Update on diagnosis of feline infectious peritonitis (FIP)

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Plan

• What causes FIP?
• Clinical FIP disease
• Definitive diagnosis vs presumptive diagnosis
• Diagnostic tests available to us

FIP is a fatal systemic disease caused by feline coronavirus (FCoV) infection

Generally:
FCoV infection is very common esp. multicat households
but
FIP is uncommon (1-5% FCoV infected cats)

FCoVs: feline coronaviruses

• LARGE enveloped RNA viruses
• Replication of genome prone to mistakes

Pathogenesis of FIP?

VIRAL FACTORS

Mutations allow more efficient replication within monocytes & macrophages → FIP

HOST FACTORS

Immune response (humoral immune response → ↑FIP), genetics/breed, age

ENVIRONMENTAL FACTORS

Level of stress (e.g. overcrowding), degree of FCoV exposure → ↑FIP

Diagnosis – one of the big problems with FIP

......a single minimally invasive FIP test to diagnose FIP in all cases does not exist
**Definitively** diagnosing FIP.....

Histopathology + immunological staining of FCoV antigen in lesions = immunohistochemistry = regarded as gold standard for FIP diagnosis

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**Presumptively** diagnosing FIP....

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**Clinical signs**

- Signs of effusive (wet) or non-effusive (dry) disease
- Overlap can be seen
- Neurological & ophthalmic examination
- Progressive disease – re-examine sequentially

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**Wet or effusive FIP**

< 80% FIP cases esp. young cats
- acute disease; progresses in wks
- peritoneal / pleural / pericardial effusions
- fever, anorexia, lethargy, weight loss
- jaundice
- ocular & neurological signs less common

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**Historical factors**

- Young cats (< 3 yrs; esp < 1 year) but also cats > 10 yrs
- Often multicat household history
- Pedigrees > non-pedigrees – certain breeds?
  - e.g. British shorthair, Abyssinian, Rexes in Oz study
  - Birmans, Ragdolls, Bengals, Rexes in US study
- Recent history of stress?
  - e.g. neutering, rehoming, change in grouping, vaccination

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**Signs of effusive (wet) or non-effusive (dry) disease**

Overlap can be seen

Neurological & ophthalmic examination

Progressive disease – re-examine sequentially
Dry or non-effusive FIP

more chronic disease course; can be months
fever, anorexia, lethargy, weight loss
ocular or neurological signs in nearly half of cases
renomegaly / irregular kidneys
mesenteric LNs
jaundice (skin)

Haematology

Non-specific – can be normal!

6 month MN Russian Blue with dry neurological FIP

Lymphopenia: 55-77%
Neutrophilia: 39-55%

Haematology

5 month ME Scottish Fold with wet (thoracic) FIP

Lymphopenia: 55-77%
Mild to moderate non-regenerative anaemia: 37-54%

Biochemistry

5 month ME Scottish Fold with wet (thoracic) FIP

Hyperglobulinaemia: 60% usually with ↓ or low-normal albumin
Hyperlirubinaemia: 21-36% esp. wet FIP, worsens with FIP disease progression ± ↑ liver values (ALP, GGT, ALT)

Biochemistry

7 month ME British Shorthair with wet (thoracic) FIP

Hyperglobulinaemia with ↓albumin:globulin ratio (A:G ratio); < 0.4 – FIP likely
Hyperlirubinaemia: ALP ‘normal’, ALT↑
Biochemistry

AGP = α1 acid glycoprotein
- major feline acute phase protein made in liver under the influence of cytokines released at site of inflammation
- FIP cases often have markedly elevated AGP levels
- not 100% specific; terminal FIV, haemoplasma infection!

Value of α1-acid glycoprotein in the diagnosis of feline infectious peritonitis

S. Bats, D.J. Edmundson, D.R. Adey, C.P. Lawrence, G. Jessell

Biochemistry

FIP diagnosis – get fluid if you can as it helps!

• Re-examine, look for effusions

Effusion analysis: peritoneal or pleural

1 year MN British Shorthair with wet (peritoneal) FIP

- Usually viscous, yellow: exudate or modified transudate
- High protein >35 g/l with >50% globulins:
  low (<0.4) A:G ratio like in serum
- Often poor cellularity:
  1.6 – 20 x 10^9/l: macrophages & non-degenerate PMNs

Effusion analysis: peritoneal or pleural

7 month ME British Shorthair with wet (thoracic) FIP

- Usually viscous, yellow: exudate or modified transudate
- High protein >35 g/l with >50% globulins:
  low (<0.4) A:G ratio like in serum
- Often poor cellularity:
  1.6 – 20 x 10^9/l: macrophages & non-degenerate PMNs

Performances of different diagnostic tests for feline infectious peritonitis in challenging clinical cases

- FIP diagnosed by +ve immunological staining of FCoV Ag
- Serum AGP had 100% sensitivity & specificity

FIP cases tend to have high CoV titres but overlap between FIP & non-FIP cases

~10% FIP cases are CoV antibody –ve

FIP diagnosis by +ve immunological staining of FCoV Ag

FIP cases had 100% sensitivity & specificity

NB. Serum or effusion AGP

? FIP > 1.5
Normal < 0.48

Biochemistry

FCoV Serology

Detects antibodies to any CoV, including maternally derived antibodies

<table>
<thead>
<tr>
<th>FCoV titre</th>
<th>No. of Cases</th>
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<tr>
<td>FIP</td>
<td>Non-FIP</td>
</tr>
<tr>
<td>0</td>
<td>2</td>
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<tr>
<td>10</td>
<td>29</td>
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<tr>
<td>2560</td>
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</tr>
</tbody>
</table>

FIP n=7

Non-FIP n=4

Detects antibodies to any CoV, including maternally derived antibodies

FIP cases had 100% sensitivity & specificity

Non-FIP cases had 100% sensitivity & specificity

~10% FIP cases are CoV antibody –ve
Reverse-transcriptase PCR

RT-PCR detects FCoV RNA
RT-PCR = reverse transcriptase PCR
FCoV RNA → cDNA → PCR.
If real-time RT-PCR, then also quantifies FCoV = qRT-PCR
Current PCRs detect ANY FCoV (i.e. not FIP specific)
Where shall we look for FCoV via qRT-PCR?....?

qRT-PCR: where shall we look?

Tissues & effusions qRT-PCR – another piece of the jigsaw, but not a definitive diagnosis

Histopathology

Ante-mortem (ultrasound guided, laparoscopy or exploratory laparotomy) or post-mortem biopsies
Specific – if consistent changes present, likely to be FIP?
Sensitivity – may miss lesions with small biopsies & sometimes typical lesions not seen (even with large biopsies)

Performances of different diagnostic tests for feline infectious peritonitis in challenging clinical cases

BLOOD

FIP tissues usually +ve (correlates with pathological changes) with far higher FCoV levels than non-FIP tissues (which are usually, but not always, -ve)

TISSUES

Most FIP effusions are +ve (85% in UoB study) and most non-FIP effusions are -ve (100% UoB study)

EFFUSIONS – wet FIP cases only

5/8 FIP cases did not have totally typical lesions; here immunological staining used for diagnosis

FIP diagnosis….it’s still not easy 😐

• Diagnosis – in most cases, histopathology &/or immunostaining are reliable for definitive diagnosis
• Exceptions occur – look at all results combined to help you decide if FIP is likely
• Sometimes a presumptive diagnosis is all that you can get – becoming confident in making that call is important

Immunological staining: FCoV antigen (Ag) in macrophages

Biopsies: in association with pathology - specificity good, sensitivity may be limited by varied distribution of FCoV Ag to stain up
Effusions: needs to be done on relatively fresh sample, generally specificity good, sensitivity an issue if antibodies mask FCoV Ag or not much Ag present

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