>3</td>
</tr>
<tr>
<td>Tear film breakup time (secs)</td>
<td>11.8</td>
<td>2</td>
</tr>
<tr>
<td>Corneal touch threshold (cm)</td>
<td>3.0</td>
<td>0.5</td>
</tr>
<tr>
<td>Corneal endothelial cell density (cells/mm²)</td>
<td>2247</td>
<td>163</td>
</tr>
<tr>
<td>Corneal anterior stromal cell density (cells/mm²)</td>
<td>587</td>
<td>27</td>
</tr>
</tbody>
</table>

Results

Central Nervous System Assessments

The TG and TREZ were histologically unremarkable in all SPF cats, and no FHV-1 antigen was detected via IHC. Some cats had small amounts of lipofuscin in scattered neuronal cell bodies (an incidental aging change).

Figure 1. Schirmer tear test (A), tear film breakup time (B), slit lamp examination (C) and confocal microscopic image of a nerve fiber within the anterior stroma of the cornea of a FHV-naive cat (D).

Figure 2. Sampling locations for extraction of the trigeminal ganglion (A) and trigeminal root entry zone (B). Samples from each side were fixed in formalin for histopathology or in DNA/RNA preservation solution for PCR. Trigeminal ganglion from a FHV-naive cat: Hematoxylin and eosin (C); FHV-1 immunohistochemistry, demonstrating lack of antigen. Hematoxylin counter stain (D). Scale bars = 100 µM

Discussion

Similar data are currently being collected from FHV-exposed cats and will be statistically compared to the data presented here. Corneal nerve fiber density is currently being processed for FHV-naive and exposed cats. FHV DNA in the trigeminal ganglion, trigeminal root entry zone and conjunctiva is currently being quantified using PCR. Corneal, lacrimal glands, and conjunctiva from FHV-1-naive and exposed cats are currently being assessed using histopathology and immunohistochemistry.

We expect FHV-infected cats will have lower basal tear production, corneal sensitivity and corneal nerve density. Results of this study will provide important insights into the pathogenesis of herpetic disease in cats and morbidity at the ocular surface and augment management strategies for cats with FHV and dry eye.

Further research will be required to collect data specifically from a subset of FHV-exposed cats and concurrent decreased tear production. This group will allow us to compare clinical parameters, nerve fiber density and histological characteristics among FHV-1 naive, FHV-1 exposed but unaffected, and FHV-1 exposed and affected cats.

Acknowledgments

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References