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Case Report *Olgu Sunumu* DOI: 10.5281/zenodo.12571027

A Case of Severe Proteinuria Due to Glomerulonephritis in a Cat

Bir Kedide Glomerulonefritise Bağlı Şiddetli Proteinüri Olgusu

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ABSTRACT

Glomerulonephritis is characterized by inflammation of the glomeruli. It is rare in cats glomerulonephritis and its etiology is not fully understood, although it can occur in many diseases such as feline leukemia virus (FeLV) feline immunodeficiency virus (FIV) and panleukopenia. Glomerulonephritis in cats presents with clinical signs such as proteinuria, hypoalbuminemia and ascites, among others. In this case presentation a detailed evaluation of glomerulonephritis was aimed a 7-year-old neutered male tabby cat presenting with complaints of ascites, peripheral edema, loss of appetite, and weakness, and diagnosed based on clinical, laboratory and ultrasonography findings. Consequently, in cats exhibiting symptoms like proteinuria and ascites, glomerulonephrıtıs should be thoroughly assessed.

Keywords: Ascites, Cat, Glomerulonephritis, Proteinuria

ÖZ

Glomerulonefritis, glomerulların yangısıyla karakterize bir durumdur. Kedilerde glomerulonefritis nadir görülmektedir ve etiyolojisi tam olarak bilinmemekle birlikte kedi lösemi virüsü (FeLV), kedi immun yetmezlik virüsü (FIV) ve panlokopeni gibi birçok hastalıkta meydana gelebilmektedir. Glomerulonefritis kedilerde proteinüri, hypoalbuminemi, asites, gibi klinik bulgularla seyretmektedir. Bu olgu sunumunda asites, periferal ödem, iştahsızlık ve halsizlik şikâyeti ile getirilen, klinik ve laboratuvar ve ultrasonografi bulguları doğrultusunda glomerulonefritis tanısı konulan 7 yaşlı erkek, tekir ırkı kısır bir kedide glomerulonefritis detaylı bir şekilde değerlendirilmesi amaçlanmıştır. Sonuç olarak proteinüri ve asites gibi bulguları olan kedilerde glomerulonefritis mutlaka değerlendirilmelidir.

Anahtar Kelimeler: Asites, Glomerulonefritis, Kedi, Proteinüri

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INTRODUCTION

The nephron, which is the functional unit of the kidney, consists of glomeruli, Bowman capsule and renal tubule. The glomerular basement membrane surrounds the capillaries and acts as a glomerular filter.[1] Glomerulonephritis (GN) is a condition characterised by inflammation of the glomeruli in the kidneys, leading to proteinuria and renal dysfunction.[2-4] Although both dogs and cats are affected by glomerulonephritis, glomerulonephritis is more common in dogs and less common in cats.[5,6] According to the World Small Animal Veterinary Association-Renal Standardisation Study Group (WSAVA-RSSG), glomerulonephritis is classified as immune complex glomerulonephritis and non-immune complex glomerulonephritis, and according to histopathological definitions, it is classified as membranous glomerulonephritis, proliferative (mesangioproliferative) glomerulonephritis and membranoproliferative glomerulonephritis.[7,8] Although little is known about the types and prevalence of glomerular disease in cats, the most common form of membranous glomerulonephritis is reported.[9,10] Glomerulonephritis in cats is a complex condition that may be associated with various underlying diseases.[11] These diseases include feline leukaemia virus (FeLV), feline immunodeficiency virus (FIV), immune-mediated diseases, panleukopenia and congenital heart diseases.[10-13] It is observed in cats between 3-4 years of age on average. In addition, although it is determined that it is more common in male cats (64% to 100%), there is no explanation for this finding.[14,15] Glomerulonephritis is a clinically important disease characterised by proteinuria and renal failure in cats.[16] Clinically, findings such as weight loss, anorexia, lethargy, polyuria, polydipsia, vomiting, ascites or peripheral edema may be observed.[5] Laboratory findings include anemia, azotemia, hypertension, hypercholesterolemia and hypoalbuminemia.[4] Treatment of glomerulonephritis in cats usually involves a combination of therapies including corticosteroids and benazepril. In addition, studies are investigating the use of telmisartan in combination therapy in the treatment of nephrotic syndrome due to non-immune-mediated glomerulonephritis in cats.[17] Studies show that high doses of telmisartan can improve glomerular and tubulointerstitial damage in glomerulonephritis.[18] The mechanism of action of telmisartan includes anti-inflammatory effects through PPARγ activation in mesangial cells and contributes to its efficacy in the treatment of glomerulonephritis.[19] Also, Acetylsalicylic acid (ASA), commonly known as aspirin, has been studied in the context of glomerulonephritis, a condition characterised by inflammation in the glomeruli of the kidneys. Research suggests that ASA may play a role in the treatment of glomerulonephritis with its anti-inflammatory properties.[20]

Albumin is one of the major proteins lost in glomerulonephritis. Albumin is a large molecule protein and its passage is largely prevented by normal glomeruli due to its net negative charge. However, the damage occurring in glomerulonephritis disrupts the glomerular filter and permeability and causes the excretion of proteins, especially albumin, in the urine.[1] Hypoalbuminemia, which is characterised by low serum albumin levels due to proteinuria, leads to a decrease in vascular colloid osmotic pressure and causes ascites formation.[21]

This case report aims to give detailed information about a cat diagnosed with glomerulonephritis.

CASE PRESENTATION

The material of the case consisted of a 7-year-old male tabby cat with complaints of ascites, peripheral edema (Figure 1), anorexia and malaise. On examination, fluctuations were observed in the abdomen and subcutaneous tissues.

Figure 1. Peripheral edema in a cat diagnosed with glomerulonephritis.

Haemogram, serum biochemistry and urine analysis were performed. In haemotological analysis, anemia due to low hemoglobin was detected, while other values were between reference values. Serum biochemical analysis revealed hypoalbuminemia, hypoproteinaemia, globulin and decreased alanine aminotransferase (ALT) values, while urea (BUN) and BUN/creatinine ratio increased. Ultrasonographic examination revealed normal right kidney (Renal L: 4.52 cm, Renal H: 3.00 cm, Renal Width: 3.03 cm, Cortex: 0.98 cm) and left kidney (Renal L: 4.43 cm, Renal H: 3.08 cm, Renal Width: 2.91 cm, Cortex: 0.83 cm) (figure 2).

Figure 2. In a cat diagnosed with glomerulonephritis, ultrasonography of the kidney

Alkaline phosphatase, creatinine and glucose were found to be within the reference values. At the same time, increased urine protein to creatinine ratio (UPC) and urinary protein (UPRO) values were detected in serum biochemical analysis. The results of haematology and serum biochemical analyses are shown in Table 1 and Table 2. In urine analysis, proteinuria (300 mg/dL) was detected and the presence of blood in the urine (0.6 mg/dL) was also detected. The pH (5) was determined to be low. Other values were found to be within the reference ranges.

Table 1. Results of hematology analyses and normal reference values

HEMATOLOGY	CASE	REFERENCE RANGE
Hematocrit(HCT)	22.5 %	26-47 %
Hemoglobin (HGB)	8 g/dL	8,5 - 15,3 g/dL
Mean Corpuscular Volume (MCH)	14.9 pg	11,8- 18,0 pg
Mean Corpuscular Hemoglobin Concentration (MCHC)	35,4 g/dL	29,0-36,0 g/dL
Red Cell Distribution Width (RDW)	17,5 %	16,0- 23,0 %

A diagnosis of glomerulonephritis was made considering the clinical and laboratory findings. Telmisartan 1 mg/kg, q24h dose peroral and acetylsalicylic acid 18.75 mg/cat 3 times a week, peroral were used in the treatment. After 10 days of treatment, serum biochemical analyses and urine analyses were repeated. In serum biochemistry, BUN value (36 mg/dL) decreased compared to the first value, but it was still higher than the reference values. Other values were found to be within normal limits. UPRO (50 mg/dL) values decreased compared to the initial value, but were still higher than the reference values. UPC (0.17) decreased to normal reference values. After the treatment, all values in the urine analysis were found to be within normal reference values and the cat was discharged in a healthy condition.

Table 2. Results of serum biochemical analyses and normal reference values

SERUM BIOCHEMISTRY	CASE	REFERENCE RANGE
Albumin (ALB)	1 g/dL	2,3- 3,5 g/dL
Total Protein (TP)	3.1 g/dL	5,7- 7,8 g/dL
Alanine Aminotransferase (ALT)	20 u/L	22,0- 84,0 u/L
Urea (BUN)	58.3 mg/dL	17,6- 32,8 mg/dL
BUN/Creatinine Ratio	36.4 mg/dL	4,0- 33,0 mg/dL
Alkaline Phosphatase (ALP)	20 u/L	9,0- 53,0 u/L
Creatinine	1.6 mg/dL	0,8- 1,6 mg/dL
Glucose	106 mg/dL	71-148 mg/dL
Globulin	2.1 g/dL	2,6-5,1 g/dL
Urine Protein to Creatinine Ratio (UPC)	3.89	0- 0,4
Urinary Protein (UPRO)	350 mg/dL	1-30 mg/dL

DISCUSSION

Although glomerulonephritis is rare in cats, various types of glomerulonephritis have been reported in many studies.[4,9,11] A retrospective study based on clinicopathological data provides valuable information about immune complex glomerulonephritis in cats.[11] Collectively, these studies emphasise the importance of addressing feline glomerulonephritis to improve feline renal health.[4,11]

Proteinuria is a finding in cats with glomerulonephritis and may be associated with various underlying conditions.[23] In addition, some cats with glomerulonephritis have a relatively good prognosis despite severe proteinuria.[24] Cavana et al. reported severe proteinuria in a 5-year-old female cat with non-amyloidotic fibrillary glomerulonephritis in a case report.[22] In the presented case, proteinuria was found in the cat with glomerulonephritis. This was explained by the disruption of the glomerular filter and permeability by the damage occurring in glomerulonephritis and increased excretion of proteins in the urine due to impaired permeability.[1]

Hypoalbuminemia is a common finding in cats with glomerulonephritis.[4,25] In a retrospective study conducted by Rayhel et al. in cats with proteinuria, they reported that hypoalbuminemia was one of the clinicopathological variables observed in cats with glomerulonephritis.[4] In addition, Asano et al. reported the association of hypoalbuminemia with proteinuric renal disease and immune complex-mediated glomerulonephritis in cats in a study on membranoproliferative glomerulonephritis in young cats and also reported that hypoalbuminemia may be an indicator of the severity of glomerular damage and protein loss in affected cats.[16] In the presented case, hypoalbuminemia was found in the cat with glomerulonephritis. Glomeruli prevent the passage of net negatively charged molecules larger than 70.000 D. Albumin is approximately 65,000 D. However, its passage is largely prevented by normal glomeruli because of its net negative charge. The formation of hypoalbuminemia in glomerulonephritis may be explained by inability to prevent passage due to glomerular damage due to glomerulonephritis and intense albumin loss.[1]

Glomerulonephritis is a common cause of protein-losing nephropathy in cats and causes fluid accumulation in the abdominal cavity known as ascites.[4] Ascites is a clinical sign that can be observed in cats with various renal diseases including glomerulonephritis. In a study by Rossi et al. on immune complex glomerulonephritis in cats, it was found that ascites were a common finding in cats diagnosed with glomerulonephritis.[11] In the presented case, intense ascites and peripheral edema were found in the cat with glomerulonephritis. The cause of ascites was thought to be transudations resulting from the imbalance of hydrostatic and oncotic pressures along the intact vascular system or exudations resulting from the passage of fluid from leaking blood vessels into the pleural cavity. A decrease in oncotic pressure occurs due to hypoalbuminemia and intravascular fluid exudates out of the vessel and causes ascites formation.[26] Ascites formation in glomerulonephritis may be explained by a decrease in oncotic pressure due to hypoalbuminemia.

Anemia is a common condition in cats and may be associated with various underlying diseases including glomerulonephritis. It has also been associated with various clinicopathological features including glomerulonephritis, hypertension and azotemia in cats.[4] In a study by Nash et al. in 13 cats with membranous nephropathy, anemia was found in 85% of the cats.[10] In a retrospective study conducted by Rayhel et al. in cats with proteinuria, anemia was found in cats with glomerulonephritis. In the same study, hypertension and azotemia were also found in cats with glomerulonephritis.[4] In the presented case, anaemia, hypertension and azotemia were found in the cat with glomerulonephritis. Glomerulonephritis is an important cause of chronic kidney disease in cats and may lead to anemia due to decreased erythropoietin production and shortened life span of erythrocytes.[4] The anemia that occurs in glomerulonephritis may be explained by decreased production of the hormone erythropoietin due to kidney involvement. Studies show that mild to moderate hypertension is common in cats with chronic renal failure.[27] In addition, the renin-angiotensin-aldosterone system (RAAS) is thought to play a role in the development of hypertension associated with renal failure in cats.[28] Abnormalities in laboratory analysis are usually non-specific and reflect the underlying disease.[29] Azotemia is a common condition in cats with renal failure.[30] Glomerulonephritis is a condition leading to renal dysfunction.[2,3,4] The formation of azotemia and hypertension in glomerulonephritis can be explained by renal dysfunction.

In conclusion, glomerulonephritis is a rare but important condition in cats. Among the symptoms of glomerulonephritis, anemia, vomiting, weight loss, abdominal swelling, and low albumin levels may be observed, but the most prominent indicator is proteinuria. Understanding the relationship between proteinuria and glomerulonephritis in cats is very important for the correct diagnosis and treatment of this condition.

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REFERENCES

1. Grant DC, Forrester SD. Glomerulonephritis in dogs and cats: glomerular function, pathophysiology, and clinical signs. Compendium on Continuing Education for the Practising Veterinarian-North American Edition. 2001;23(8):739-747.
2. Syme HM, Markwell PJ, Pfeiffer DU, Elliott J. Survival of cats with naturally occurring chronic renal failure is related to severity of proteinuria. *J. Vet. Intern. Med.* 2006;20(3):528.
3. Kuwahar Y, Nishii N, Takasu M, Ohba Y, Maeda S, Kitagawa H. Use of urine albumin/creatinine ratio for estimation of proteinuria in cats and dogs. *J Vet Med Sci*. 2008;70(8): 865-867.
4. Rayhel LH, Quimby JM, Cianciolo RE, Cléroux A, McLeland S, Fränken T. Clinicopathologic and pathologic characteristics of feline proteinuric kidney disease. *J Feline Med Surg.* 2020;22(12):1219-1229.
5. Vaden SL. Glomerular disease. *Top. Companion Anim. Med.* 2011;26(3):128-134.
6. Cook AK, Cowgill LD. Clinical and pathological features of protein-losing glomerular disease in the dog: A review of 137 cases (1985–1992). *J Am Anim Hosp Assoc.* 1996;32:313–322.
7. Cianciolo RE, Mohr FC, Aresu L, et al. World small animal veterinary association renal pathology initiative: classification of glomerular diseases in dogs. *Vet. Pathol.* 2016;53(1):113-135.
8. Grauer GF, DiBartola SP. Glomerular disease, in Ettinger SJ, Feldman EC (eds): Textbook of Veterinary Internal Medicine. Diseases of the Dog and Cat. Philadelphia, WB Saunders Co, 2000; pp:1662–1678.
9. Gross C, Cianciolo RE, Lees GE, Brown CA, Foster JD. Proliferative, necrotizing and crescentic immune complex-mediated glomerulonephritis in a cat. *J. Feline Med. Surg. Open Rep.* 2015;1(2):2055116915603995.
10. Nash AS, Wright NG, Spencer AJ, Thompson H, Fisher EW. Membranous nephropathy in the cat: a clinical and pathological study. *Vet. Rec.* 1979;105(4):71-77.
11. Rossi F, Aresu L, Martini V, et al. Immune-complex glomerulonephritis in cats: a retrospective study based on clinico-pathological data, histopathology and ultrastructural features. *BMC Vet. Res.* 2019;15(1):1-9.
12. Thornburg LP, Kinden D, Digilio K. Immune glomerulitis in a cat. *Vet. Pathol.* 1979;16(5):604-606.
13. Reinacher M. Diseases associated with spontaneous feline leukemia virus (FeLV) infection in cats. *Vet. Immunol. Immunopathol*. 1989;21(1):85-95.
14. Arthur JE, Lucke VM, Newby TJ, Bourne FJ. The long-term prognosis of feline idiopathic membranous glomerulonephropathy. *J Am Anim Hosp Assoc*. 1986;22:731-737.
15. Lucke VM. Glomerulonephritis in the cat. *Vet. Annu*. 1982;22:270-278.
16. Asano T, Tsukamoto A, Ohno K, Ogihara K, Kamiie J, Shirota K. Membranoproliferative glomerulonephritis in a young cat. *J Vet Med Sci*. 2008;70(12):1373-1375.
17. Casado Bregón D, Cianciolo RE, Smith VA. The use of telmisartan in combination therapy in the management of nephrotic syndrome due to non-immune-mediated glomerulonephropathy in a young cat. *Vet. Rec. Case Rep.* 2021;9(4):e210.
18. Ranjbar R, Shafiee M, Hesari A, Ferns GA, Ghasemi F, Rezayi M. The potential therapeutic use of renin–angiotensin system inhibitors in the treatment of inflammatory diseases. *J. Cell. Physiol.* 2018;234(3):2277-2295.
19. Han W, Zhao H, Jiang B, Liu F. Epa and dha increased pparγ expression and deceased integrin-linked kinase and integrin β1 expression in rat glomerular mesangial cells treated with lipopolysaccharide. *Biosci. Trends*. 2014;8(2):120-125.
20. Hirahashi J, Hanafusa N, Wada T, et al. Aspirin and eicosapentaenoic acid may arrest progressive iga nephropathy: a potential alternative to immunosuppression. *J. Intern. Med.* 2015;54(18):2377-2382.
21. Buob S, Johnston AN, Webster CRL. Portal hypertension: pathophysiology, diagnosis, and treatment. *J. Vet. Intern. Med.* 2011;25(2):169-186.
22. Cavana P, Capucchio MT, Bovero A, et al. Noncongophilic fibrillary glomerulonephritis in a cat. *Vet. Pathol.* 2008;45(3):347-351.
23. Brown CA, Elliott J, Schmiedt CW, Brown SA. Chronic kidney disease in aged cats. *Vet. Pathol.*

2016;53(2):309-326.
24. Kuwahara Y, Ohba Y, Kitoh K, Kuwahara N, Kitagawa H. Association of laboratory data and death within one month in cats with chronic renal failure. *J Small Anim Pract*. 2006;47(8):446-450.
25. DeClue AE, Delgado C, Chang CH, Sharp CR. Clinical and immunologic assessment of sepsis and the systemic inflammatory response syndrome in cats. *J Am Vet Med Assoc*. 2011;238(7):890-897.
26. Muzumdar H. Pleural effusion. *Pediatr Rev*. 2012;33(1):45-47.
27. Bijsmans E, Jepson R, Chang Y, Syme HM, Elliott J. Changes in systolic blood pressure over time in healthy cats and cats with chronic kidney disease. *J. Vet. Intern. Med.* 2015;29(3):855-861.
28. Brown SA, Brown CA, Jacobs G, Stiles J, Hendi RS, Wilson S. Effects of the angiotensin converting enzyme inhibitor benazepril in cats with induced renal insufficiency. *Am. J. Vet. Res.* 2001;62(3):375-383.
29. Grant DC, Forrester SD. Glomerulonephritis in dogs and cats.Diagnosis and treatment. Compendium on Continuing Education for the Practising Veterinarian. 2011;23.
30. Brown CA, Jeong KS, Poppenga RH, et al. Outbreaks of renal failure associated with melamine and cyanuric acid in dogs and cats in 2004 and 2007. *J. Vet. Diagn. Invest.* 2007;19(5):525-531.

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Uterine Torsion in a Pregnant Tabby Cat

Gebe Bir Tekir Kedide Uterus Torsiyonu

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ABSTRACT

Uterine torsion, which is rarely observed in queens and bitches, is known as one of the causes of dystocia. In the anamnesis, it is noted that the patient was brought due to a general condition disorder rather than abdominal contractions. Lethargy, hypothermia (37°C), stomach pain, and bloody vaginal discharge were noted during the clinical examination. Doppler ultrasonography were used to assess the viability of palpable foetuses from the abdominal wall. Upon the patient's owner request, it was decided to perform ovariohysterectomy (OHE). The diagnosis following midline laparotomy was a unilateral uterine torsion. There was evidence of a 270° longitudinal axis torsion at the left cornu uteri. The right cornu uteri appeared normal, but the left cornu uteri was cyanotic. To relieve the tension on the uterus, a small incision was made in the torsionized cornu uteri to remove the two dead kittens. The incision site was tamponaded with a sponge to prevent leakage of uterine contents into the abdomen. However, no incision was made in the other cornu uteri. At the end of the procedure, ovariohysterectomy was performed and the operation line was closed. In conclusion, this case report summarizes the clinical signs, approaches and intraoperative management of uterine torsion, a rare condition in pregnant queens.

Keywords: Dystocia, Ovariohysterectomy, Pregnant, Tabby Cat, Uterine Torsion.

ÖZ

Kedi ve köpeklerde nadir görülen uterus torsiyonu, güç doğum nedenlerinden biri olarak bilinmektedir. Anamnezde hastanın abdominal kontraksiyonlardan ziyade genel durum bozukluğu nedeniyle getirildiği belirtilmiştir. Klinik muayene sırasında letarji, hipotermi (37°C), karın ağrısı ve kanlı vajinal akıntı kaydedildi. Karın duvarından palpe edilebilen fetüslerin canlılığını değerlendirmek için doppler ultrasonografi kullanıldı. Hasta sahibinin isteği üzerine ovariohisterektomi (OHE) yapılmasına karar verildi. Median hattan yapılan laparotomi ile torsio uteri teşhisi konuldu. Sol cornu uterinin uzun ekseninde 270°'lik torsiyon belirgindi. Sağ cornu uteri normal görünürken, sol cornu uteri siyanotikti. Uterus üzerindeki gerilimi hafifletmek için, ölen iki yavruyu çıkarmak üzere torsiyona uğramış kornu uteri'ye küçük bir kesi yapıldı. Uterus içeriğinin karın içine sızmasını önlemek için kesi yapılan bölge spançla tamponlandı. Ancak, diğer kornu uteriye herhangi bir ensizyon yapılmadı. İşlem sonunda ovaryohisterektomi yapılarak operasyon hattı kapatıldı. Sonuç olarak, bu vakada gebe kedilerde nadiren karşılaşılan bir durum olan uterus torsiyonu vakalarında, klinik belirtiler, yaklaşımlar ve operasyon sırasında ki tedavi özetlenmiştir.

Anahtar Kelimeler: Gebelik, Güç Doğum, Ovariohisterektomi, Tekir kedi, Torsiyo uteri.

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INTRODUCTION

Dystocia is defined as difficulties in the parturition process caused by abnormalities in the mother cat or the kitty, or both.[1-3] One of the conditions causing dystocia is uterine torsion (UT). Uterine torsion, which is not common except in cows, occurs when the uterus or its cornu rotates around its axis to varying degrees.[4,5] Although the cause is uncertain, laxity of the uterine ligaments, movement of the foetuses and physical activity predispose to UT.[6,7] Since there is no specific symptom, the diagnosis is made by experimental laparotomy.[3] The viability of the kittens should be evaluated by Doppler USG before the operation.[3] If the kittens are alive, C-section can be attempted.[7] However, if the kittens die, ovariohysterectomy (OHE) should be considered due to the risk of possible release of endotoxin or inflammatory mediators.[3,8] Since UT is life-threatening for both the kittens and the mother, fluid therapy or, if possible, blood transfusion should be given throughout the operation.[7,8] In this case report, the diagnosis, surgical procedure and prognosis of UT in a tabby cat are discussed and the clinical approach is summarized.

CASE PRESENTATION

In the anamnesis taken from the owner of the pregnant cat, we were told that the patient was brought to our clinic due to general condition disorder rather than abdominal contractions. Lethargy, coldness (37°C), stomach pain, and bloody vaginal discharge were noted during the clinical examination. Additionally, the skin turgor and capillary filling time were used to understand the existence of dehydration of up to 5-10%. The conjunctiva and oral cavity mucous membranes were paler, and the capillary refill time was longer. Doppler ultrasonography were used to assess the viability of palpable foetuses from the abdominal wall. Due to the absence of signs of viability in one horn, emergency cesarean section was recommended. Upon the patient's request, it was decided to perform ovariohysterectomy (OHE). Subsequent to the pre-anesthesia phase, an induction procedure was conducted using medetomidine hydrochloride 0.12 mg (0.04 mg/kg, im, Domitor®, Zoetis, Turkey), 0.12 mg butorphanol (0.04 mg/kg, sc, Butomidor®, Richter Pharma®, Austria), and 6 mg (3 mg/kg, iv, Propofol-Lipuro®, Braun, Germany). Once the righting reflex was absent, a 3-mm internal diameter cuffed tube (Sheridan/CF, Teleflex, NC, USA) was used to intubate the trachea. The anesthetic used for inhalation was % 5 isoflurane (Isoflurane; Piramal Critical Care Inc., PA, USA) with 50% oxygen (5L/min) circulating through the system. 30 ml of dextran 70 (10 ml/kg/day, iv, Profileks, Turkey) and 100 ml of Ringer's lactate (5 ml/kg/hour, iv, S.A.L.F. S.p.A, Italy) were the fluids used in the pre-operative fluid therapy. The diagnosis following midline laparotomy was a unilateral uterine torsion. There was evidence of a 270° longitudinal axis torsion at the left cornu uteri. The right cornu uteri appeared normal, but the left cornu uteri was cyanotic (Figure 1).

Figure 1. *Cyanotic left cornu uteri with 270° torsion and nornal cornu uteri*

Hemostatic forceps were applied to the apical and basal part of the torsion horns to avoid excessive tension and to shorten the uterine stump. The torsion horn was cut through a small incision to remove the two dead kittens and a second incision was made outside the surgical line. No further attempt was made to prevent leakage of the uterine contents into the abdomen; however, the other horn was not incised and the ovaries and uterus were removed en bloc technique. None of the kittens survived because they didn't complete their development. As a matter of fact, it was seen that the kittens removed from the cyanotic cornu had a cyanotic color (Figure 2). Although the mother queen woke up at the end of the operation, she was kept under observation for a day. The patient was discharged after making sure that the condition was stable.

Figure 2. *Kittens removed from cyanotic cornu (two on the left) and normal cornu uterus (three on the right)*

DISCUSSION

Uterine torsion (UT), which is rarely seen in cats, is one of the causes of difficult delivery, which is usually encountered in the last trimester of pregnancy.[9] In the presented case, UT occurred approximately on the 45th day of pregnancy.[4,6] The fact that the anamnesis included information about the habit of constantly climbing and jumping to high places in the house indicates that the presented case overlaps with previous cases.[7] In addition, the clinical symptoms in the case were similar to those in the literature.[6,10] Since the contrast enhanced computed tomography device, which is widely used in human medicine, was not available in our clinic, the diagnosis was made by laparotomy.[7,9,11] The choice of operation was based on the lack of viability in some kittens on Doppler USG examination and the deteriorating general condition of the pregnant queen.[3,9,12] As described in previous cases, UT was diagnosed by laparotomy. Again, considering the warnings in previous cases, the tissue was tried to be removed before the torsion dissolved. Otherwise, endotoxic shock or excessive inflammatory response could have occurred.[13,14] Blood sampling could not be performed due to the urgency of the situation. However, it is known to be necessary to summarize the patient's condition before every operation.[15] Fluid therapy should be performed intraoperatively in such risky cases to maintain general condition stability. Even blood transfusion should be performed if possible.[7] In this case, fluid therapy was administered throughout the operation. In previous cases, it was said that late intervention or side effects of anesthesia could result in death.[7,16] Eventually, the patient's condition was stabilized and the operation was completed. However, since the UT occurred at the beginning of the last trimester and the kittens had not completed their development, none of the kittens survived.

Uterine torsion may be suspected in pregnant cats in the presence of the symptoms presented in the case. Although UT in queens is rare, it should be kept in mind that it is a case that can be encountered. In conclusion, this case summarizes the possible clinical signs, and approaches, for cases of UT in queens.

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REFERENCES

1. Mota-Rojas D, Martínez-Burnes J, Napolitano F, et al. Dystocia: factors affecting parturition in domestic animals. *CAB Rev.* 2020;1-16.
2. Pretzer SD. Medical management of canine and feline dystocia. *Theriogenology.* 2008;70:332-336.
3. Tohumcu V, Çiplak AY, Aydin ŞA. Unilateral Uterine Horn Torsion in a Pregnant Angora Cat. *J Vet Case Rep.* 2021;1:14-17.
4. Thilagar S, Yew YC, Dhaliwal GK, et al. Uterine horn torsion in a pregnant cat. *Vet. Rec*. 2011;157:558-560.
5. Weldeyohanes G, Haben F. Dystocia in domestic animals and its management. *Int J Pharm Biomed Res.* 2020;7(3):1-11.
6. Ali M, Suresh A, Sarath T, et al. Surgical Management of Dystocia Due to Unilateral Uterine Torsion in a Domestic Shorthair Cat. *Top Companion Anim Med.* 2021;45:100577.
7. Kuroda K, Osaki T, Harada K, et al. Uterine torsion in a full-term pregnant cat. *J Feline Med Surg Open Rep.* 2017;3:1-4.
8. Stanley SW, Pacchiana PD. Uterine torsion and metabolic abnormalities in a cat with a piometra. *Can Vet J.* 2008;49:398-400.
9. Hendy EAA, Elgohary BK. Unilateral uterine torsion in a pregnant cat. *J. Adv. Vet. Res.* 2023;13(1):138-140.
10. Dal-Bó ÍS, Corrêa TO, Ferreira MP. Uterine torsion in domestic feline–case report. *Ars Vet Jab*. 2013;29:88-92.
11. Doğruer G, Köse AM, Koldaş Ürer E, Doğruer A. Unilateral uterine torsion in a pregnant bitch. *Eurasian J Vet Sci.* 2018;34(1):60-64.

12. Kumru IH, Seyrek-Intas K, Seyrek-Intas D, Tek HB, Wehrend A. Clinical case: unilateral en bloc ovariocornuectomy as a treatment for uterine torsion in a bitch. *Revue Med Vet.* 2011;162:76-78.
13. Ridyard AE, Welsh EA, Gunn-Moore DA. Successful treatment of uterine torsion in a cat with severe metabolic and haemostatic complications. *J Feline Med Surg.* 2000;2:115–119.
14. De La Puerta B, McMahon L, Moores A. Uterine horn torsion in a non-gravid cat. *J Feline Med Surg.* 2008;10:395–397.
15. Traas AM. Surgical management of canine and feline dystocia. *Theriogenology*. 2008;70(3):337-342.
16. Brodbelt DC, Flaherty D, Pettifer GR. Anesthetic risk and informed consent. In: Grim KA, ed. Veterinary Anesthesia and Analgesia. New Jersey: Wiley Blackwell; 2015:11-22.

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Histopathologic and Immunohistochemical Approach to a Case of Invasive Cribriform Carcinoma in Mammary Tissue of Sprague Dawley Rat

Sprague Dawley Ratının Meme Dokusunda İnvaziv Kribriform Karsinom Olgusuna Histopatolojik ve İmmünohistokimyasal Yaklaşım

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ABSTRACT

Breast cancer is a neoplastic disease that originates in the breast tissue and can metastasize to other tissues and organs, especially the lung and liver. It is one of the most common cancers in dogs and cats, especially in humans. Breast cancers exhibit striking genetic and phenotypic diversity and have a highly complex mechanism. There are many subtypes of mammary cancer with different biological and pathologic features and different clinical course. In this case report, the mass detected in the abdominal region of the rat was removed under general anesthesia. The mass was examined macroscopically, histopathologically and immunohistochemically. As a result of the examinations, invasive cribriform carcinoma was diagnosed in mammary tissue. In immunohistochemical analysis, Ki67 and α-SMA expressions were detected in the mass. In this case report, we contributed to the literature by determining the histopathologic findings of Invasive Cribriform Carcinoma in mammary tissue of rats and the expression levels of Ki67 and α-SMA in these carcinomas.

Keywords: Cancer, Histopathology, Immunohistochemistry, Mammary, Rat

ÖZ

Meme kanseri, meme dokusundan kaynaklanan ve başta akciğer ve karaciğer olmak üzere diğer doku ve organlara metastaz yapabilen neoplastik bir hastalıktır. Köpek ve kedilerde, özellikle de insanlarda en sık görülen kanserlerden biridir. Meme kanserleri çarpıcı genetik ve fenotipik çeşitlilik gösterir ve oldukça karmaşık bir mekanizmaya sahiptir. Meme kanserinin farklı biyolojik ve patolojik özellikleri ve farklı klinik seyri olan pek çok alt tipi bulunmaktadır. Bu olgu sunumunda sıçanın karın bölgesinde tespit edilen kitle genel anestezi altında çıkarıldı. Kitle makroskobik, histopatolojik ve immünohistokimyasal olarak incelendi. Yapılan incelemeler sonucunda meme dokusunda invazif kribriform karsinom tanısı konuldu. İmmunhistokimyasal analizde kitlede Ki67 ve α-SMA ekspresyonları tespit edildi. Bu olgu sunumunda, sıçanların meme dokusunda İnvazif Kribriform Karsinom'un histopatolojik bulgularını ve bu karsinomlarda Ki67 ve α-SMA ekspresyon düzeylerini belirleyerek literatüre katkı sağladık.

Anahtar Kelimeler: Kanser, Histopatoloji, İmmunohistokimya, Meme, Rat

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INTRODUCTION

In all living organisms, the processes of renewal of cells and tissues, functioning of organs and systems, growth, development, stopping growth when necessary and apoptosis (programmed cell death) continue within the framework of an order called homeostasis. Disruption occurring at any stage of homeostasis adversely affects physiologic stages and hyperplasia or neoplasms occur in cells, especially as a result of problems in the apoptosis process.[1] The breast is an organ with a very large area and a high risk for cancer.[2] Breast tumors are tumors that start directly in the mammary gland or can spread from the primary tumor focus to the entire breast tissue by metastasis. At the same time, tumors originating from the breast tissue may metastasize to regional and distant lymph nodes and other organs, especially the lung and liver.[3] Tumors in the mammary glands occur at an advanced age and are perceived as subcutaneous masses. Mammary tumors are one of the most common tumors in many rat species. The incidence and nature of mammary tumors in aged female rats varies in different species.[3-5] In laboratory rats, the mammary gland is an important organ, especially in terms of evaluation for potential carcinogenic effects. Tumors in the mammary gland occur at an advanced age and are perceived as subcutaneous masses. Mammary tumors are one of the most common tumors in many rat and rat species. The incidence and nature of mammary tumors in aged female rats may vary in different breeds. Invasive cribriform carcinoma (ICC) is a special type of mammary cancer that has different biological and pathological characteristics of breast cancer and may have a different clinical course. ICC is a rare type of primary breast carcinoma with an incidence of 0.3-3.5%.[6-8]

In this case report, we aimed to reveal the histopathologic findings of Invasive Cribriform Carcinomas (ICC) detected in rat mammary tissue and the expression levels of Ki67 and alpha-smooth muscle actin (α-SMA) in these carcinomas.

CASE PRESENTATION

This case was observed in an 8-month-old sprague dawley rat. Clinical examination revealed difficulty in walking, depression and loss of appetite. A mass formation in the inguinal region and hypersensitivity in this region were also detected. The mass in the abdominal region was removed under general anesthesia. Macroscopic examination of the mass revealed that the mass had a lobular structure and its surface had a mottled appearance (Figure 1). The weight of the mass was 19 g and its dimensions were calculated to be 4*4*2 cm. The mass was fixed in 10% neutral buffered formaldehyde solution and routine histopathologic examination procedure was performed.

Figure 1. *Macroscopic appearance of the mass taken from breast tissue.*

Histopathologic examinations revealed a cribriform pattern of invasive carcinoma and the presence of irregular islets throughout the mass. Exudate accumulations were observed in the center of the masses. The anaplastic cells in the mass were well differentiated, smaller, more homogeneous and had a round or oval nucleus with mild to moderate nuclear atypia. Very rare mitotic figures were observed (Figure 2).

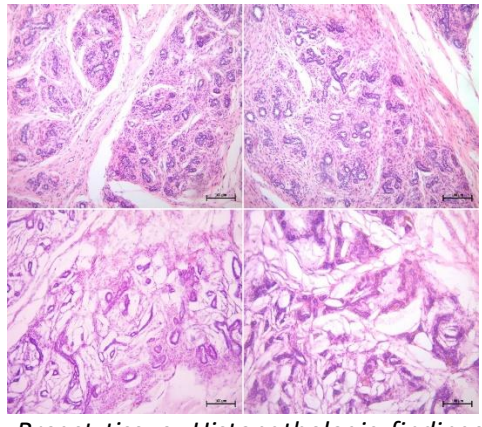

Figure 2. *Breast tissue, Histopathologic findings seen in Invasive Cribriform Carcinoma, H&E, Bars: 100µm.*

Immunohistochemical examinations revealed severe Ki67 and α-SMA expressions in anaplastic cells (Figure 3).

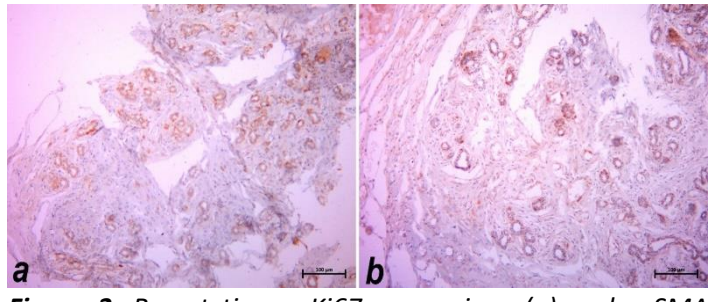

Figure 3. *Breast tissue, Ki67 expressions (a) and α-SMA expressions (b), IHC-P, DAB, Bars: 100µm.*

DISCUSSION

Different types of cancer are seen in rats, as in many domestic animal species and humans. The most prominent of these cancers is breast cancer. In rats used in many experimental breast cancer models, breast cancer can develop naturally with advancing age.[1]

In case reports, it was reported that histopathological examination of breast tumors revealed milk duct epithelial cells, glandular and lobular structures consisting of papillary, tubular, cribriform and comedo patterns, papillary pattern, multiple branched papillae covered by cuboidal to columnar epithelium, increased neoplastic cells (mitotic figure), thickened tissues with a few glandular structures spread in stromal tissues and vascularization was very common.[9] In invasive cribriform carcinomas, it was reported that anaplastic cells were small in size, atypia could not be determined exactly and mitosis was rare. Histopathologic examinations revealed a cribriform pattern of invasive carcinoma and the presence of irregular islets throughout the mass. Exudate accumulations were observed in the center of the masses. The anaplastic cells in the mass were well differentiated, smaller, more homogeneous and had a round or oval nucleus with mild to moderate nuclear atypia. Very rare mitotic figures were observed.

Immunohistochemistry is an important method of diagnostic breast pathology. It is widely used for diagnostic purposes in most solid tumors, including breast cancer. Ki67 and alpha-smooth muscle actin (α-SMA) proteins are known to be very important in the diagnosis of breast tumors. In different studies, it has been reported that Ki67 and alpha-smooth muscle actin (α-SMA) expression levels are significantly increased in breast tumors.[10,11] In this case report, high levels of Ki67 and α-SMA expressions were found in Invasive Cribriform Carcinoma developing in breast tissue, just like in breast tumors.

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REFERENCES

1. Cabadak H. Hücre siklusu ve kanser. *ADÜ Tıp Fak Derg.* 2018;9(3):51-61.
2. Quesenberry KE, Donnelly TM, Hillyer EV. Biology, husbandry, and clinical techniques of guinea pigs and chinchillas. In: Quesenberry KE, Carpenter JW (eds) Ferrets, Rabbits, and Rodents: Clinical Medicine and Surgery, 2nd edn, Elsevier/Saunders, St Louis. 2004: 232–327.
3. Davis RK, Stevenson GR, Busch KA. Tumor incidence in normal Sprague-Dawley female rats. *Can Res.* 1956;16:194-197.
4. Durbin PW, Williams MH, Jeung N, Arnold JS. Development of spontaneous mammary tumors over the life-span of the female Charles River (Sprague-Dawley) rat: The influence of ovariectomy, thyroidectomy and adrenalectomy-ovariectomy. *Can Res.* 1966;26:400-411.
5. Solleveld HA, Haseman JK, McConnell EE. Natural history of body weight gain, survival and neoplasia in the F344 rat. *J Natl Can Inst*. 1984;72:929-940.
6. Curtis MR, Bullock FD, Dunning WF. A statistical study of the occurrence of spontaneous tumors in a large colony of rats. *Am J Can.* 1931;15:67-121.
7. Wright AW, Klinck GHJ, Wolfe JM. The pathology and pathogenesis of mammary tumors occurring spontaneously in the Albany strain of rats. *Am J Pathol*. 1940;16:817-834.
8. Komitowski D, Sass B, Lamb W. Rat mammary tumor classification; Notes on comparative aspects. *J Natl Can Inst.* 1982;68:147-156.
9. Venable JG, Schwartz AM, Silverberg SG. Infiltrating cribriform carcinoma of the breast: a distinctive clinicopathologic entity. *Hum. Pathol.* 1990;21(3):333-338.
10. Buchsbaum RJ, Oh SY. Breast cancer-associated fibroblasts: where we are and where we need to go. *Cancers*. 2016;8(2):19.
11. Kadthur JC, Suguna Rao SR, Sonnahallipura BM, Thimmanahalli DS, Laxmikanth SM. Prognostic value of Ki 67 proliferation antigen in canine malignant mammary gland tumours. *Braz. J Vet. Pathol.* 2011:36-40.

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Successful Management of Cardiogenic Thromboembolism in a Cat

Bir Kedide Kardiyojenik Tromboembolinin Başarılı Yönetimi

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ABSTRACT

Cardiogenic arterial thromboembolism (CATE) is a critical and often life-threatening condition seen in both human and veterinary medicine. Cats with underlying cardiac conditions are predisposed to developing intracavitary thrombi due to hypertrophic cardiomyopathy (HCM). A two-year-old Scottish Fold neutered male cat presented to Atapet Animal Hospital with acute dyspnea. The patient was found to be tachypneic and tachycardic. Latero-lateral radiographic evaluation indicated pulmonary edema, and a ventro-dorsal view demonstrated a valentine heart shape, while echocardiography demonstrated a significantly enlarged left atrium, a "smoke" appearance suggestive of blood stasis, and an accompanying atrial thrombus, along with increased left ventricular wall thickness and pericardial effusion. Subsequent echocardiographic evaluations on the 3rd and 30th days post-treatment demonstrated absence of thrombus, resolution of tachycardia, and overall improvement in clinical status. Echocardiographic examinations were crucial for the early diagnosis of CATE and HCM, and starting treatment with heparin derivatives and then clopidogrel helped manage CATE.

Keywords: Cardiogenic thromboembolism, Cat, Successful management

ÖZ

Kardiyojenik arteriyel tromboembolizm (CATE), hem insan hem de veteriner hekimliğinde görülen kritik ve sıklıkla yaşamı tehdit eden bir durumdur. Altta yatan kalp rahatsızlığı olan kediler, hipertrofik kardiyomiyopatiye (HCM) bağlı olarak intrakaviter trombüs geliştirmeye yatkındır. İki yaşında Scottish Fold kısırlaştırılmış erkek kedi, akut nefes darlığı şikayetiyle Atapet Hayvan Hastanesi'ne başvurdu. Hastanın taşipneik ve taşikardik olduğu belirlendi. Latero-lateral radyografik değerlendirme pulmoner ödemi gösterdi ve ventro-dorsal görünümde sevgililer günü kalp şekli görüldü; ekokardiyografide ise sol atriyumda belirgin bir genişleme, kan stazını düşündüren bir "duman" görünümü ve buna eşlik eden atriyal trombüs ile birlikte sol atriyumda artış görüldü. ventriküler duvar kalınlığı ve perikardiyal efüzyon. Tedaviden sonraki 3. ve 30. günlerde yapılan ekokardiyografik değerlendirmelerde trombüs olmadığı, taşikardinin düzeldiği ve klinik durumda genel iyileşme olduğu görüldü. CATE ve HCM'nin erken tanısı için ekokardiyografik incelemeler çok önemliydi ve heparin türevleri ve ardından klopidogrel ile tedaviye başlanması, CATE'nin yönetilmesine yardımcı oldu.

Anahtar Kelimeler: Başarılı Yönetim, Kardiyojenik Tromboembolizm, Kedi

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INTRODUCTION

Cardiogenic arterial thromboembolism is a critical and often life-threatening condition seen in both human and veterinary medicine.[1] Despite its severity, successful management strategies remain limited, particularly in feline patients.[2-4] These events are termed cardiogenic due to their origin in a cardiac chamber, typically the left auricle. They are closely linked with underlying myocardial diseases, encompassing a spectrum that includes hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy, restrictive cardiomyopathy, and unclassified/ischemic cardiomyopathy.[5-9] Cats with underlying cardiac conditions are predisposed to developing intracavitary thrombi due to factors encompassed by the Virchow triad: blood stasis, endothelial injury, and a potential hypercoagulable state.[10] When left ventricular function is impaired, it can lead to left atrial dilation and dysfunction in the left auricle, promoting blood stasis.[11] This stasis is often detectable on echocardiograms as spontaneous contrast, colloquially referred to as "smoke".[11-13] Moreover, the gold standard test for diagnosing HCM is echocardiography[14], and many of the most important prognostic markers in these domestic felines are echocardiographic variables.[15] Asymptomatic HCM is common, affecting approximately 15% of apparently healthy cats and up to 25% of cats older than 9 years.[14] Therefore, it is very important to screen cats for probable asymptomatic HCM by echocardiography, especially the younger ones. This case report presents a successful approach to the management of cardiogenic thromboembolism in a domestic cat. Through a combination of prompt diagnosis, aggressive treatment, and meticulous care, the feline patient not only survived this acute cardiac event but also demonstrated remarkable recovery and long-term stability. The case highlights the importance of early recognition, multidisciplinary collaboration, and tailored therapeutic interventions in achieving favorable outcomes in feline CATE cases.

CASE PRESENTATION

A two-year-old Scottish Fold neutered male cat, who had no previous illness, was presented to Atapet Animal Hospital with a complaint of acute dyspnea. The patient was found to be tachypneic (40 breaths per minute) and tachycardic (210 beats per minute) and had no neurological findings. However, a complete blood examination revealed no abnormalities (Table 1), latero-lateral radiographic evaluation indicated pulmonary edema (Figure 1), and a ventro-dorsal view demonstrated a valentine heart shape (Figure 2), while echocardiography demonstrated a significantly enlarged left atrium, a "smoke" appearance (Figure 3), suggestive of blood stasis, and an accompanying atrial thrombus (Figure 3), alongside increased left ventricular wall thickness and pericardial effusion (Figure 4).

Table 1. *Haematological parameters of cat with CATE.*

Parameters	Result	Reference value
WBC (x10³/µL)	12.26	3.5 – 17.5
LYM (x10³/µL)	1.31	0.7 – 7.4
MON (x10³/µL)	0.12	0.1 – 1.0
NEU (x10³/µL)	10.68	2.0 – 11.5
EOS (x10³/µL)	0.14	0.0 – 1.5
BAS (x10³/µL)	0.01	0.0 – 0.3
RBC (x10⁶/µL)	8.46	6.3 – 11.8
HGB (g/dL)	10.9	9.0 – 16.0
HCT (%)	34.8	26.0 – 50.2
PLT (x10³/µL)	154	140 – 595

Figure 1. *Pulmonary edema in the latero-lateral radiographic view of the cat.*

Figure 2. *The valentine heart shape in the ventro-dorsal radiographic view of the cat.*

The vertebral heart score (VHS) is only 51% accurate in cat radiography.[15] Therefore, VHS was not measured, and echocardiography, which is considered the gold standard in the diagnosis of HCM, was used. Echocardiography was performed using the Mindray® VETUS-8 echocardiography scanner. The left atrial (LA)-to-aortic (Ao) diameter ratio

(LA/Ao) was measured in the right parasternal short-axis view at the level of the basal heart (Table 2). The end-diastolic interventricular septal thickness (IVSd), LV end-diastolic internal diameter (LVIDd), LV end-diastolic posterior wall thickness (LVPWd), LV end-systolic interventricular septal thickness (IVSs), LV end-systolic internal diameter (LVIDs), LV end-systolic posterior wall thickness (LVPWs), and fractional shortening (FS) were measured in the right parasternal short-axis view at the level of the chordae tendineae (Table 2).

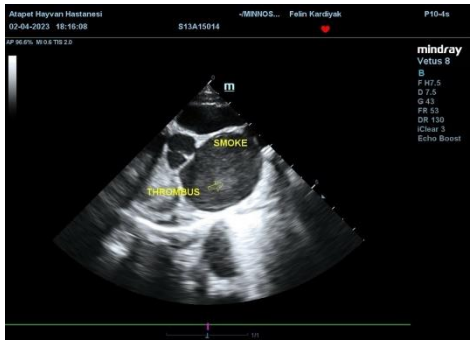

Figure 3. *Smoke and thrombus appearance in the left atrium before the treatment on day one.*

Figure 4. *Pericardial effusion appearance in the left atrium before the treatment on day one.*

Figure 5. *The left atrium view of the cat on day three after treatment.*

and echocardiographic examinations (Table 2), HCM with a cardiogenic thrombus was diagnosed in the patient. Blood gas analysis could not be performed on the patient due to the inability of the patient's owner to meet the budget due to the high treatment costs. After informed consent was obtained, treatment was started with oxygen administration, and oxygen administration was continued throughout the treatment. Because the patient was tachycardic, diltiazem (0.25 mg/kg PO, BID, 30 days), a negative inotropic agent approved for use in cats with HCM, was started. Furosemide (1 mg/kg IV, 3 days) was started for the treatment of pulmonary edema because it reduces the pressure caused by excess fluid in the lungs. According to Bonagura (2), sodium heparin was initially administered at 100 IU/kg IV, diluted with 10 ml of saline on the first day, followed by subsequent subcutaneous injections of 200 IU/kg once every 8 hours on the second day. The furosemide application was continued for 3 days. By the third day of treatment, control echocardiography revealed dissolution of the atrial thrombus (Figure 5) and decreased "smoke" appearance, prompting the initiation of clopidogrel at 18.75 mg/cat PO every 24 hours. More frequent checks could not be carried out due to the financial concerns of the patient owner. Therefore, echocardiographic evaluations performed on the 3rd and 30th days after treatment showed that there was no thrombus, tachycardia improved, and there was a general improvement in the clinical condition. Moreover, at the 1-month follow-up, clinical and echocardiographic examinations revealed successful management of the cardiogenic thromboembolism in the presented case.

Table 2. *M-mode echocardiographic indices in the presented case and reference ranges*[25]

Parameter	Presented case measurements	Reference ranges
LA (mm)	**17.9**	7-14
Ao (mm)	8.3	8-11
LA/Ao	**2.15**	≤1.6-17
IVSd (mm)	**7**	≤5.5
LVIDd (mm)	12.1	12-18
LVPWd (mm)	**9.8**	≤5.5
IVSs (mm)	8.1	≤9
LVIDs (mm)	**3.9**	5-10
LVPWs (mm)	**12.6**	≤9
FS (%)	**67.44**	35-65

Based on the clinical symptoms, radiographic (Figure 2),

DISCUSSION

Cardiogenic arterial thromboembolism poses a significant threat in feline cardiomyopathy, where fragments of intracavitary thrombi can obstruct distant arteries, resulting in tissue damage or organ infarction.[6] Paraplegia, paralysis, and severe pain have been reported in ATE cases. Additionally, tachypnea (91%), hypothermia (66%), and loss of limb motor function (66%) were commonly observed in cats with ATE.[16] In this case, emergency treatment was started when the patient came with only a complaint of dyspnea and tachypnea and a thrombus was detected in the left atrium on echocardiography. Thus, clinical findings such as paraplegia and paralysis due to CATE were not observed. In a study, when the underlying diseases were investigated in 127 cats with ATE, it was observed that the most common causes were cardiac in origin and were classified as dilated, unclassified, hypertrophic obstructive, and hypertrophic cardiomyopathy. It has been reported that one of the most common causes is hypertrophic cardiomyopathy.[16] Similarly, a thrombus mass was detected in the left atrium of the cat in this case, and HCM was detected in the cat as a result of echocardiographic measurements.

The reported prevalence of ATE in cats is approximately 0.3% in general practice and 0.6% in the referral population.[16,17] Two large studies found that 9% to 11% of cats with HCM developed ATE.[16,18] The mean or median age at presentation with ATE is 8–12 years, with a range of 0.1–21 years.[16,17] On the other hand, the incidence of ATE in young cats with HCM (<2.5 years) was reported to be only 0.7% in a large, multicenter study.[19] In this case report, the patient was only 2 years old. The diagnosis of a disease that is very rare at this age can be based on the use of echocardiography, as seen in this case. As a matter of fact, a thrombus in the left atrium was detected by echocardiography performed on the patient who complained of dyspnea, and the disease could be diagnosed before the clinical findings progressed.

Unfortunately, effective strategies to prevent recurrent CATE are lacking, often leading to euthanasia as the chosen course of action.[20] Antithrombotic drugs are the standard of care for cardioembolic prevention in humans[21] and have been incorporated into clinical protocols for cats.[22] Optimising medical management is crucial to prevent intracardiac thrombosis and subsequent ATE in at-risk cases or recurrence in post-ATE cases, as cats with HCM are at high risk of this condition. According to recent consensus guidelines on feline cardiomyopathies from the American College of Veterinary Internal Medicine, clopidogrel, an antiplatelet medication, should be started when there are echocardiographic risk factors.[23] Early heparinization and subsequent use of oral clopidogrel, as in this case, were found to be effective in the treatment. Similarly, in their study, Lo et al.[24] used clopidogrel and rivaroxaban in the treatment of cats with ATE. They reported that dual antithrombotic therapy resulted in fewer side effects, a lower relapse rate, and provided effective thromboprophylaxis in cats with intracardiac thrombus or spontaneous echocardiographic contrast.

As a result, HCM should be suspected in cats with respiratory emergencies, especially shortness of breath, echocardiography should be performed as soon as the patient calms down, and the left atrium should be evaluated for a possible thrombus. It was observed that echocardiographic examinations played a very important role in the early diagnosis of CATE and HCM, and that starting treatment with heparin derivatives and then using clopidogrel provided beneficial results in the management of CATE.

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REFERENCES

1. Harpster NK. Feline myocardial diseases. In: Kirk RW, ed. Current veterinary therapy IX. Philadelphia: WB Saunders; 1986:380-398.
2. Bonagura JD, Fox PR. Restrictive cardiomyopathy. In: Bonagura JD, ed. Kirk's current veterinary therapy XII. Philadelphia: WB Saunders; 1995:863-867.
3. Laste NJ, Harpster NK. A retrospective study of 100 cases of feline distal aortic thromboembolism: 1977-1993. *J Am Anim Hosp Assoc.* 1995; 31(6):492-500.
4. Atkins CE, Gallo AM, Kurzman ID, et al. Risk factors, clinical signs, and survival in cats with a clinical diagnosis of idiopathic hypertrophic cardiomyopathy: 74 cases (1985-1989). J *Am Vet*

Med Assoc. 1992;201(4):613-618.
5. Baty CJ, Malarkey DE, Atkins CE, et al. Natural history of hypertrophic cardiomyopathy and aortic thromboembolism in a family of domestic shorthair cats. *J Vet Intern Med*. 2001;15(6):595-599.
6. Moore KE, Morris N, Dhupa N, et al. Retrospective study of streptokinase administration in 46 cats with arterial thromboembolism. *J Vet Emerg Crit Care.* 2000;10(4):245-257.
7. Rush JE, Freeman LM, Fenollosa NK, et al. Population and survival characteristics of cats with hypertrophic cardiomyopathy: 260 cases (1990-1999). *J Am Vet Med Assoc.* 2002;(2):202-207.
8. Peterson EN, Moise NS, Brown CA, et al. Heterogeneity of hypertrophy in feline hypertrophic heart disease. *J Vet Intern Med.* 1993;7(3):183-189.
9. Smith SA, Tobias AH, Jacob KA, et al. Arterial thromboembolism in cats: acute crisis in 127 cases (1992-2001) and long-term management with low-dose aspirin in 24 cases. *J Vet Intern Med.* 2003;17(1):73-83.
10. Payne JR, Borgeat K, Connolly DJ, et al. Prognostic indicators in cats with hypertrophic cardiomyopathy. *J Vet Intern Med.* 2013;27(6):1427-1436.
11. Stokol T, Brooks M, Rush JE, et al. Hypercoagulability in cats with cardiomyopathy. *J Vet Intern Med.* 2008;22(3):546-552.
12. Helenski CA, Ross JN. Platelet aggregation in feline cardiomyopathy. *J Vet Intern Med.* 1987;1(1):24-28.
13. Welles EG, Boudreaux MK, Crager CS, et al. Platelet function and antithrombin, plasminogen, and fibrinolytic activities in cats with heart disease. *Am J Vet Res.* 1994;55(5):619-627.
14. Luis Fuentes V, Wilkie LJ. Asymptomatic hypertrophic cardiomyopathy: diagnosis and therapy. *Vet Clin North Am Small Anim Pract.* 2017;47(5):1041-1054.
15. Haggstrom J, Luis Fuentes V, Wess G. Screening for hypertrophic cardiomyopathy in cats. *J Vet Cardiol.* 2015;17(Suppl 1):S134-149.
16. Laste NJ, Harpster NK. A retrospective study of 100 cases of feline distal aortic thromboembolism: 1977-1993. *J Am Anim Hosp Assoc.* 1995;31(6):492-500.
17. S.A. Smith, A.H. Tobias, K.A. Jacob, D.M. Fine, P.L. Grumbles. Arterial thromboembolism in cats: acute crisis in 127 cases (1992-2001) and long-term management with low-dose aspirin in 24 cases. *J Vet Intern Med*. 2003;17(1):73-83.
18. K. Borgeat, J. Wright, O. Garrod, J.R. Payne, V.L. Fuentes. Arterial thromboembolism in 250 cats in general practice: 2004-2012, *J Vet Intern Med*. 2014;28(1):102-115.
19. J.R. Payne, K. Borgeat, D.C. Brodbelt, D.J. Connolly, V. Luis Fuentes. Risk factors associated with sudden death vs. congestive heart failure or arterial thromboembolism in cats with hypertrophic cardiomyopathy. *J Vet Cardiol*. 2015;17(1):5318-5328.
20. P. R. Fox, B.W. Keene, K. Lamb, K.A. Schober, V. Chetboul et al. International collaborative study to assess cardiovascular risk and evaluate long-term health in cats with preclinical hypertrophic cardiomyopathy and apparently healthy cats: the REVEAL Study. *J Vet Intern Med*. 2018;32(1):930-943.
21. Schoeman JP. Feline distal aortic thromboembolism: a review of 44 cases (1990-1998). *J Feline Med Surg.* 1999;1(4):221-31.
22. Deedwania PC, Huang GW. Role of emerging antithrombotic therapy in the prevention of cardioembolic complications in patients with atrial fibrillation. *Am J Cardiovasc Drugs.* 2011;11(4):265-275.
23. Hogan DF, Fox PR, Jacob K, et al. Secondary prevention of cardiogenic arterial thromboembolism in the cat: The double-blind, randomized, positive-controlled feline arterial thromboembolism; clopidogrel vs. aspirin trial (FAT CAT). *J Vet Cardiol.* 2015;17(Suppl 1):S306-17.
24. Luis Fuentes V, Abbott J, Chetboul V, et al. ACVIM consensus statement guidelines for the classification, diagnosis, and management of cardiomyopathies in cats. *J Vet Intern Med.* 2020; 34:1062–1077.
25. Nelson RW, Couto CG. Small Animal Internal Medicine-E-Book: Small Animal Internal Medicine-E-Book. Elsevier Health Sciences, 2019.

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Morphopathological Examination of Anencephaly and Concomitant Congenital Malformations in a Lamb

Kuzuda Anensefali ve Eşlik Eden Konjenital Malformasyonların Morfopatolojik İncelenmesi

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ABSTRACT

The macro-pathology changes of anencephaly and other accompanying congenital anomalies in a lamb are described in this report. Anencephaly is a condition in which a large part of the brain does not develop or is not formed at all as a result of incorrect closure of the neural sulcus during the development of the offspring in the intrauterine period. Anencephaly is generally not manifested alone and includes various anomalies. Although congenital malformations are very common in domestic ruminants, there is no report in the literature reporting an anencephaly anomaly in lambs. In this study, for the first time in the world, anencephaly in a lamb and some concomitant anomalies were presented. In this case in which morphological changes were examined, anencephaly anomalies, as well as anomalies of acrania, arhinia, anotia, anophthalmia, agnathia and microglossia were also encountered. Thanks to this case, the macroscopic findings of congenital head anomalies in a lamb that had not been previously reported were presented and evaluations were made on their possible etiological causes.

Keywords: Anencephaly, Congenital anomaly, Lamb, Morphopathology.

ÖZ

Bu olgu sunumunda bir kuzuda anensefali ve eşlik eden diğer konjenital anomalilerin makro-patoloji değişiklikleri anlatılmaktadır. Anensefali, intrauterin dönemde yavrunun gelişimi sırasında nöral sulkusun yanlış kapanması sonucu beynin büyük bir bölümünün gelişmemesi veya hiç oluşmaması durumudur. Anensefali genellikle tek başına ortaya çıkmaz ve çeşitli anomalileri içerir. Evcil ruminantlarda konjenital malformasyonlar oldukça yaygın olmasına rağmen literatürde kuzularda anensefali anomalisini bildiren bir yayın bulunmamaktadır. Bu çalışmada dünyada ilk kez bir kuzuda anensefali ve buna eşlik eden bazı anomaliler sunulmuştur. Morfolojik değişikliklerin incelendiği bu olguda anensefali anomalilerinin yanı sıra akrania, arhinia, anotia, anoftalmi, agnati ve mikroglossia anomalilerine de rastlandı. Bu vaka sayesinde bir kuzuda daha önce bildirilmemiş konjenital kafa anomalilerinin makroskobik bulguları sunulmuş ve bunların olası etiyolojik nedenleri üzerine değerlendirmeler yapılmıştır.

Anahtar Kelimeler: Anensefali, Konjenital anomali, Kuzu, Morfopatoloji

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INTRODUCTION

Congenital malformations may manifest as any organ or organs in the body not forming at all during or after the intrauterine period, their inadequate development, and various developmental deformities.[1,2] Congenital anomalies of the central nervous system (CNS) are more common than other system or organ anomalies in domestic animals.[3,4] Anencephaly, which is one of the most important CNS anomalies, is the case where both hemispheres that form the brain are not shaped. Closure errors in the cranial part of the neural tube are involved in the pathogenesis of anencephaly. In anencephaly anomalies the offspring are usually born dead. Even if live-borns usually don't have a chance to survive. Anencephalic cases generally do not have skin, and hemispheriums are replaced by the area cerebrovasculosa an irregular mass consisting of a mixture of nerve tissue and blood vessels.[5,6] The phenomenon of anencephaly often does not occur as a single anomaly. Anencephalic anomalies occur along with developmental disorders such as acrania, agnathia, anophthalmia, arhinia, anotia, aglossia, craniosynostosis, myeloschisis, cheiloschisis, and palatoschisis. Acrania is the absence of the calvarial bone that preserves the brain; arrhinia is the absence of the nose; anotia is the absence of the ear; aglossia is the absence of the tongue. Craniosynostosis is the bifidity of the calvarian bone; myeloschisis is the bifidity of the cheek; cheiloschisis is of the lip; and palatoschisis is of the palate. Although the etiology of the congenital malformations of the CNS has not been definitively explained, toxic-infectious diseases, hereditary and environmental factors have been suggested to play a role.[1,7,8]

The case being presented here might be of interest because it reports anencephaly and other head anomalies that have not been previously reported in lambs. In addition, some evaluations were made on the etiology of congenital anomalies based on this case.

CASE PRESENTATION

The case material consisted of the offspring of a five-year-old Akkaraman breed sheep brought to Yüzüncü Yıl University, Faculty of Veterinary Medicine, Department of Obstetrics and Gynecology with the complaint of difficult birth. Examination of the birth canal revealed that the fetus was swollen and therefore could not leave the canal. When it was understood that there could be no normal delivery, a cesarean section was decided. The lamb, which was removed from the birth canal after the operation was performed by obtaining the consent form from the patient owner, was found to have no vital activity. In addition, the examination showed that the fetus died in the womb. No significant clinical symptoms were observed in the mother, who was kept under surveillance for 24 hours. The offspring with congenital malformations were sent to the Department of Pathology to determine the existing anomalies and undergo a macroscopic examination.

Macroscopic Findings

Examination revealed that the offspring died approximately three days earlier. It was observed that the placenta carried with the offspring was dark. It was determined that the congenital malformations in the offspring were mostly located in the head and neck region (Fig. 1A). It was the first remarkable finding that the calvarial bone was not shaped in the offspring, i.e., acrania. The presence of a cystic pouch with a fluctuant content was detected instead of the head, which was not protected by the skin.

Figure 1. *A) Cystic structure under the undeveloped scalp (arrowhead). B) The mouth, nose, ears and eyes are not formed (arrowhead). C) Air sacs containing otolytic fluid in the cystic structure (arrowhead). D) Fully formed hyoid bone, larynx, trachea, and esophagus under the air sacs (arrowhead).*

A rudimentary residue consisting of immature nerve and vein formations was detected in and around the connective area of this cystic formation. Since the facial bones did not form to a large extent, it was observed that no facial organs such as the jaw (agnotia), nose (arhinia), ear (anotia), and eye (anophthalmia) were formed (Fig. 1B). With the opening of the cystic formation in the head, two small air sacs in the form of gas bubbles and autolytic tissue residues with some amount of smelly brownish fluid were detected in the sac (Fig. 1C). Inside this cystic formation, a small unformed tongue and hyoid bone were found. It was

found that the larynx and the following esophagus and trachea were formed when advanced to the throat region (Fig. 1D).

The spinal cord was very regular and reached exactly the os occipitale, and there was a blocked spinal canal just after the atlanto-occipital joint, just like a plug (Fig. 2A). With this plug-like behavior, it was seen that the nervous system pathway was blocked and the nervous system ended in this region (Fig. 2B). It was found that hemispherium, cerebellum, mesencephalon, and pons were not shaped at all in this anencephalic case (Fig. 2C). Medulla oblongata was found to be present as a rudimentary remnant. It was determined that labor could not be started because the hypothalamus did not form, and therefore, the tissues were severely autolytic (Fig. 2D). Autolytic changes were quite common in the rest of the body.

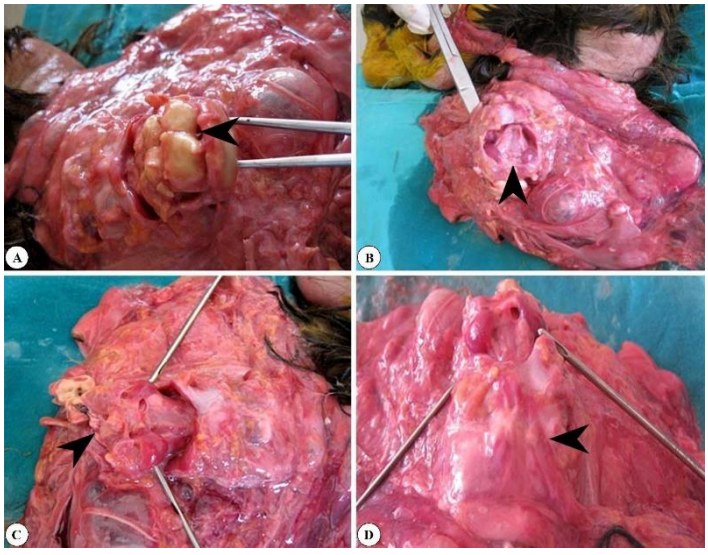

Figure 2. *A) The spinal cord forms a plug at the atlanto-occipital joint (arrowhead). B) Termination of the nervous system with the plug formed by the spinal cord (arrowhead). C) The hemispheres, cerebellum, mesensefalon and pons are not formed at all (arrowhead). D) Excessive autolysis and adhesions in other internal organs (arrowhead).*

DISCUSSION

Although studies on mammalian anomalies caused by inadequate development in the intrauterine period are quite insufficient, the incidence of congenital malformations in sheep has been reported to be between 0.5-1%.1,9 This prevalence cannot be underestimated, taking into account the cases that may not have been reported. In order to address the importance of congenital anomalies and draw attention to their etiologies, such cases should be reported, and their etiology should be scrutinized. CNS anomalies are among the most common congenital malformations in domestic animals. CNS anomalies are more common than other system and organ anomalies. This is due to the fact that the embryonic development of the CNS is earlier than other systems and organs. It has also been suggested that complications in the embryonic development of the CNS may be effective in the development of abnormal encephalon.[5,6] Although anomalies of the CNS, which has a complex embryogenesis and a long intaruterine process since the early stages of pregnancy, are more common, few reports have been made regarding this system.[2,4] In Turkey, Hazıroğlu et al., for the first time, reported a calf case with anencephaly and various accompanying congenital malformations.[10] Dogan et al., in their examination of 6 calves with congenital anomalies, they reported that they found findings related to head anomalies in 3 of them.[11] Due to the fact that the head region consists of important organs, anomalies here have vital consequences. Especially the anomalies in the CNS, which is the root of the organism, are the causes of functional disorders in other organs and systems of the body that appear morphologically normal.

Cranial malformations do not usually occur alone and more than one anomaly is observed together.[3,12] Many cranial anomalies were also present in this case. Lakkawar et al. who reported a calf case with anencephaly and associated malformations, reported that they observed erroneous and inadequate development of the tongue and mandibula, acrania, anophthalmia, anotia, and arhinia.[13] In addition, Lakkawar et al., stated that there was no skin in the skull area and that there were three cystic formations present here.[13] Hazıroğlu et al., in their study describing anencephaly and accompanying malformations in a calf fetus reported that the upper jaw was short (brachiganti supeior), the upper lip had a cleft (cheiloschisis), the palate had a cleft (palatoschisis), the ear was rudimentary (microtia), the eye was small (microphthalmia), and there were no hemispheriums (anencephaly).[10] Hazıroğlu et al. reported in their cases that although hemispheriums were not shaped, calvarial bone was formed, the cerbellum was larger than usual and pituitary was existent.[10] In this presented case, it was observed that more severe malformations were present compared to the case reported by Hazıroğlu et al. However, similar to the case reported by Lakkawar et al. anophthalmia, anotia, arhinia, acrania and anencephilia were detected.

Various factors, such as genetic disorders, infectious and toxic diseases, fetal hypoxia, nutritional deficiency, trauma, and irradiation play a role in the etiology of CNS anomalies.[14,15] According to the anamnesis obtained from this case, it was stated that such anomalies were not previously seen in the herd, one-way nutrition was performed, there was no epidemic infection in the herd, and there was no condition that would lead to poisoning.

In light of the anamnesis and literature information obtained, it was thought that the anomaly in this case may have been caused by nutritional deficiency.

As a result, the findings of a case with anencephaly and related malformations such as anophthalmia, arhinia, anotia, and agnathia in a lamb were reported for the first time in the world with this study. In addition to these morphological changes determined in the case of congenital anomalies, an evaluation was made on possible etiological causes, and it was thought that malnutrition may have a role in the pathogenesis of such anomalies.

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REFERENCES

1. Jubb KVF, Kennedy PC, Palmer N. Pathology of domestic animals. Fourth Edition. Academic Press. United Stated. Vol. 1, 2013, pp. 270-286.
2. Singh M, Parrah JUD, Moulvi BA, Athar H, Kalim MO, Dedmari, FH. A review on pectus excavatum in canines: A congenital anomaly. *Iran J Vet Surg.* 2013;8(1):59-64.
3. Dos Anjos Nonato I, Teixeira MR, De Miranda JL, Braz HMB, Machado JP. Cranioschisis and anencephaly in a dog-challenging etiology. *Acta Sci Vet.* 2019;47(1):449.
4. İşler CT, Altuğ M, Gönenci R, Aytekin İ. Evaluation of anomaly cases detected in calves in Bolu region between 2005-2009. *Harran Üniv Vet Fak Derg.* 2016;5(2):100-104.
5. Di Muro G, Cagnotti G, Bellino C, Capucchio MT, Colombino E, D'Angelo A. Multiple Cephalic Malformations in a Calf. *Animals.* 2020;10(9):1532.
6. Silva LF, Rabelo RE, Santos GP, et al. Multiple congenital encephalic malformations in a calf. *Braz J Vet Pathol.* 2016;(9):103-107.
7. Islam MR, Roh YS, Cho A, et al. Multiple congenital anomalies in a Korean native calf (Bos taurus coreanae). *Korean J Vet Res.* 2011;51(1):63-67.
8. Ortega-Pacheco A, Lezama-García MA, Colín-Flores R. Presence of congenital anomalies in three dog litters. *Reprod Domest Anim.* 2020;55(5):652-655.
9. Raoofi A, Dehghan MM, Mardjanmehr SH, et al. Cranium bifidum with meningocele in a lamb. *Small Rumin Res.* 2004;55(1-3):253-256.
10. Haziroğlu RM, Atasever A, Yildiz D. Anencephaly and other congenital malformations in a calf [Turkısh]. *Ankara Univ Vet Fak Derg.* 1996;(43):303-305.
11. Doğan GK, Karakurt E, Kuru M, Nuhoğlu, H. Anatomical and pathological evaluation of congenital anomalies in calves: 6 cases. *Pakistan J Zool.* 2022;54(3):1345-1354.
12. Yurdakul İ, Yalçin M, Karataş Ö. A Case of Multiple Congenital Anomaly in a Calf. *Erciyes Üniv Vet Fak Derg.* 2020;17(3):342-345.
13. Lakkawar AW, Kumar R, Nair MG, Varshney KC. Anencephaly and Associated Malformations in a Ovine Foetus. *Folia Vet.* 2002;46(1):39-41.
14. Rousseaux CG, Ribble CS. Developmental anomalies in farm animals: II. Defining etiology. *Can Vet J.* 1988;29(1):30-40.
15. Samuel M, Wanmi N, Usende L, Ozegbe PC. Review of Some Developmental Anomalies in Domestic Species in North Central Region of Nigeria-Contributions of Normadism and Climate Changes in Embryo-toxicicitity. *Anim Mol Breed.* 2016;6(1):1-7.