Terminal feline infectious peritonitis in a domestic short hair cat: a case report

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Abstract

A year old spayed female DSH cat was presented to the Milford Veterinary Clinic on April 1, 2019 with a recent history of sneezing episodes, lethargy and moist eyes with no apparent health issues earlier. In-house thoracic radiographs revealed an extensive enhanced radiopacity area, suggestive of growth, such as lymphoma. Therefore, following quick oxygen recoupment and subcutaneous fluid therapy, with the owner's consent, the case was referred to the Oakland Veterinary Emergency/Critical Care (OVECC). Thoracentesis revealed pleural effusion, consistent with the fatal effusive (wet) form of viral feline infectious peritonitis (FIP). On extraction of voluminous viscous exudate with fibrin clots, the respiratory efficiency improved markedly. Cardiac involvement eliminated through echocardiography, phyllite IV fluid therapy in the night was followed with routine IV fluid therapy next morning. The clinical condition improved, and the pet was transferred to the owner's care with advisory on April 3, 2019. After uneventful two days, the pet with aggravated respiratory distress was referred back to the OVECC on 8th April, 2019. In view of the poor prognosis with recurrent bouts of highly embarrassing pleural effusion, deteriorating clinical condition, the owner opted for humane euthanasia.

Keywords: Feline infectious peritonitis, Viral, Pathogenesis, Treatment, Prognosis, Euthanasia

Immune-augmented feline infectious peritonitis (FIP) is the end-result of infection of the macrophages by mutant strains of endemic feline corona virus (FECV), culminating almost invariably in mortality (Foley and Leutenegger, 2001). FIP is clinically manifested mainly in the effusive wet form, or non-effusive dry form, the latter commonly involving the nervous system (Rand *et al*., 1994). Cat specific Type I FECV, RNA virus is more prevalent (Benetka *et al*., 2004),and cats from catteries/ multiple-cat environment are at increased risk of oral infection following ingestion of fecal contaminated food (Foley *et al*.,1997).

FIP may be associated with neurological dysfunction. CNS involvement with inflammatory episodes, mostly affecting young cats below 4 years age (Rand *et al*., 1994), pure-bred males more vulnerable (Norris *et al*., 2005). The well-documented reports (Marioni-Henry *et al*., 2004; Barnes *et al*., 2004; Boettcher *et al*., 2007) chronicle multiple forms of neurological disorder: seizures, abnormal behavioral profile/postural responses, cranial nerve deficits, and ataxia in the affected cats. Wide ranging clinical signs: anorexia, weight loss, debility, lethargy, fever, pica, and ocular lesions (Rand *et al*., 1994) indicate involvement of diffuse areas of CNS (Diaz and Poma, 2009).

Critical appraisal of the complete case history, systematic physical examination and proper interpretation of the diagnostic panel data: CBC, serum biochemical profile, definitive demonstration of anti-corona virus antibodies in the CSF and serum, imaging protocols: radiography, CT scan, and MRI remain the mainstay of diagnosis.

The pathogenesis of feline infectious peritonitis has not been completely elucidated till date (Olsen, 1993; Perlman, 1998). Recent studies have established the role of several viral proteins,varying receptor specificity/genomic differences between feline enteric corona viruses (FECVs) and FIP viruses (FIPVs). FECVs replicate mainly in the intestinal epithelium and are shed in the feces, but FIPVs replicate in the monocytes.

Key events in the pathogenesis of FIP are accelerated systemic infection following RNA viral replication in the monocytes, and transformation of the infected monocytes → macrophages. The bio-activation significantly contributes to pathogenesis manifested in the form of vasculitis, body cavity effusions and inflammatory fibrinous lesions (Kipar and Meli, 2014). The host's genetics and immune status also play an important role (Brown, 2009).

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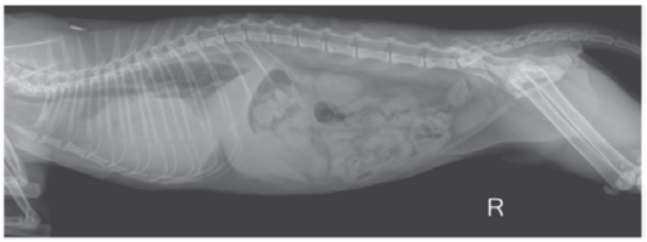
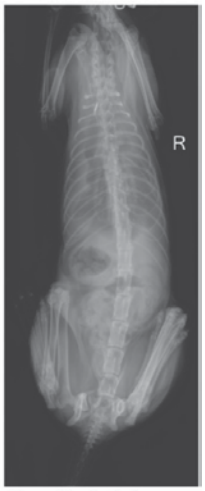


Right Lateral View: Note the lung position and radiopacity in thoracic cavity

Case History and Observations



Dorso-Ventral view

Female DSH cat was presented to the Milford Veterinary Clinic on April 1st, 2019 with a recent history of sneezing episodes with running nose, lethargy and watery eyes, but no apparent health issues in the past. Physical examination: RT 103.2^0 F, HR 210/ minute, RR 32/ minute, BCS 2/5, CRT < 2 seconds, and the visible mucous membranes pink. The pet exhibited labored breathing and appeared slightly dehydrated. In-house thoracic radiographs revealed an extensive area of increased opacity, suggestive of possible growth. Oxygen therapy was initiated for interim relief from dyspnea. Supportive fluid therapy (100 ml) was given SC+ Vitamin B_{12} (10 ml) SC at multiple sites. Then with the owner's informed consent the case was referred to the Oakland Veterinary Emergency/ Critical Care (OVECC), Bloomfield Hills, MI.

1. Hemato-biochemical profile (OVECC).

Table 1A. Patient's hematological profile on April 1, 2018, 8 PM

Parameter (units)	Value	Reference interval	Status
TEC ($1x10^6$/µL)	3.03	6.54-12.2	L
Hematocrit (%)	11.5	30.3-52.3	L
Hemoglobin (g/dL)	3.6	9.8-16.2	L
MCV (fL)	38.0	35.9-53.1	N
MCH (pg)	11.9	11.8-17.3	N
MCHC (%)	31.3	28.1-35.8	N
RDW (%)	30.2	15.0	H
Reticulocyte (%)	20.3	3.0-50.0	N
Reticulocyte-Hb (pg)	13.8	13.2-20.8	N
TLC ($1x\ 10^3$/µL)	13.98	2.87-17.0	N
Neutrophil (%)	84.7		
Lymphocyte (%)	10.4		
Monocyte (%)	2.8		
Eosinophil (%)	1.9		
Basophil (%)	0.2		
Neutrophil ($1x10^3$/µL)	11.84	2.30-10.29	H
Lymphocyte($1x10^3$/ µL)	1.45	0.92-6.88	N
Monocyte ($1x10^3$/µL)	0.39	0.05-0.67	N
Eosinophil ($1x10^3$/µL)	0.27	0.17-1.57	N
Basophil ($1x10^3$/µL)	0.03	0.01-0.26	N
Thrombocyte ($1x10^3$/ µL)	280	151-600	N
CBC Auto Analyzer			

Table 1B. Patient's blood biochemical profile on April 1, 2018, 8.24 PM (OVECC).

Parameter (units)	Value	Reference interval	Status
Glucose (mg/dL)	148	74-159	N
Creatinine (mg/dL)	0.8	0.8-2.4	N
BUN (mg/dL)	18	16-36	N
BUN/ Creatinine ratio	20		
Phosphate (mg/dL)	7.1	3.1-7.5	N
Total calcium (mg/dL)	9.0	7.8-11.3	N
Total protein (g/dL)	8.1	5.7-8.9	N
Albumin (g/dL)	2.5	2.3-3.4	N
Globulin (g/dL)	5.6	2.8-5.1	H
A/G ratio	0.4		
ALT (U/L)	25.0	12-130	N
ALKP (U/L)	14.0	14-111	N
GGT (U/L)	0.0	0-4	N
Amylase (U/L)	738.0	500-1500	N
Lipase (U/L)	367.0	100-1400	N
Total Bilirubin (mg/dL)	0.2	0.0-0.9	N
Cholesterol (mg/dL)	164.0	65-225	N
Na^+ (mmol/L)	158	150-165	N
K^+ (mmol/L)	3.9	3.5-5.8	N
Cl^- (mmol/L)	121.0	112-129	N
Osmotic Ca	327.0		

Blood Chemistry Auto Analyzer N: Normal, L: Low, H: High

II. a/t FAST scan on 1st April, 2019

Pleural fluid accumulation (bilateral) with echogenic swirling was clearly perceptible, with no peritoneal/ pericardial fluid.

III. Echocardiogram

The image, with no evidence of LV hypertrophy or chamber enlargement, is absolutely normal. However, some residual pleural effusion is noted with evidence of poorly inflated lung near the dorsal aspect of right atrium. The left apical four-chamber view revealed a pocket of highly cellular thick fluid. The cardiology specialist's inference was some unidentified pulmonary disease: FIP/ lymphoma/ diaphragmatic hernia with confirmed non-existence of cardiovascular disorder

I. Pleural effusion cytology April 2, 2019 (OVECC). This test, aimed to rule out pathogenic infection, has not detected any bacterial rods or cocci; only a few red blood cells and white blood cells seen. TS of fluid is 5.2.

II. Abdominal fluid (ascites) analysis with cytology on April 2

2019 (IDEXX Lab). Aspirate: 1.5 ml straw colored turbid (protein 6 g/dL), RBCs < 0.1x 10^6 µL. Microscopic picture: evidence of increased cellularity: the nucleated cell count (1 x 10^3/ µL) 3.83 The stained slides reveal 94% pyknotic to moderately degenerated neutrophils, and the remaining 6% macrophages (some exhibiting phagocytized cell debris). No infectious agent discernible. Pathologist's interpretation: mild neutrophilic/ mixed white cell inflammatory response, suggestive of low-grade peritonitis.

Treatment

The diagnostic panel data indicate the strong possibility of feline infective peritonitis (FIP), though presently concurrent lymphoma cannot be ruled out. The treatment at the OVECC is scheduled accordingly.

April 1, 2019 (9 PM)

Flow-by oxygen started, followed by IM injection of butorphanol. The right thorax is clipped; the skin cleansed with alcohol. After intra-dermal injection of the local anesthetic, lidocaine, the area sanitized with chlorhexidine and alcohol. Thoracentesis with a small 18g IV catheter, cranial to the 9th rib: total 79 ml viscous bright yellowish, mountain dew colored fluid aspirated off. The same procedure repeated on the left thorax: total 62 ml fluid of identical color and consistency with fibrin clots removed. The patient is anemic with low TEC and Hb (Table 1), but the hepatic function (albumin, ALT, ALKP values normal) and renal function (BUN, creatinine values normal) remain unimpaired (Table 2). Post-thoracentesis BP: 72 mm-mercury; radiographs: substantially reduced quantity of pleural effusion is reflected clinically in significantly improved respiratory efficiency. On assured elimination of cardiac involvement in the electrocardiogram profile, phyllite IVF therapy was given @ 10 ml/ hr. The BP at one hr interval (11 PM): 106 mm-mercury; SpO_2 95%.

April 2, 2019 (3 AM): Rectal temperature 104.2^{0}F, BP 84 mm-mercury;SpO_2 96%.6 AM: Recheck radiographs: slightly more pleural effusion visible in the left cranial thoracic region; air bubbles in the pleural effusion observed in the right thoracic region; a/t FAST scan: no significant pockets of accumulated fluid visible, reminiscent of the post-chest tapfast scan. Most of the pleural fluid is observed in the cranial thorax near the heart.

Physical examination: RT 105.2^0 F, HR 224, RR 74.

Respiratory efficiency increased; slightly lethargic but alert and responsive; Abdominal palpation SNP, eating well. CP auscultation normal heart rate and rhythm with no murmur; right/ left thorax normal BV sounds dorsally, quieter BV ventrally; BP 72 mm-mercury. Total 20 ml fluid infused IV slowly in 15 minutes, BP 80 mm-mercury.

April 3, 2019

10 AM: The OVECC formal discharge instructions with detailed homecare advisory and need-based recheck guidelines issued to the pet owner. A copy with details of diagnosis and treatment was received in the home clinic.

April 8, 2019

4:15 PM Cat was referred back to the OVECC with accentuated respiratory distress, apparently because of pleural re-effusion. However, in view of the poor prognosis, fast deterioration in the clinical condition, and not wanting Athena to suffer further, the owner opted for humane euthanasia (TVC, Propofol 3 ml IV, Fatal 3 ml IV).

Discussion

The primary differentials in the young feline patient FIP and lymphoma. In the Cardiology specialist's report, the normal echocardiograph profile is emphasized. Markedly increased radio-density over the heart, in both R/L and L/L views suggest the

possibility of underlying pulmonary disease. Scanning of the 3-view thoracic survey radiograph by the Radiologist highlights the dorsal displacement of lung parenchyma, and the cardiac silhouette away from the sternum because of abnormal accumulation of gas-filled fluid in the pleural spaces. The alveolar pattern in the bilateral cranial lung lobes, and the pulmonary vascular histo-architecture are intact. The soft tissues juxtaposed in the R/L thorax appear indurated. These pathomorphologic anomalies are highly suggestive of pleural effusion associated with an inflammatory response with exfoliated neutrophils/ mixed white blood cells.

Murphy *et al*. (2018) demonstrated that the synthetic nucleoside analog GS-441524 (C_{12} H_{13} N_5 O_4, mol. wt. 291.27), non-toxic to feline cells at concentrations as high as 100 µM, effectively inhibits FIP viral replication in cell cultures (infected feline peritoneal macrophages harvested from clinical cases) at as low as 1 µM concentration. The drug pharmacokinetics reveal that a single dose @ 5 mg/ kg SC or IV sustains effective blood titers for 24 hr. Experimental infection of severe effusive form FIP in disease-free laboratory cats in the UC Davis campus has clearly established that GS-441524 promotes rapid reversal of the clinical signs and return to normalcy within two weeks of treatment @ 2 or 5 mg/kg SC or IV OD. The bio-mechanisms are well-established: nucleoside triphosphate (NTP), the *in vivo* potentiated derivative gets incorporated in the nascent single-stranded virulent RNA viral transcript and induces premature chain termination in the infected tissue macrophage. In the follow-up clinical trials (Pedersen *et al*., 2019),GS-441524 is shown to be a safe and effective treatment of FIP in different forms/ severity grades: non-effusive, dry-to-effusive, and effusive. The optimum dose is 4.0 mg/kg SC, OD for 12 weeks. The well-planned and executed clinical trial has led to a historic breakthrough in the treatment of feline infectious peritonitis (FIP), considered an 'untreatable' silent killer till now.

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