DIAGNOSIS OF CORONAVIRUS AND FIP IN CATS

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Although most cats infected with FCoV remain perfectly healthy, around one in ten cats infected with FCoV develops feline infectious peritonitis (FIP), usually at the first exposure. FIP is now believed to be the leading infectious cause of cat death, yet it remains one of the most difficult of conditions to diagnose. The most effective treatment, feline interferon omega, isn’t available in the USA. There is currently only one FIP vaccine, Primucell® and, like all vaccines, it is not 100% effective.

After infection with FCoV, there are 4 possible outcomes:

1. develop FIP (about 10% of cats)
2. become transiently infected, shed FCoV for 2 – 3 months, become seropositive, stop shedding virus, become seronegative. Be susceptible to re-infection. (Most cats.)
3. become a healthy lifelong carrier cat (13%)
4. there is a tiny minority of cats who are naturally resistant to FCoV infection

This manuscript is about the first of these outcomes – the development of FIP.

STEP 1 DIAGNOSIS:
CLINICAL SIGNS AND HISTORY SUGGEST FIP

Clinical signs suggest to you a possibility of FIP: e.g. ascites, pleural effusion, weight loss, chronic mild pyrexia of unknown origin, icterus, intraocular signs, neurological signs.....

If you understand that FIP is an immune-mediated vasculitis it becomes easier to understand how it is able to manifest with so many varied clinical signs. Any blood vessel to any organ can be affected and the clinical signs will result from damage to that organ. FIP is generally defined as either "wet" (effusive) or "dry" (non-effusive) but neither is clear-cut and an effusive case can become non-effusive or vice versa. Effusive FIP is the more acute condition – occurring within 4-6 weeks of a stressful event in the cat’s life, whereas non-effusive FIP can incubate for months to years. In effusive FIP, many blood vessels are affected, allowing fluid to leak out into the abdomen or thorax or both. Thus the cat presents with ascites or pleural effusion. The ascitic cat may appear to have put on weight, although ribs are usually more palpable. The Orion Foundation call FIP “the purring disease” because the cat may still be bright and eating, though some are dull and anorexic. The temperature of cats with FIP rarely goes above 103°F. A cat with a pleural effusion will present with dyspnoea.

In the more chronic, non-effusive, FIP, fewer blood vessels are affected. The cat loses weight gradually, becomes dull and anorexic. Most cats with dry FIP have palpably enlarged mesenteric lymph nodes and intraocular lesions. Clinical signs will depend on which organs are involved:

♦ liver ➔ jaundice
♦ meninges/hydrocephalus ➔ neurological signs (ataxia, nystagmus, fits, loss of reflexes)
♦ eyes ➔ uveitis, aqueous flare, vitreous flare, retinal vessel cuffing, corneal precipitates, haemorrhage into anterior or posterior chambers

STEP 2 DIAGNOSIS: LABORATORY TESTS

Correct diagnosis is essential, we have found that only 18% of cats clinically diagnosed as having FIP were likely to really have FIP when tested by our FIP profile. There is no such thing as a single “FIP” test and there may never be one – be very wary of any single test which claims to be diagnostic of FIP. The definitive diagnostic test remains histopathology of a biopsy and even then it can be difficult to interpret, when immunohistochemical staining might also be necessary. In our laboratory, we use a careful selection of tests as indicated in table 1.

To diagnose FIP, all the above parameters should be met. If only some are met, consider differential diagnoses carefully. In non-effusive FIP there should also be an enlarged mesenteric lymph node and intra-ocular signs.

Table 1. FIP profile from Companion Animal Diagnostics, University of Glasgow

<table>
<thead>
<tr>
<th>Laboratory result</th>
<th>Effusive</th>
<th>Non-effusive</th>
</tr>
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<tbody>
<tr>
<td>High FCoV antibody titer</td>
<td>Usually</td>
<td>over 640</td>
</tr>
<tr>
<td>High 1-acid glycoprotein (AGP)</td>
<td>Yes (&gt;1500 g/ml)</td>
<td>Over 1000 g/ml</td>
</tr>
<tr>
<td>Non-regenerative anemia (Hct 30 or less)</td>
<td>Possibly</td>
<td>Yes</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>Possibly</td>
<td>Yes</td>
</tr>
<tr>
<td>Neutrophilia with shift to left</td>
<td>Probably</td>
<td>Probably</td>
</tr>
<tr>
<td>Cytology of effusion</td>
<td>Total wbc count &lt; 2.0 x 10^9/l: neutrophils and macrophages. Sterile – no bacteria!</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Raised globulins</td>
<td>In effusion: total protein &gt; 35g/l. If less, it’s not FIP</td>
<td>In plasma, globulins &gt; 40g/l</td>
</tr>
<tr>
<td>Albumin: globulin ratio</td>
<td>In effusion: &lt; 0.4 – FIP very likely</td>
<td>In plasma &lt; 0.4 – FIP very likely</td>
</tr>
<tr>
<td></td>
<td>&gt; 0.8 – FIP very unlikely</td>
<td>&gt; 0.8 – FIP very unlikely</td>
</tr>
<tr>
<td></td>
<td>between 0.4 and 0.8 - FIP possible</td>
<td>between 0.4 and 0.8 - FIP possible</td>
</tr>
</tbody>
</table>
In House Testing

Within your own surgery it should be possible to conduct a number of the tests listed above – for example the albumin:globulin ratio. In a suspect case of effusive FIP, measuring the total protein of the effusion alone may eliminate the possibility of a diagnosis of FIP, for example, in ascites produced as a result of cardiomyopathy the total protein is often less than 5g/l. You can probably measure Hct and may be able to perform a differential or do cytology of the effusion. In her paper (2003), Katrin Hartmann describes the Rivalta test: one drop of 98% acetic acid is added to 5mls of distilled water and mixed thoroughly, a drop of effusion is carefully layered on top, if it disappears and the solution remains clear, the test is negative. If the drop retains its shape, stays attached to the surface or floats slowly down the tube, then it’s positive. Predictive value positive is 0.86, predictive value negative is 0.97.

FCoV Antibody Tests

The indirect immunofluorescent antibody test (IFAT) from the University of Glasgow is the gold standard. It gives an antibody titer that is useful for comparison in sequential testing and contains an internal negative control at each dilution, so that false positive results do not occur. Samples divided into 5 and sent to 5 different laboratories in the USA gave 5 different results (Postorino Reeves, personal communication).

FCoV Virus Tests

RT-PCR detects the RNA of FCoV. Detection of FCoV RNA in the blood or faeces is not diagnostic of FIP, since around 25% of healthy seropositive cats, or animals with non-FIP illness, are also positive. However, positive RT-PCR of an effusion may well be diagnostic of FIP. The usefulness of an RT-PCR which detects replicating virus in peripheral blood mononuclear cells is unclear at time of writing, but will be mentioned in my presentation.

Detection of FCoV in macrophages in an effusion by immunofluorescence is diagnostic of FIP, but a negative result is more difficult to interpret (Hartmann et al, 2003).

STEP 3: TREATMENT

Since FIP is immune mediated, treatment aims at diminishing the immune reaction, usually using quite high doses of prednisolone, as a sliding dose (i.e. 4mg/kg/day for 10-14 days, reducing to 2 mg/kg/day for 10-14 days, and so on). Until recently, FIP was incurable and so-called “recovered” cats were probably simply misdiagnosed. However, in Europe, feline interferon omega (Virbagen Omega®) has been introduced which has effected a cure in around 25% of cats and remission in others. Unfortunately, human interferon doesn’t have a similar efficacy.

<table>
<thead>
<tr>
<th>Table 2. Interferon Omega protocol</th>
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<tbody>
<tr>
<td><strong>Wet FIP</strong></td>
</tr>
<tr>
<td>Prednisolone: 2mg/kg s.i.d.</td>
</tr>
<tr>
<td>reduce to 0.5mg/kg after remission</td>
</tr>
<tr>
<td>Virbagen Omega: 1M IU s/c e.o.d.</td>
</tr>
<tr>
<td>reducing to once weekly if remission occurs</td>
</tr>
<tr>
<td><strong>Dry FIP</strong></td>
</tr>
<tr>
<td>Prednisolone: 2mg/kg s.i.d.</td>
</tr>
<tr>
<td>reduce to 0.5mg/kg after remission</td>
</tr>
<tr>
<td>Virbagen Omega: 50,000 i.u. per cat orally s.i.d.</td>
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</tbody>
</table>

Watari et al (1998) describe remission of 2 cases of FIP using thromboxane synthetase inhibitors: dose - ozagrel hydrochloride 5 mg/kg bid.
For further information on FIP treatment, visit www.catvirus.com and www.felinecoronavirus.com (abstracts page for the Ishida abstract).

HOW TO SUBMIT SAMPLES FOR AN FIP PROFILE

Samples to Send

**Effusive FIP**
- 1-2 ml effusion in plain tube
- 1-2 ml effusion in EDTA tube
- 1ml heparin blood

**Non-effusive FIP**
- 2 air-dried blood smears
- 1 ml EDTA blood
- 2 x 1ml heparin blood

Send samples by air mail to:
Companion Animal Diagnostics, University of Glasgow Veterinary School, Bearsden, Glasgow, G61 1QH, United Kingdom
Tel: + 44 (0)141 330 5777
Fax: + 44 (0)141 330 5748
Email: Companion@vet.gla.ac.uk
www.gla.ac.uk/companion

REFERENCES


INFORMATION FOR CLIENTS

- http://www.catvirus.com
- Orion Foundation
- http://www.devonheaven.com/users/orionsociety/