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Research Article/Araştırma Makalesi

Investigations of Adenosine Deaminase and C-reactive Protein in Cats with Feline Infectious Peritonitis

Felin İnfeksiyöz Peritonitli Kedilerde Adenozin Deaminaz ve C-reaktif Protein Düzeylerinin Araştırılması

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Abstract: The aims of the present study were to evaluate T-cell-mediated immune response and acute phase response in cats with infectious peritonitis (FIP). In the study, 20 cats with FIP and 10 clinically healthy cats were used. Cats with FIP were divided into two groups as dry form (n=10) and wet form (n=10) based on clinical, radiographic and necropsy findings. Adenosine deaminase (ADA-1) and C reactive protein (CRP) levels were determined by using cat-specific ELISA kits. Serum concentrations of total protein (TP) and albümin (A) were measured by photometric methods. In the study, both serum and peritoneal effusion concentrations of ADA-1 ($p<0.001$) and CRP ($p<0.001$) were significantly higher in cats with FIP than control cats. A high positive correlation was obtained between serum concentrations of ADA-1 and CRP in cats with FIP ($r=0.62$, $p<0.001$). Significant increases in TP ($p<0.01$) and globulin ($p<0.01$) levels and decreases in A ($p<0.01$) values and A/G ratio ($p<0.01$) were obtained in cats with FIP. Serum TP ($p<0.05$) and G ($p<0.05$) levels were significantly higher, whereas ADA-1 activitiy ($p<0.01$) was lower in cats with dry form than in cats with wet form of FIP. As a conclusion, both serum and peritoneal effusion samples can be used to determine ADA-1 and CRP, and they can be useful biomarkers for evaluating T-cell-mediated immune responses, inflammation and possibly organ damages in cats with FIP.

Keywords: Adenosine Deaminase-1 (ADA-1), Cat, C-Reactive Protein (CRP), Feline Infectious Peritonitis (FIP).

Öz: Çalışmada felin infeksiyöz peritonitli (FİP) kedilerde T-lenfosit aracılı immun yanıt ve akut faz yanıtın değerlendirilmesi amaçlanmıştır. Çalışmada 20 FİP'li ve 10 adet klinik olarak sağlıklı kedi kullanıldı. FİP'li kediler klinik, röntgen ve nekropsi bulguları ışığında yaş form (n=10) ve kuru form (n=10) FİP'li olarak iki gruba ayrıldı. Adenozin deaminaz-1 (ADA-1), C-reaktif protein (CRP) düzeyleri kedi spesifik ELISA testleri kullanılarak belirlendi. Serum total protein (TP) ve albümin (A) düzeyleri ise fotometrik metodla saptandı. Çalışmada FİP'li kedilerin hem serum hem de peritoneal efuzyonlarındaki ADA-1 ($p<0,001$) ve CRP ($p<0,001$) düzeyleri sağlıklı kedilerin düzeylerine göre anlamlı düzeyde yüksek olduğu belirlendi. FİP'li kedilerin serum ADA-1 konsantrasyonu ile CRP konsantrasyonları arasında yüksek düzeyde pozitif korelasyonun olduğu belirlendi ($r=0,62$, $p<0,001$). FİP'li kedilerin serum TP ($p<0,01$) ve globülin (G) ($p<0,01$) düzeylerinde anlamlı artışlar belirlenirken albümin ($p<0,01$) düzeyleri ve albümin globülin oranlarında (A/G) ise anlamlı düzeyde düşüşler saptandı. Kuru form FİP'li kedilerin serum TP ($p<0,05$), ve G ($p<0,05$) düzeyleri yaş form FİP'li kedilerinki ile karşılaştırıldığında anlamlı düzeyde yüksek iken ADA-1 $p<0,01$) aktivitesinin ise anlamlı düzeyde düşük olduğu saptandı. Sonuç olarak, FİP'li kedilerde hem serum hem de peritoneal efüzyonların ADA-1 ve CRP düzeylerinin ölçümünde kullanılabileceği ve bu parametrelerin FİP'li kedilerde T-lenfosit aracılı immun yanıt, yangı ve olası organ hasarlarının değerlendirilmesinde yararlı biyomarkırlar olduğu düşünülmektedir.

Anahtar Kelimeler: Adenozin Deaminaz-1 (ADA-1), C-Reaktif Protein (CRP) Felin İnfeksiyöz Peritonitis (FIP), Kedi.

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Introduction

Feline infectious peritonitis (FIP) is a highly fatal viral disease that caused by feline coronavirus (FCoV) (Addie et al., 2009, Pedersen, 2014). FCoV generally cause either asymptomatic infection or mild diarrhea (Addie et al., 2009; Decaro and Buonaiglia, 2011; Pedersen, 2014).

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Some of the healthy and diarrheic cats are become carrier and these cats are potentially at risk for developing FIP (Addie et al., 2009; Kipar et al., 2010; Vogel et al., 2010; Wotrhing et al., 2012). FCoV can be mutate and a mild gastrointestinal disease progresses into clinical FIP, that is progressive and almost always fatal (Sharif et al., 2009; Ehman et al., 2018; Li et al., 2019). FIP develop in two forms as an effusive (wet) and a non-effusuve (dry) form. The effusive form is characterized by an accumulation of protein-rich fluid in the abdomen and/or chest. In dry form of FIP, granulomatous or pyogronulomatous lesion develop in various organs and the developing clinic symptoms are related to these organ dysfunctions (Addie et al., 2009; Diaz and Poma, 2009; Sharif et al., 2009; Oguzoglu et al., 2010; Tasker, 2018).

In studies, severe hematologic and biochemical alterations have been reported in cats with FIP. In these studies, total protein (TP) and globulin (G) concentrations were found to be elevated, while albumin (A) concentrations and albumin/globulin ratio were shown to decrease in cats with FIP. None of these findings are specific for FIP and definitive diagnosis of FIP is very difficult. Single positive or negative diagnostic test is meaningless and does not rule out the either presence or absence of FIP in cats. Therefore, a combination of a complete history, clinical examination, laboratory tests, post-mortem examination and histopathology may help its confirmatory diagnosis. Furthermore, clinical signs consistent with FIP and a positive diagnostic test result may indicate the presence of active FIP in cats (Diaz and Poma, 2009; Sharif et al., 2010; Pedersen, 2014; Tasker, 2018).

Adenosine deaminase (ADA), a purine catalytic enzyme, plays a vital role in the maturation of the immunological system and it is essential for proliferation and differentiation of lymphocytes (Martinez-Navio et al., 2011; Antonioli et al., 2012; Sauer et al., 2012; Brigida et al., 2014; Flinn and Gennery, 2018). Elevated ADA activities reflect the activation of cell-mediated immunity, while decreased values are associated with immunodeficiency (Climent et al., 2009; Poursharifi et al., 2009; Antonioli et al., 2012; Flinn and Gennery, 2018). Adenosine deaminase has been shown to have diagnostic value in several diseases and it is considered to be a marker of T-cell activation and inflammation for both human and animals (Castro et al., 2003; Ellah et al., 2004; Baba et al., 2008; Martinez-Navio et al., 2011; Rodriques et al., 2012; Afrasibian et al., 2013; Akhtardanesh et al., 2013; Brigida et al., 2014). In studies, ADA test has shown to have a high sensitivity and specificity in the diagnosis of pleural tuberculosis and suggested to be a useful diagnotic marker for tuberculosis (Castro et al., 2003; Baba et al., 2008; Afrasibian et al., 2013). Furthermore, a positive corelation was determined between serum ADA activity and the degree of hepatocellular damage. It was suggested to have a dignostic value for liver disease in cattle (Ellah et al., 2004).

C-reactive protein, a positive acute phase protein (APP), is synthesized primarily in liver hepatocytes and its concentration increases during inflammatory events (Clyne and Olshaker 1999; Gokce and Bozukluhan, 2009; Sproston and Ashworth 2018). It is an acute marker for inflammation and its levels shown to increase in several diseases including pneumonia (Ruiz-Gonzalez et al., 2018), neonatal sepsis (Xu et al., 2016), viral and bacterial infections (Sproston and Ashworth 2018; Chiu et al., 2019), rheumatoid arthritis (Nalesnik et al., 2011; Sridevi et al., 2018) and cardiovascular diseases (Ridger et al., 2002; Osman et al., 2006). CRP is also used to distinguish between patients with bacterial and viral infections, and no infections (Sasaki et al., 2002; Haran et al 2012; Sproston and Ashworth 2018; Chiu et al., 2019). It has been reported that CRP is not just a market of inflammation, it is also an important regulator of inflammatory processes. It plays a key role in the host's defence against infections (Clyne and Olshaker 1999; Sproston and Ashworth 2018).

Up to date, serum and pleural effusion ADA-1 and CRP levels have not been studied and their diagnostic values have not been established in cats with FIP. Therefore, in the present study, ADA-1, CRP, total protein, albumin and globulin

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values were measured to determine T-cell activation, acute phase responses and their diagnostic values in cats with FIP.

Material and Methods

Animals

Twenty FIP-suspected cats and 10 clinically healthy cats in different breeds and ages were used in the study. Cats with respiratory distress, weight loss, depression, loss of appetite, nervous signs, accumulation of effusion either within the abdominal cavity or chest cavity were accepted as suspicious to FIP. Chest or abdominal radiography was also applied to the cats suspicious to FIP. Cat-specific FCoV antigen, FCoV antibody, feline leukoma virus (FLeV) and feline immunodefficieny virus (FIV) rapid test kits were used to detect FCoV infected cats according to the manufacturer instructions (Bionote, Korea). Furthermore, necropsy was performed for each cat either died or euthanized. Twenty cats with positive results for either antigen or antibody tests of FCoV and with supportive clinical, X-ray and necropsy findings of FIP were accepted as FIP and used in the study (Diaz and Poma, 2009; Tasker, 2018). Cats positive to FLeV or FIV were not used in the study. Control cats were negative for all the tests applied. Cats with abdominal effusion (n=10) detected by radiography and necropsy were accepted as wet form, while cats with granulomatous lesions in various organs observed in necropsy were accepted as dry form of FIP.

This study was performed according to the requirements of the ethical committee of the Faculty of Veterinary Medicine, Burdur Mehmet Akif Ersoy University, Turkey (Approval No: 2018/392).

Laboratory Analysis

Serum samples were collected from all the animals and used to analyse CRP, ADA-1, TP, A and G values. Peritoneal effusions were also collected from 10 cats with wet form of FIP and used to determine CRP and ADA-1 levels. Serum concentrations of TP, G, and A were determined by photometric methods (Abbott Architect Ci8200 Biochemstry Analyser USA). Serum and pleural effusions ADA-1 (SunRed, Shanghai, CHINA) and CRP (Bioassay Technology Laboratory, Shanghai, CHINA) levels were measured by commercially available cat-specific ELISA kits according to the manufacturer's instructions. Serum globulin concentrations were calculated by subtracting albumin values from total protein values.

The optical density (OD) of each well for ADA-1 and CRP was determined with a micro-ELISA plate reader (MR-96A, Minray, China) at a test wave-length of 450 nm. The concentrations of ADA-1 and CRP were calculated regression analysis on the basis of standard curve derived from two-fold dilutions of each standard stock solution. The sensitivities of ADA and CRP were 0.075ng/ml and 0.12mg/mL, respectively.

Statistical analysis

Kolmogorov Smirnov test was used to determine normality of distribution of the data, which were normally distributed. The significance of the differences in values between cats with FIP and control cats were determined by Student's t test. Student's t test also used to compare the differences in values between wet and dry form of FIP. Pearson's correlation coefficient (r) analysis was performed to determine the correlations between the parameters obtained from cats with FIP. All the values were expressed as mean and standard deviations of the mean (mean ± SD). The level of significance was accepted as $p<0.05$ for both Student's t test and Pearson's correlation coefficient analysis. SPSS software computer programme (version 14.01 for Windows, SPSS Inc, Chicago) was used to perform all the statistical analyses.

Results

Clinical Findings

Anorexia, weight loss and depression were common clinical findings observed in cats with either wet or dry form of FIP. In addition to these, effusions in abdominal or chest cavity with

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breathing difficulties were also observed in cats with wet form of FIP. In dry form, nervous symptoms including weakness, incoordination, *opisthotonus*, paraplegia were dominant clinical symptoms observed. Presence of excessive fluid accumulation in chest and/or abdominal cavity (wet form) and granulomatous lesions (dry form) in various organs such as liver, lungs and intestines were confirmed by chest and/or abdominal radiography and necropsy.

Biochemical Findings

In the study, serum concentrations of TP ($p<0.01$), G ($p<0.05$), ADA-1 ($p<0.001$) and CRP ($p<0.001$) were significantly higher in cats with FIP than those of obtained from control cats. Whereas, serum concentrations of A ($p<0.01$) and A/G ratio ($p<0.01$) were significantly low in cats with FIP compared to that of control cats (Table 1).

Table 1. Biochemical findings of cats with feline infectious peritonitis (FIP) and control cats. (Mean ± Standard deviation).

Parameters	Control (n=10)	FIP	Min-max	p value
ADA-1 (ng/ml)	2.53±0.75	4.40±0.80	2.49-5.12	0.001
CRP mg/L	1.75±0.36	2.67±0.44	1.9-3.53	0.001
TP (g/dl)	7.33±0.73	8.71±1.48	6.4-14.1	0.003
A (g/dl)	2.70±1.88	2.34±0.41	1.1-2.9	0.015
G (g/dl)	4.63±0.73	5.67±1.42	3.7-8.6	0.039
A/G	0.59±0.09	0.43±0.12	0.23-0.67	0.001

ADA-1: Adenosine deaminase, CRP: C-reactive protein, TP: Total protein, A: Albumin, G: Globulin, A/G: Albumin/Globulin ratio. Significant level was accepted as $p<0.05$.

Table 2. Serum and peritoneal effusion concentrations of adenosine deaminase (ADA-1) and C-reactive protein (CRP) in cats with wet form of feline infectious peritonitis (FIP) and control cats. (Mean ± Standard deviation).

Parameters	Control Serum (n=10)	FIP Serum (n=10)	FIP Effusion (n=10)
ADA-1 (ng/ml)	2.53±0.75 [a]	4.75±0.82 [b]	4.92±0.70 [b]
CRP mg/L	1.75±0.36 [a]	2.77±0.51 [b]	2.64±0.52 [b]

ADA-1: Adenosine deaminase, CRP: C-reactive protein. *Different letters* above the *columns indicate significant difference* between the groups. Significant level was accepted as $p<0.05$.

Furthermore, both ADA-1 ($p<0.001$) and CRP ($p<0.001$) values were also high in effusions as determined in serum samples (Table 2).

There were positive correlations between serum ADA-1 and CRP ($r=0.62$, $p<0.01$), TP ($r=0.40$, $p<0.05$), while negative correlations were obtained between ADA-1 and A ($r=-0.42$, $p<0.05$), A/G ($r=-0.49$, $p<0.05$). Furthermore, positive correlation were also detected between TP and G ($r=0.62$, $p<0.01$), and between A and A/G ($r=0.68$, $p<0.01$). On the other hand, negative correlations were obtained between TP and A/G ($r=-0.56$, $p<0.01$), and between G and A/G ($r=-0.79$, $p<0.001$) (Table 3). A positive correlation was determined between serum and effusion concentrations of CRP in cats with wet form of FIP ($r=0.52$, $p<0.01$), while a negative correlation was obtained between ADA-1 values of serum and effusion of these cats ($r=-0.43$, $p<0.05$).

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Table 3. Correlations (r) between the parameters of serum samples obtained from Cats with FIP.

Parameters	ADA (ng/ml)	CRP (mg/ml)	TP (g/dl)	A (g/dl)	G (g/dl)	A/G
ADA (ng/ml)	1	0.62**	0.40*	-0.42*	0.29	-0.49*
CRP (mg/L)		1	0.26	-0.28	-0.02	-0.14
TP (g/dl)			1	-0.16	0.62**	-0.56*
A (g/dl)				1	-0.16	0.68**
G (g/dl)					1	-0.79***
A/G						1

ADA-1: Adenosine deaminase, CRP: C-reactive protein, TP: Total protein, A: Albumin, G: Globulin, A/G: Albumin/Globulin ratio. Significant levels were indicated by symbols, *:p<0.05, **:p<0.01, ***: p<0.001.

Comparison of the parameters obtained from dry and wet form of FIP showed that serum ADA-1 levels were significantly higher in cats with wet form compared to those of cats with dry form of FIP (p<0.01). Serum concentrations of CRP were also high in cats with wet form of FIP, but there was no statistically significance between wet form and dry form of FIP (Table 4). In addition to these, serum TP and G values were significantly higher in cats with dry form of FIP than that of values obtained from cats with wet form of FIP (p<0.05, Table 4).

Table 4. Serum biochemical findings of cats with dry form and wet form of feline infectious peritonitis (FIP), and control cats. (Mean ± Standard deviation).

Parameters	Control (n=10)	Dry Form (n=10)	Wet form (n=10)
ADA-1 (ng/ml)	2.53±0.75 [a]	4.04±0.63 [b]	4.75±0.82 [c]
CRP (mg/L	1.75±0.36 [a]	2.57±0.34 [b]	2.77±0.51 [b]
TP (g/dl)	7.33±0.73 [a]	9.35±1.84 [b]	8.07±1.18 [a]
A (g/dl)	2.70±1.88 [a]	2.47±0.27 [ab]	2.21±0.49 [bc]
G (g/dl)	4.63±0.73 [a]	6.28±1.04 [b]	5.06±1.52 [a]
A/G	0.59±0.09[a]	0.40±0.09 [b]	0.46±0.14 [b]

ADA-1: Adenosine deaminase, CRP: C-reactive protein, TP: Total protein, A: Albumin, G: Globulin, A/G: Albumin/globulin. *Different letters* above the *columns indicate significant difference* between the groups. The significant level was accepted as p<0.05.

Discussion

Feline infectious peritonitis caused by FCoV is a higly contagious and deadly infection of domesticated and wild cats (Addie et al., 2009; Pedersen, 2014; Tasker,2018). Most of the cats are seropositive to feline coronavirus (FCoV) and be come cariers (Addie et al., 2009; Kipar et al., 2010; Vogel et al., 2010; Wotrhing et al., 2012; Pedersen, 2014; Li et al., 2019). These cats are highly susceptible to develop FIP due to mutation of FCoV and FIP can be seen in any time of the cat's life (Sharif et al., 2009; Fehr and Perlman, 2015; Ehman et al., 2018; Li et al., 2019). Up to date, differrential diagnosis of cats from FCoV to FIPV and their treatments are still insufficient and available vaccines are not able to fully protect cats agains FIP (Addie et al., 2009; Pedersen, 2014; Tasker, 2018).

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It has been demostrated that severe hematologic and boichemical alterations occur in cats with FIP (Addie et al., 2009; Pedersen, 2014). Elevated serum concentrations of TP and G, and decrease in A and A/G values have been reported in cats with FIP (Hartmann et al., 2003; Addie et al., 2009; Jeffery et al., 2012; Pedersen, 2014). These alterations have been implicated to have some diagnostic value for differentiating cats form FIP to healthy ones (Hartmann et al., 2003; Addie et al., 2009; Diaz and Poma, 2009; Sharif et al., 2010; Jeffery et al., 2012; Pedersen, 2014; Tasker, 2018). In the present study, elevated serum concentrations of TP ($p<0.01$) and G ($p<0.05$) and decreased in concentration ($p<0.01$) and A/G ratio ($p<0.01$) were determined in cats with FIP as reported elsewere (Hartmann et al., 2003; Addie et al., 2009; Sharif et al., 2010; Jeffery et al., 2012; Pedersen, 2014). It is known that globulin synthesis increases in chronic disease, while albumin values decrease in association with liver and renal insufficieny (Kaneko, 1997). It was reported that hipoalbuminemia obtained in cats with FIP occured due to renal insufficiency and accumulation of protein-rich effusions in cavities (Addie et al., 2009). It's synthesis may also be decreased in response to acute phase responses as it is a negative APP (Clyne and Olshaker, 1999; Gokce and Bozukluhan, 2009; Sproston and Ashworth 2018). Total protein concentrations implicated to increase due to increased globulin synthesis, resulting decrease in A/G ratio in cats with FIP (Hartmann et al., 2003; Addie et al., 2009; Sharif et al., 2010; Jeffery et al., 2012; Pedersen, 2014). In the present study, A/G ratio were found to be significantly low in cats with FIP. The decrease in A/G ratio is most probabily occur due to elevated globulin and decreased in albumin concentrations. Furthermore, high positive correlations were obtained between TP and G ($r=0.62$, $p<0.01$), and also between A and A/G ($r=0.68$, $p<0.01$). On the other hand, high negative correlation was detected between G and A/G ($r=-0.79$, $p<0.001$). These correlations indicate that A, G and A/G ratio may have diagnostic value in cat with FIP as mentioned elsewhere (Hartmann et al., 2003; Addie et al., 2009; Sharif et al., 2010; Jeffery et al., 2012; Pedersen, 2014). In addition to these, in the present study, the differences in biochemical values were also compared between wet and dry form of FIP. It was found that serum TP and G values were significantly higher in cats with dry form of FIP than that of wet form of FIP. Albumin values were similarly low but not significantly different in both groups. These findings indicate that liver function may not be affected to produce globulin but it may be insufficient to produce albumin in both groups of cats. As reported before, accumulation of protein-rich effusions may not be the cause of low albumin concentrations obtained in cats with FIP (Addie et al., 2009), because, in the present study, low albumin values were obtained in both dry and wet form of FIP. Therefore, in combination of renal and hepatic dysfunction, and also some other unknown factors may play a role in reduced albumin concentrations obtained in both dry and wet form of FIP.

C-reactive protein, a positive APP, is synthesized primarily in liver hepatocytes and its concentrations increases during the inflammatory events (Clyne and Olshaker 1999; Gokce and Bozukluhan, 2009; Sproston and Ashworth 2018). It has been used to diagnose inflammation and also differentiate bacterial infections from viral infections (Clyne and Olshaker 1999; Haran et al 2012, Xu et al., 2016; Ruiz-Gonzalez et al., 2018; Sproston and Ashworth 2018; Chiu et al., 2019). In previous studies, elevated serum and abdominal effusions haptoglobin (Hb) α^1-acid glycoprotein (α_1-AGP) and serum amyloid A (SAA) were reported in cats with FIP (Duthie et al., 1997; Giordano et al., 2004; Hazuchova et al., 2017). Effusion AGP levels were implicated to be useful in differentiating between FIP and other diseases (Hazuvhova et al., 2017). In the present study, both serum and effusion concentrations of CRP were found to be high in cats with FIP ($p<0.001$). A positive correlation was detected between serum and effusion concentrations of CRP in wet form of FIP ($r=0.52$, $p<0.01$). In addition to low albumin values, elevated CRP may indicate development of acute phase

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responses in cats with FIP, therefore elevated serum and effusion CRP values may have diagnostic and prognostic values in cats with both dry and wet form of FIP. However, CRP levels may not be insufficient to differentiate dry form from wet form of FIP. Because of significant high CRP levels were detected in both groups and there were no significant differences in CRP levels between these groups.

Adenosine deaminase (ADA-1) plays a vital role in the maturation of the immunological system and it is essential for proliferation and differentiation of lymphocytes (Brigida et al., 2014; Martinez-Navio et al., 2011; Antonioli et al., 2012; Sauer et al., 2012; Flinn and Gennery, 2018). It is considered to be a marker of T-cell activation and inflammation in both human and animals (Castro et al., 2003; Ellah et al., 2004; Baba et al., 2008; Martinez-Navio et al., 2011; Rodriques et al., 2012; Afrasibian et al., 2013; Akhtardanesh et al., 2013; Brigida et al., 2014). Furthermore, ADA was reported to have anti-inflammatory effects on normal levels but it was shown to cause tissue and organ damages in high levels (Baba et al., 2008; Niraula et al., 2018). A correlation between increase in serum ADA levels and severity of inflammation was reported and the increase was suggested to be related with presence of activated T-lymphocytes and monocytes, and organ damages (Baba et al., 2008; Niraula et al., 2018). Elevated ADA-1 activity was also reported in cattle with liver diseases and a positive correlation was determined between serum ADA-1 activity and the degree of hepatocellular damage (Ellah et al., 2004). Furthermore, ADA test has been shown to have a high sensitivity and specificity in the diagnosis of pleural tuberculosis in human and thus, its activity has been suggested to be a useful diagnostic marker for tuberculosis (Castro et al., 2003; Baba et al., 2008; Afrasibian et al., 2013). Concentrations of serum and pleural effusion of CRP and ADA were found to be high and a positive correlation was detected between their serum and pleural effusion increases in patients with tuberculosis. In this study, ADA was suggested to be a useful biomarker to differentiate malignant tuberculosis from nonspecific pyothorax (Kim et al., 1988). Elevated serum CRP and ADA levels were also determined in patients with rheumatoid arthritis and they were implicated to be useful biomarkers for diagnosing inflammation and following the treatment (Nalesnik et al., 2011; Sridevi et al., 2018). Therefore, ADA-1 has been suggested to be a useful biomarker for evaluating T-cell-mediated immune responses, diagnosing inflammation and organ damages (Ellah et al., 2004; Climent et al., 2009; Baba et al., 2008; Kapisyzi et al., 2009; Afrasiabian et al., 2013; Nagayasu et al., 2018; Niraula et al., 2018).

In the present study, for the first time, elevated serum ADA-1 activities were obtained in cats with both dry and wet form of FIP compared to control cats ($p<0.001$). High concentrations of ADA-1 activity was also determined in the peritoneal effusions of cats with wet form of FIP ($p<0.001$). These results may confirm T-cell activation and also reflect organ damages in both dry and wet form of FIP. Furthermore, serum ADA-1 activity was higher in wet form than that of dry form of FIP ($p<0.01$). Serum ADA-1 levels may be used to differentiate wet form from dry form of FIP, but it needs to be further investigated with a high number of cats with wet and dry form of FIP. In the study, both serum CRP and ADA-1 concentrations were elevated and a high positive correlation was detected between these parameters in cats with FIP ($r=0.62$, $p<0.01$). It is suggestive that both serum and the effusions can be used to analyse ADA-1 and CRP values and these two parameters can be useful to determine T-cell activation, inflammation and also organ damages in cats with FIP.

In conclusion, serum concentrations of TP, G, ADA-1 and CRP were high in cats with both wet and dry form of FIP, while serum concentrations of A and A/G ratio were significantly low in both groups. ADA-1 and CRP values were also high in the peritoneal effusions of cats with wet form of FIP. High serum concentrations of TP and G, and low ADA-1 activitiy were obtained in cats with dry form compared to wet form of FIP. It

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is suggestive that T-cell activation, acute phase response and possibly organ damages develop in cats with FIP. The results of the present study, indicate that both serum and effusion values of ADA-1 and CRP can be useful biomarkers to determine T-cell activitiy, inflammation and organ damages in both dry and wet form of FIP.

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