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CASE REPORT

Feline Infectious Peritonitis with Distinct Ocular Involvement in A Cat in Turkey

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Abstract

An approximately 2-year old domestic short hair female cat weighting 2.750g was presented to Firat University Veterinary Teaching Hospital with a history of depression, anorexia and weight loss for the last 15 days. Clinical examination revealed incoordination, hyperaesthesia, circling, head tilt, posterior paraparesis, absence of the pupillary reflex in both eyes, opisthotonus and anisocoria. Blood samples were examined for hematological, RT-PCR and biochemical analyses. The cat died without any improvement of clinical findings although symptomatic treatment was made. Necropsy revealed that distinct ocular lesions such as hyphema and thick proteinous exudate accumulation in vitreous in both eyes. Microscopically; there was pyogranulomatous vasculitis in meninges, sclera, corpus ciliare choroid, retina was partially detached in the right eye with retinal epithelial hypertrophy. The kidneys contained focal subcapsular, gray to yellow raised nodules varying from 3 to 10 mm in diameter, and there was discrete fatty degeneration in the liver. The RT-PCR revealed that RNA for FCoV was positive in the blood sample. As a result; the non-effusive form of FIP with distinct ocular involvement was diagnosed through clinical, pathological and polymerase chain reaction (PCR) findings.

Keywords: *Anisocoria, Cat, Eye, Feline infectious peritonitis, Hyphema*

Türkiye'de Bir Kedide Göz Lezyonlarıyla Belirgin Feline Enfeksiyöz Peritonitis Olgusu

Özet

Fırat Üniversitesi Hayvan Hastanesi'ne onbeş gündür süren depresyon, anoreksi ve canlı ağırlık kaybı şikayetiyle yaklaşık 2 yaşında ve 2.750 g ağırlığında, evcil, kısa tüylü dişi bir kedi getirildi. Klinik muayenede inkoordinasyon, hiperestezi, dönme, başı eğme, posterior paraparesis, her iki gözde pupilla refleksinin olmayışı, opistotonus ve anizokori belirlendi. Hematolojik, biyokimyasal ve RT-PCR analizleri için kan örnekleri alındı. Semptomatik tedaviye rağmen klinik bulgularda hiçbir iyileşme olmaksızın kedi öldü. Nekropside, her iki gözde vitreusta yoğun protein tabiatında eksudat birikimi ve hifem'le belirgin oküler lezyonlar ortaya konuldu. Mikroskobik olarak; meninkslerde, sklerada ve korpus silyar koroidde pyogranulomatoz vaskülitis gözlenirken sağ gözde ise retina, kısmen ayrılmış olarak epitelyal hipertrofili şekilde belirlendi. Böbrekler fokal subkapsular 3-10 mm çapına kadar değişen gri-sarı nodülller içeriyordu ve karaciğerde farklı yerlerde yağ dejenerasyonu vardı. Kan örneğinde RT-PCR ile FCoV nükleik asiti pozitif olarak tespit edildi. Sonuç olarak; klinik, patolojik ve RT-PCR bulgularına göre göz lezyonlarıyla belirgin non-efüzif feline infeksiyöz peritonitis tanısı konuldu.

Anahtar sözcükler: *Anizokori, Kedi, Göz, Feline infeksiyöz peritonitis, Hifem*

INTRODUCTION

Feline infectious peritonitis (FIP) is a fatal, immune-mediated disease triggered by infection with a feline coronavirus (FCoV) [1]. FCoV strains are subdivided into two distinct biotypes, feline enteric coronavirus (FECV) and feline infectious peritonitis virus (FIPV). Infection with FECV is highly common and specific antibodies are present in up to 90% of cats in catteries and in up to 50% of those in single-cat households. However, only about 5% of FECV-infected cats develop FIP in a cattery environment [2]. Based on widely accepted *in vivo* mutation theory, FIP

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arises by mutated enteric FECV in infected cat [3]. The average age for development of FIP is between 6 months to 2 years old [2]. Two major forms of FIP, an effusive and a non-effusive form, are recognized. In some cases of non-effusive FIP, body effusion can develop at the terminal stage of the diseases and become a mixed-type of FIP upon necropsy [1].

Cats with a strong humoral immunity and a weak or absent cell-mediated immune response against FIPV develop a persistent viremia and effusive FIP. Effusive disease results from widespread deposition of immune complexes in blood vessels and complement activation leading to vessel damage, vasculitis and leakage of serum and protein into body cavities [2,4]. Cats with partial cell-mediated immune responses along with humoral immunity develop the more chronic non-effusive form of FIP, which is characterized by immune mediated (delayed hypersensitivity-like) granulomatous, frequently perivascular, lesions in abdominal viscera, lungs, brain and eyes [2,4,5]. Ocular involvement is common, leading to a variety of changes such as iris color, dyscoria or anisocoria secondary to uveitis, sudden loss of the vision and hyphaema [6,7]. Although FIP cases were described in totally four cats [8-10] and two captive lions [11,12], there is no case report adressing ocular changes of FIP in Turkey. The aim of this report is to present clinical and pathological findings of a non-effusive FIP case with distinct ocular involvement.

CASE HISTORY

An approximately 2-year old weighting 2.750 g domestic short hair female cat was presented to Firat University Veterinary Teaching Hospital The history indicated that the cat had been adopted from street by the owner 6 month ago and she had depression, anorexia and weight loss for the last 15 days. Her vaccinations were current for feline herpesvirus-1 and feline calicivirus and feline parvovirus.

Clinical examination revealed depressed appetite, inco-ordination, hyperesthesia, circling, head tilt, posterior paraparesis, absence of the pupillary reflex, opisthotonus and anisocoria (mydriasis in the right eye and myosis in the left eye). Rectal temperature, heart and respiratory rates were 39.6ºC, 160 beats per minute and 60 breaths per minute, respectively. Abdominal ultrasounography was performed.

Following physical and ultrasonographic examination, blood samples were collected for hematological and biochemical analyses. The serum was separated by centrifugation at 2.000 g at 4ºC for 10 min and stored at -20ºC until use. Red blood cell (RBC) and white blood cell (WBC) count, hemoglobin (Hb) level, and packed cell volume (PCV), measurements were obtained by using manual methods. Serum alanin amino transferase (ALT), aspartate aminotransferase (AST), total protein (TP), total bilirubin (TB), direct bilirubin (DB), blood urea nitrogen (BUN), creatinine (CRSC), albumin (ALB) and globulin (GLB) levels were determined with a biochemistry analizator (Dimension ARX, Dade Behring). Following physical examination, blood samples were obtained for complete blood cell count (CBC), serum biochemistry (Dimension ARX, Dade Behring) and serological analyses.

Abdominal ultrasound revealed no significant finding. CBC was unremarkable including RBC: 7.3 10^6/µL, Hb: 11 g/dL, PCV 35% and WBC: 5.8 10^3/µL. Serum biochemistry analyses showed moderately elevated AST activity (108 U/L), however ALT (23 U/L), TP (7.3 g/L), TB (0.3 µmol/L), DB (0.1 µmol/L) BUN (28 mmol/L), CRSC (0.9 µmol/L) were in normal ranges. ALB was slightly under the lower limit of normal range and GLB was near the upper limit of normal range (ALB 2.5 g/dL, GLB 4.8 g/dL) [13].

Based on history and clinical findings (mild pyrexia, weight loss, dullness, depressed appetite, hyperaesthesia, circling, head tilt, opisthotonus, posterior paraperesis, absence of the pupillary reflex, uveitis, anisocoria and hyphaema), tentative diagnosis of FIP was made. Although symptomatic treatment including oral (prednisolone) and topical steroids (prednisolone acetate 1%) together with fluid therapy was instituted, the patient's condition worsened and died in following day and, subsequently complete necropsy was performed on the cat with histologic evaluation of tissues. Complete necropsy was performed and samples of kidney, eyes, liver, spleen, tongue, brain, intestines and lungs were fixed in 10% formalin and embedded in paraffin wax. Five µm sections were stained with hematoxyline and eosin (H-E) for histological examination.

A reverse transcriptase (RT)-PCR was performed in order to detect RNA of FCoV in the blood and brain tissue samples as described previously by Simons et al.[14].

Hyphyma which is more prominet in left eye, cloudy appearence of anterior chamber and bilateral pupillary dilatation *(Fig. 1A)*. Macroscopically; upon vertical sectioning of the globes, there was severe hyphema and thick proteinous fluid accumulation in vitreous of the both eyes *(Fig. 1B)*. The kidneys contained focal sub-capsular, gray to yellow raised nodules varying from 3 to 10 mm in diameter. There was discrete fatty change in the liver. The alimentary track had no abnormalities, nor spleen, heart and brain. The results of RT-PCR revealed that FCoV was positive in the blood sample *(Fig. 1C)*. For RT-PCR reactions, the primers were chosen from the highly conserved M gene sequence of the FCoV genome. As a control to check the efficiency of the RNA isolation from the blood samples and the subsequent reverse transcriptase reaction, a glyceraldehyde-3-phosphate dehydrogenase (GAPDH gene). After PCR, The DNA bands

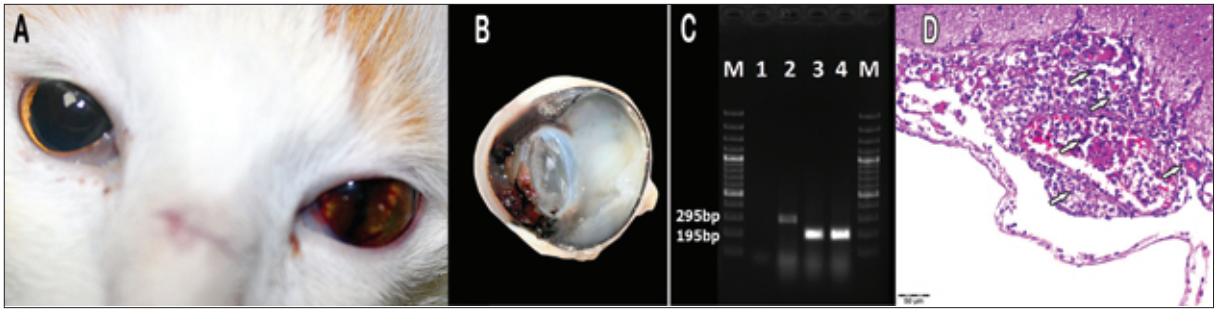

Fig 1. A- Hyphyma which is more prominet in left eye, cloudy appearence of anterior chamber and bilateral pupillary dilatation, **B-** Accumulation of proteinous exudate in vitreous and hemorrhage in anterior chamber, **C-** The RT-PCR results using primer pairs for FCoV M gene and GAPDH gene region (for FIPV 295bp, 195 bpfor GAPDH). M: 100 bp DNA ladder (Fermentas, Lithuania) Line 1: Brain tissue (FIPV), Lane 2: Leukocyte sample (FIPV), Lane 3: Brain tissue (GAPDH gene), Lane 4: Leukocyte sample (GAPDH), **D-** Vasculitis in cerebral meninges containing mixed inflammatory infiltrate in inner and outer surface of vessels *(arrows)*

Şekil 1. A- Sol gözde daha belrgin bir hifem, ön göz kamerasının bulanık görünümü ve çift taraflı pupilla dilatasyonu, **B-** Vitreusta proteinöz eksudat birikimi ve anteriyor kamarada kanama, **C-** FCoV M geni ve GAPDH gen bölgesi için kullanılan primer eşleşmelerine göre RT-PCR sonuçları (FIPV 295bp, 195 bpfor GAPDH). M: 100 bp DNA basamağı (Fermentas, Litvanya) Sıra 1: Beyin dokusu (FIPV), Sıra 2: Lökosit örneği (FIPV), Sıra 3: Beyin dokusu (GAPDH), Sıra 4: Lökosit örneği (GAPDH), **D-** Damarların iç ve dış yüzeyinde miks yangısal infiltrat içeren vaskülitis *(oklar)*

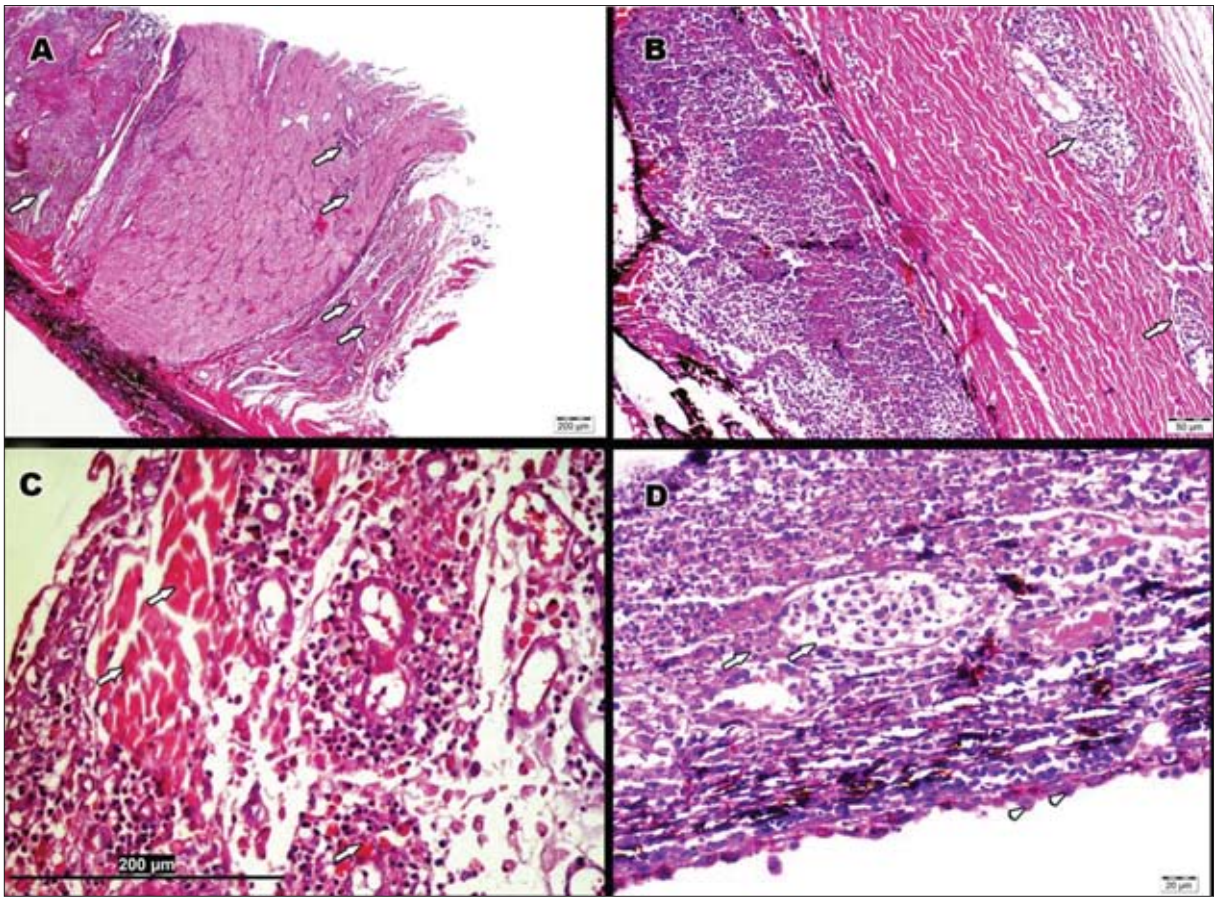

Fig 2. A- Optic nerve meningitis *(arrow)* and optic neuritis characterized by perivascular infiltration *(arrows)*, **B-** Pyogranulomatous inflammatory reaction in corpus cilliare and perivascular infiltrations in scleara *(arrows)*, **C-** Necrotic changes in muscle *(arrows)* and perivascular lymphoplasmacytic infiltrations, **D-** Vasculitis *(arrows)*, interstitial lymphohistiocytic infiltration in choroidea and hypertrophic retinal pigment epithelium *(arrow head)*

Şekil 2. A- Perivasküler infiltrasyon ile belirgin optik sinir meningitis *(ok)* ve optik nöritis *(oklar)*, **B-** Korpus siliare'de pyogranulomatoz inflamatuar reaksiyon ve sklerada perivasküler infiltrasyon, **C-** Kas liflerinde nekrotik değişimler *(oklar)* ve perivasküler lenfoplazmasitik infiltrasyonlar, **D-** Vaskülitis *(oklar)*, koroidde intersitisyel lenfohistiositik infiltrasyon ve retinal pigment epitelinde hipertrofi *(ok başı)*

were observed under UV light and photographic records were made. 195 bp band were positive reaction control provided by the Feline GAPDH gene. 295 bp band were positive as feline coronavirus. Microscopic changes were limited to the meninges, optic nerves, eyes, and kidneys. Most of these changes were characterized by mixed inflammatory reaction together with vasculitis and perivascular infiltration. Meninges showed foci of pyogranulomatous to lymphohistiocytic infiltration and vasculitis *(Fig. 1D)*. Perivascular inflammatory reaction was more prominent in orbital meninges and optic nerve *(Fig. 2A)*. There was a pyogranulomatous panuveitis and anterior uveitis in the left and right eye, respectively. The interstitial and perivascular inflammatory infiltrate contained neutrophils, lymphocytes and foamy macrophages with a higher neutrophilic component in iris, ciliary process, ciliary body and sclera *(Fig. 2B)*. Pyogranulomatous vasculitis by mixed inflammatory infiltrate was limited to the iris and sclera in the right eye. There was mild edema, focal mild perivascular lymphohistiocytic infiltrations and few hemosiderine containing macrophages in iridial stroma in the left eye. There was moderately fibrino-purulent exudate accumulation with considerable foamy macrophages in vitreous in both eyes. Rhabdomyocytes showed moderate to severe degenerative to necrotic changes and perivascular infiltrations of pure lympho-plasmacytic cells *(Fig. 2C)*. The choroid was expanded by mixed cellular infiltration, mild pigment incontinence and showed vasculitis *(Fig. 2D)*. Retina was partially detached due to subretinal exudate in non-tapetal region. The other lesions included mild corneal and conjunctival edema. Renal changes consisted of focal pyogranulomatous nephritis characterized by infiltration of cell mixture including lympho-histiocytes and neutrophiles in renal cortex and rarely medulla. Pyogranulomas were non-necrotic and there were diffuse hydropic changes in renal tubules and multifocal hyaline casts in tubular lumen.

DISCUSSION

As there is no gold standard for diagnosis of FIP and the lesions are diverse and highly variable, it is always challenge to make histo-pathological diagnosis. However, in the present case the diagnosis was based on histopathology and PCR [6]. Consistent with the earlier reports, clinical signs including mild pyrexia, weight loss, dullness, depressed appetite were determined in the present case. Mild pyrexia had probably caused to tachycardia and tachypnea. Signs referable to spinal cord involvement, such as incoordination, hyperaesthesia, circling, head tilt, posterior paraperesis were also present [2,5]. As the eye is the last effected organ in FIP and the cat could die before it's involvement, the ocular pathology might not be observed in most cases. In the present case, involvement of the organs other than eye was mild. Ocular lesions were bilateral and included protein rich fluid accumulation in ocular compartments, uveitis, vasculitis, pure lymphoplasmacytic infiltrations and rhabdomyositis were fairly characteristic and almost pathognomonic for FIP [2,6,7]. Ocular involvement is relatively common in dry form, leading to a variety of changes, such as iris colour, anisocoria secondary to anterior uveitis, sudden loss of the vision and hyphaema [6,7]. These ocular signs completely coincided with the findings determined in this case. Although there are some reports indicating ocular lesions of FIP in the worldwide, ocular lesions in FIP have not been reported in Turkey.

A very common laboratory finding in cats with FIP is an increase in total serum protein concentration caused by a rise in globulins [15]. This is found in about 50% of cats with effusion and 70% of cats without effusion [1]. Albumin level remains normal or falls slightly [16]. Low albumin level is usually associated with protein loss caused by glomerulopathy secondary to immune complex deposition or by extravasation of protein-rich fluid during vasculitis [17]. GLB level increases, possibly through stimulation of B cells by interleukin-6, which is produced as part of the disease process [16]. In the present case, although serum total protein was in the reference ranges, ALB was slightly under the lower limit of normal range and GLB was near the upper limit of normal range. Other laboratory parameters (liver enzymes, bilirubin, urea, creatinine) can be variably elevated depending on the degree and localization of organ involvement, however they are generally not diagnostic [17]. In the present case, those values were in the reference ranges out of slightly increased AST level. Slightly increased AST level was probably associated with discrete fatty change. In this study, the non-effusive FIP was diagnosed through history, clinical, pathological and polymerase chain reaction (PCR) findings.

Collectively; FIP should be considered in differential diagnosis of diseases showing similar findings in cats. Distinct ocular lesions in combination with the other findings may be useful criteria in the diagnosis of FIP.

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