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Successful Management of Feline Infectious Peritonitis with Human Recombinant Interferon-alpha and Pentoxifylline in a Cat

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Abstract : A 6-month-old intact female, domestic short hair cat was presented with dyspnea and anorexia for 2 days. Physical examination revealed muffled heart sound with labored breaths. Hyperproteinemia and hyperglobulinemia with polyclonal gammapathy was revealed. Pleural effusion was non-septic exudates, it also had hyperglobulinemia with decreased albumin:globuline ration. In addition, effusion RT-PCR for feline coronavirus was positive in this cat. Feline infectious peritonitis (FIP) was strongly suspected and aggressive treatments with human interferon-alpha, pentoxifylline, and glucocorticoids were initiated. The cat remained healthy without recurrence of pleural effusion during 5 months follow-up periods. To the author's knowledge, this is the first case report describing successful management of FIP with human interferon-alpha and pentoxifylline in Korea.

Key words **:** FIP, interferon-alpha, protein electrophoresis, pentoxifylline.

Introduction

Feline infectious peritonitis (FIP) is systemic fatal immune-mediated disease caused by mutant feline coronavirus (2,3). Most cats affected with FIP are young, between 3 months to 3 years, and purebred. Multi-cat households or shelter have a higher prevalence of the FIP (3). Clinical signs divided according to the two different forms of FIP: effusive and non-effusive (1). Both forms may have lethargy, anorexia, weight loss and poor growth and generally effusive form progresses more rapidly and more lethal than non-effusive form (2). In effusive forms, vasculitis caused by immune complex resulting in leakage of fluid into the body cavity. Otherwise, perivascular infiltrations of inflammatory cells in the parenchyma of organs are made in non-effusive forms of FIP (2,3,10). No single laboratory test is available for the definite diagnosis of FIP and no curative treatment is identified for FIP (4,9).

The following case report describes the clinical and laboratory features of effusive form of FIP and successful management of this disease through human recombinant interferon-alpha and pentoxifylline in a cat.

Case History

A 6-month-old intact female, domestic short hair cat was admitted with dyspnea. The owner adopted street cat 4 months ago. The cat had no vaccination, but otherwise healthy until 2 days ago. Abrupt dyspnea was noticed 2 days ago and the cat was anorexic. When presented, the cat was mildly depressed, but was alert and responsive. Physical examination revealed muffled heart sound with labored breaths. No other abnormalities were noted on the physical examination.

The hemogram showed leukocytosis (30,090/μl, reference range, 5,500-19,500/μl) with stress leukogram. Serum chemistry profiles showed an electrolyte imbalance with hypokalemia (3.2 mmol/L; reference range, 3.5-5.8 mmol/L), and elevated creatine kinase (CK) (4697 U/L, reference range; 73-260 U/L). Hyperproteinemia (9.8 g/dl; reference range, 6.6-8.4 g/dl) with low albumin:globulin ratio (A:G; 0.58) was noticed. Radiologic examination revealed severe pleural effusion (Fig 1). Due to the respiratory distress was severe, thoracocentesis was performed and 140 mL of straw-colored, cloudy fluid was removed. The fluid has a low cell count (1,050 cells/μl), with a specific gravity 1.035, and a protein concentration 6.3 g/dl. The A:G ratio of the pleural fluid was 0.5. Most cells were neutrophils and macrophages (Fig 2). A cellularity was low

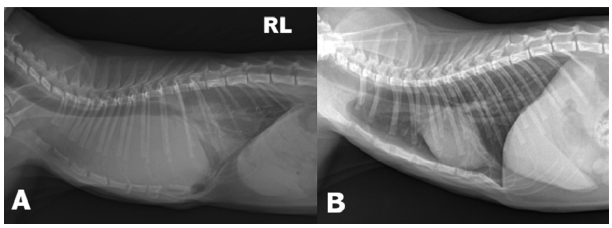

Fig 1. Thoracic radiographs of a cat with pleural effusion. Heart visualization was impaired on day 0 (A). Visualization of intrathoracic structures improved after treatment (day 10) (B).

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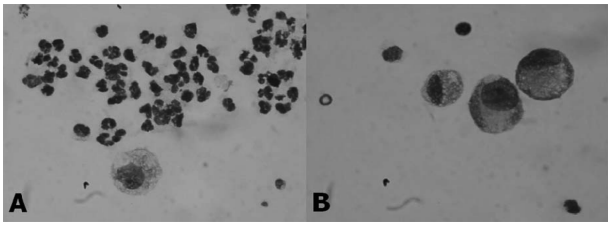

Fig 2. Cytology of pleural effusion fluid. Pyogrnulomatous inflammation was noted with neutrophils and macrophages in the fluid (Diff-Quik stain A: × 400, B: × 1000).

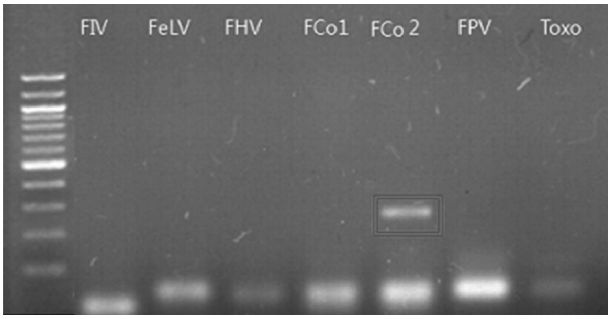

Fig 4. Agarose gel electrophoresis with ethidium bromide of RT-PCR products of serum and pleural effusion in a cat. Pleural effusion sample revealed positive results to coronavirus. Lane 1; molecular weight marker (100 bp), FIV; Feline immunodeficiency virus, FeLV; Feline leukemia virus, FHV; Feline herpes virus, FCo1; serum sample for feline coronavirus, FCo2; pleural effusion sample for feline coronavirus, FPV; Feline parvovirus, Toxo; Toxoplasma.

but, specific gravity and protein concentration was higher. Due to the pleural fluid was culture negative, the effusion was characterized as a non-septic exudate. Feline infectious peritonitis (FIP) was strongly suspected and further examinations were performed to confirm this condition. Protein electrophoresis for serum and pleural effusion revealed polyclonal gammopathy (Fig 3). Reverse transcription polymerase chain reaction (RT-PCR) in effusion fluid identified feline coronavirus (Fig 4). Based on the history, clinical signs, physical examinations and laboratory findings, the present case was diagnosed as an effusive form of FIP.

Table 1. Hematologic findings in a cat with FIP before and after treatment

Parameters	Interval after first examination				Reference Range
	0	D3	D10	D30	
WBC(× 10^3/μl)	30.09	8.25	6.48	6.85	5.5-19.5
BUN(mg/dl)	20	23	22	20	18-33
CREA (mg/dl)	1.0	0.7	0.6	0.6	1.0-1.6
ALT (U/L)	20	29	28	22	28-106
AST (U/L)	44	26	18	16	12-46
ALP (U/L)	56	16	40	28	14-71
T P(g/dl)	9.8	8.7	8.3	7.8	6.6-8.4
ALB (g/dl)	3.6	3.4	4.4	4.3	1.9-3.9
A:G ratio	0.58	0.64	1.12	1.22	0.9-1.3

*ND : not done, D : days

Table 2. Serum protein electrophoresis in a cat with FIP before and after treatment

Parameters	Interval after first examination			Reference Range (g/dl)
	0	D3	D10	
Albumin	3.7	4.3	4.15	3.28-3.96
Alpha 1	0.28	0.43	0.43	0.46-0.77
Alpha 2	1.86	1.36	1.4	0.53-0.88
Beta	1.2	1.12	0.97	0.72-1.15
Gamma	2.73	1.42	1.31	0.96-1.86

*ND : not done, D : days

Medical management was instituted with human recombinant interferon-alpha (Intermax alpha, 6×10^5 IU/cat 5 days a week for 3 weeks, SC; LG life sciences, Seoul, Korea), pentoxifylline (Trental, 10 mg/kg q12hrs, PO; Handok, Seoul, Korea) and prednisolone (Solondo, 2 mg/kg q 12hrs, PO; Yuhan medica, Seoul, Koare). The clinical signs of the cat were improved over the next 3 days, and serum A:G ratio was increased (A:G = 1.12) 10 days after presentation (Table 1). Monitoring of serum protein electrophoresis at day 3 and 10 revealed decreased serum gamma-globulin concentration (Table 2). The

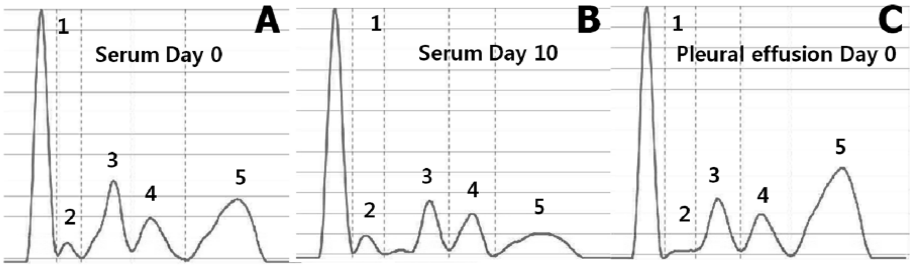

Fig 3. Protein electrophoresis of serum and pleural effusion fluid in a cat. Polyclonal gammopathy with elevated alpha-2 and gamma- fraction were noted on day 0 (A: serum, C: pleural effusion fluid). 10 days after treatment, decreased serum gamma-fraction were marked (B). (1: albumin, 2: alpha-1, 3: alpha-2, 4: beta, 5: gamma).

cat was in good condition and clinically healthy for 5 months without recurrence of the pleural effusion.

Discussion

Several studies of diagnosis of FIP have been published, however no single test is available for definite diagnosis of FIP and it is often misdiagnosed (4,9). Non-regenerative anemia, lymphopenia, neutrophilia and thrombocytopenia are common hematologic abnormalities, but it is not specific for FIP (3). Hyperglobulinemia and low serum albumin:globulin ratio (A:G) is observed in most cats with FIP and polyclonal or monoclonal gammopathy is also revealed through serum protein electrophoresis (4,10). In effusive forms of FIP, typical features of effusion fluid is also helpful for the diagnosis and other serologic tests (anticoronavirus antibodies) or reverse transcription polymerase chain reaction (RT-PCR) has good predictive values (3). Histopathologic examination is gold standard of FIP diagnosis; however antemortem examination is not always available. Thus, diagnosis must be made based on the history, physical examination, and several laboratory findings (1,4,8). This cat was young and abrupt pleural effusion was noted when presented. Differential diagnoses such as FIP, multifocal lymphosarcoma, heart disease, feline immunodeficiency virus, feline leukemia virus and toxoplasmosis were considered. Laboratory examination revealed leukocytosis with stress leukogram and hyperglobulinemia with polyclonal gammopathy. The effusion was a non-septic exudates with high protein and low A:G ratio, which was typical features of FIP in cats. Moreover, RT-PCR of effusion sample revealed positive results to coronavirus only. Effusion RT-PCR of FIP has more diagnostic value than serum RT-PCR results (4). Definitive diagnosis of FIP without histopathologic confirmation is impossible, however based on the history, signalment and several laboratory examinations, effusive FIP was highly suspected in this cat and more aggressive treatment methods were tried.

In this cat, high dose recombinant human interferon-alpha was tried. High dose injectable human interferon-alpha has effective antiviral effect in some reports (5,11), however it has limitation for long-term management due to cats develop neutralizing antibodies for this treatment. Thus pentoxifylline and prednisolone was also used as palliative care. Prednisolone was traditional immunosuppressive drug for FIP cats and currently good supportive treatment of choice (5). Pentoxifylline was used for treating vasculitis but no clinical studies were established and decreasing tumor necrosis factor-a level in feline leukemia virus infection was revealed (7). Several other treatments were tried for FIP treatment; however no effective treatment has been identified. Oral low dose human interferon-alpha (4) has immunomodulatory effects but which cause progression of FIP and not recommended. Feline interferon-omega (6,8) for antiviral treatment and thromboxane synthesis inhibitor, ozagrel hydrochloride (10) were also used for treatment of FIP however further study was required (1,3,5).

In this case report, we described management of FIP with human recombinant interferon-alpha and pentoxifylline. Recently, no effective treatment has been identified in FIP and use of several antiviral and immunosuppressive drugs need further studies to establish their efficacy.

In conclusion, this case demonstrates that long-term management of FIP with human recombinant interferon-alpha and pentoxifylline was successful in this cat.

Acknowledgement

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재조합 인간 인터페론 알파와 Pentoxifylline을 이용한 고양이 전염성 복막염의 치료 증례

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요 약 : 6개월령의 잡종 수컷 고양이가 갑작스런 호흡곤란과 식욕부진 증상으로 내원 하였다. 신체검사상 심음의 감소와 함께 확연한 호흡곤란이 확인 되었다. 혈액학적 검사에서 고글로블린 혈증을 동반한 고단백혈증이 관찰되었으며, 다클론성 감마글로블린병증이 확인 되었다. 환축은 흉부 방사선 검사에서 흉수가 확인 되었으며, 흉수는 비감염성 삼출물로, 흉수 역시 다클론성 감마글로블린병증을 동반한 고글로블린증과 감소한 알브민 대 글로블린 비율이 관찰되었다. 또한 흉강 삼출물을 통한 역전사 중합효소연쇄반응에서 고양이 코로나바이러스에 양성반응을 확인하였다. 따라서, 환축은 고양이 전염성 복막염이 강하게 의심되었으며, 재조합 인간 인터페론 알파, pentoxifylline 과 스테로이드제를 이용한 적극적인 치료가 시작 되었다. 환축은 초기 치료에 반응이 좋았으며, 치료 이후 5개월간 재발 증상이 관찰되지 않았다. 결론적으로 본 증례는 재조합 인간 인터페론 알파와 pentoxifylline을 이용한 고양이 전염성 복막염의 치료 반응에 대한 국내 첫 증례보고이다.

주요어 : 고양이 전염성 복막염, 재조합 인간 인터페론 알파, 단백 전기영동법, pentoxifylline