PROTEINURIA IN A CAT

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SIGNALMENT, CASE HISTORY AND CLINICAL PRESENTATION

"Bartolomeo" is a 15-month-old intact male domestic shorthair cat. He is an indoor cat and a previous FIV- FeLV test resulted negative.

He was admitted to the San Francesco Veterinary Hospital for a history of exercise intolerance, stiff gait and polyuria - inappropriate urination. In the previous 6 months, the owner noticed some white nodules appearing and spontaneously regressing on the tongue.

At the clinical presentation, the cat was bright, alert, and no abdominal pain or respiratory distress were noted.

LABORATORY FINDINGS

A complete cell blood count (CBC. ProCyte Dx, Idexx Laboratories), biochemical analysis (BT 1500 vet, Futurlab Italia), urinalysis which included urinary protein to creatinine (UPC) ratio (spectrophotometric measurement with pyrogallol red and Jaffè methods, respectively) and urinary culture were performed.

CBC results were unremarkable except for a mild eosinopenia (confirmed by manual differential count) and a mild increase in hemoglobin (Hgb) concentration. - **Table 1**

Parameter	Result	Reference Intervals
RBC ($x10^6/\mu L$)	11.66	6.54 – 12.20
Hgb (g/dL)	**16.3**	9.8 – 16.2
HCT (%)	49.4	30.3 – 52.3
MCV (fL)	42.4	35.9 – 53.1
MCH (pg)	14	11.8 – 17.3
MCHC (g/dL)	33	28.1 – 35.8
RDW (%)	27	15 - 27
Reticulocyte count ($x10^3/\mu L$)	43.1	3 - 50
WBC ($x10^3/\mu L$)	10.77	2.87 – 17.02
Neutrophils (%)	42	-
Neutrophils ($x10^3/\mu L$)	4.52	2.30 – 10.29
Lymphocytes (%)	51	-
Lymphocytes ($x10^3/\mu L$)	2.31	0.92 – 6.88
Monocytes (%)	5	-
Monocytes ($x10^3/\mu L$)	0.54	0.05 – 0.67
Eosinophils (%)	1	-
Eosinophils ($x10^3/\mu L$)	**0.11**	0.17 – 1.57
Basophils (%)	0	-
Basophils ($x10^3/\mu L$)	0	0.01 – 0.26
PLT ($x10^3/\mu L$)	419	151 - 600

Table 1: *Hematological results of the cat. Mild eosinopenia and mild increase in Hgb concentration are present (Procyte Dx, Idexx Laboratories).*

Serum had normal aspect and biochemical results showed a severe increase in CK activity, moderate increase of ALT and AST activities and mild hyperlipasemia – **Table 2**

Parameter	Result	Reference Intervals
ALT (UI/L)	**283**	25 – 87
AST (UI/L)	**427**	10 – 35
ALP (UI/L)	32	19 – 70
GGT (UI/L)	2	0 – 8
DGGR Lipase (UI/L)	**36**	12 – 31
CK (UI/L)	**45577**	91 – 326
Total Bilirubin (mg/dL)	0.12	0 – 0.26
Cholesterol (mg/dL)	129	95 – 210
Triglycerides (mg/dL)	29	19 – 81
Glucose (mg/dL)	130	72 – 136
Total proteins (g/dL)	7.3	6 – 8.2
Albumin (g/dL)	**4.2**	3 – 4.2
Globulin (g/dL)	3.1	1.8 – 5.5
A:G ratio	**1.35**	0.5 – 1.3
Creatinine (mg/dL)	1.0	0.6 – 1.8
Urea (mg/dL)	61	30 – 65
Calcium (mg/dL)	9.3	7.3 – 11.5
Phosphorus (mg/dL)	5.8	2.6 – 6.2
Sodium (mmol/L)	152	146 – 159
Potassium (mmol/L)	4.3	3.8 – 5.3
Chloride (mmol/L)	115	108 - 130
SDMA Idexx (µg/dL)	9	0-14

Table 2: *Biochemical results of the cats. Severe increase of CK activity, moderate increase of ALT and AST activities, mild hyperlipasemia are present (BT1500 vet, Futurlab).*

The mild hyperlipasemia was considered unremarkable. Moderate increase of ALT and AST activities can be due to hepatocellular damage (both primary and secondary hepatic diseases). However, the concurrent severe increase in CK activity, which is the most sensitive enzyme indicator of muscle necrosis (Shelton, 2004), along with the major increase of AST compared to ALT activity supported most likely a muscular damage. Albumin concentration (also increase of A:G ratio) and concurrent RBC and HCT values near to the upper reference limits associated with mild increase in Hgb concentration suggested a probable mild dehydration.

The urine sample was collected by cystocentesis. Complete urinalysis (chemical and physical analysis performed by visual inspection, refractometric urine specific gravity (USG) measurement, dipstick test, and microscopic sediment evaluation) showed a marked positive reaction to pads of heme-containing compounds and proteins; sediment was inactive and UPC ratio was increased. The urinary culture was negative. – **Tables 3 and 4.**

Chemical – physical analysis	Result	Reference Intervals
Color and aspect	Clear yellow	Clear yellow
USG	1.050	1.015 – 1.060
pH	**5**	6.5 - 7
Proteins	**+++**	Negative
Glucose	Negative	Negative
Ketones	Negative	Negative
Heme-containing compounds	**+++**	Negative
Bilirubin	Negative	Negative
UPC ratio	**1.1**	0.2 – 0.4

Sediment evaluation	Result	Reference Intervals
Leucocytes	Absent	<5/HPF
RBC	Absent	<5/HPF
Clusters	Absent	Absent - rare
Crystals	Absent	Absent
Epithelial cells	Absent	Rare
Bacteria	Not seen	Absent
Others	Lipid droplets	-

Tables 3 - 4: *Urinalysis of the cat. The urine was acid and marked positive reaction to heme – containing compounds and proteins pads are seen. Sediment is inactive and proteinuria is identified.*

Positive reaction to heme-containing compounds indicates the presence of Hgb, myoglobin (Mgb), or erythrocytes in urine. The latter was ruled out based on the urinary sediment evaluation and *in vitro* erythrocytes' lysis was considered unlikely as the sample was processed immediately after collection and the USG was adequate. Hemoglobinuria was excluded due to normal serum aspect and the absence of anemia. Thus, myoglobinuria was the most likely cause of the peroxidase reaction of the pad. This hypothesis was further supported by the concurrent biochemical alterations suggestive of muscular injury.

Urine pH could be affected by both renal and extrarenal factors. Aciduria could be secondary to metabolic or respiratory acidosis, or due to proximal tubular acidosis: unfortunately, blood gas analysis was not performed in this case.

The positive reaction to the dipstick pad suggested a high urinary proteins concentration. However, this test has poor accuracy and specificity in detecting proteinuria in cats even if combined with USG (Pérez-Accino et al., 2020). UPC ratio confirmed the presence of proteinuria which could be pre-renal, renal (tubular, glomerular or mixed damage) or post renal.

Sodium dodecyl sulfate-agarose gel electrophoresis (SDS-AGE; Hydragel 5 Proteinuria, Sebia Italia) was performed to investigate the urinary protein profile and revealed a mixed (glomerular and tubular) proteinuria.

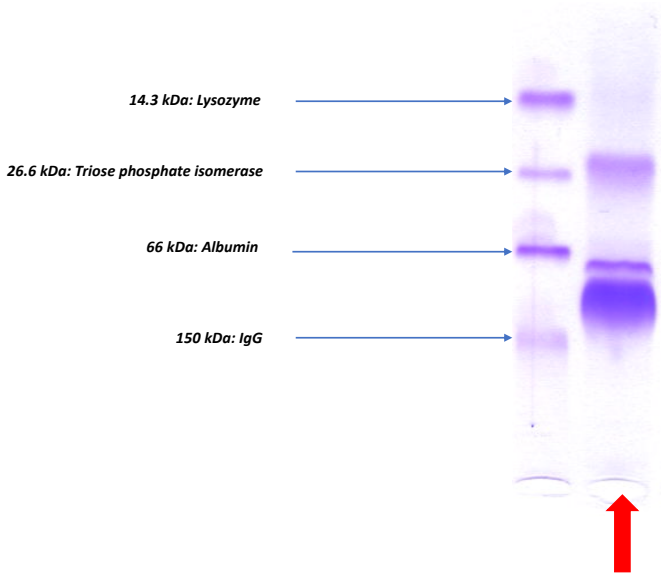

Image 1: *SDS- AGE of the cat. The first line (left) shows the control sample with known molecular weights (Molecular Mass Control; Sebia Italia) corresponding to lysozyme (14.3 kDa), triose phosphate isomerase (26.6 kDa), bovine albumin (66 kDa) and human IgG (150 kDa).* ***The second line (right) is the cat (red arrow)*** *(Hydragel 5 Proteinuria, Sebia Italia).*

The marked band slightly above 26.6 kDa was consistent with the presence of tubular proteins suggesting tubular damage (bands of molecular weight (MW) lower than that of albumin). Overload pre-renal proteinuria had to be considered as differential diagnosis: free light chains proteins (25 kDa) were considered unlikely as there was no further evidence of plasma cells or lymphoproliferative disorder. Despite the absence of a clear band at the MW of Mgb (17 kDa), myoglobinuria cannot be ruled out. Mgb is unstable, particularly, as in this case, in acidic urine (Chen-Levy et al., 2005); however, Mgb fragmentation may have resulted in the presence of homogeneous protein traces in the low MW region. The marked band just below 66 kDa was consistent with albuminuria: the MW of albumin in cats is 67 kDa (Maeda et al., 2015). Other marked bands between 66 and 150 kDa were consistent with high MW proteins, such as transferrin (77 kDa; Maeda et al., 2015): this finding associated with albuminuria may suggest a glomerular damage. However, cauxin (carboxylesterase-like urinary excreted protein) which is a 70 kDa glycoprotein produced mostly in mature intact male cats by epithelial cells of the distal tubules of the kidney, (Miyazaki et al., 2003; Miyazaki et al., 2006) migrates in the same region of transferrin.

Biochemical findings associated with urinalysis and SDS-AGE results were consistent with muscular damage (rhabdomyolysis) and suggested a possible secondary myoglobinuric renal damage with both tubular and glomerular involvement.

ADDITIONAL TESTS AND INVESTIGATIONS

Infectious causes of myopathy were investigated. Serology for *Toxoplasma gondii* was performed (Butts and Langley-Hobbs, 2020). Strong positivity for IgG (results: > 1:3200. RI: positive result above to 1:50) and low positivity for IgM (results: 1:100. RI: positive result above to 1:50) were found. The cat started treatment with clindamycin (10 mg/kg PO, q24h); however, after one month from the

beginning of antimicrobial therapy, no clinical improvements were seen and both serology titers remained unchanged.
Further investigations were carried out. Cytological findings of the white nodules on the tongue were consistent with *calcinosis*.

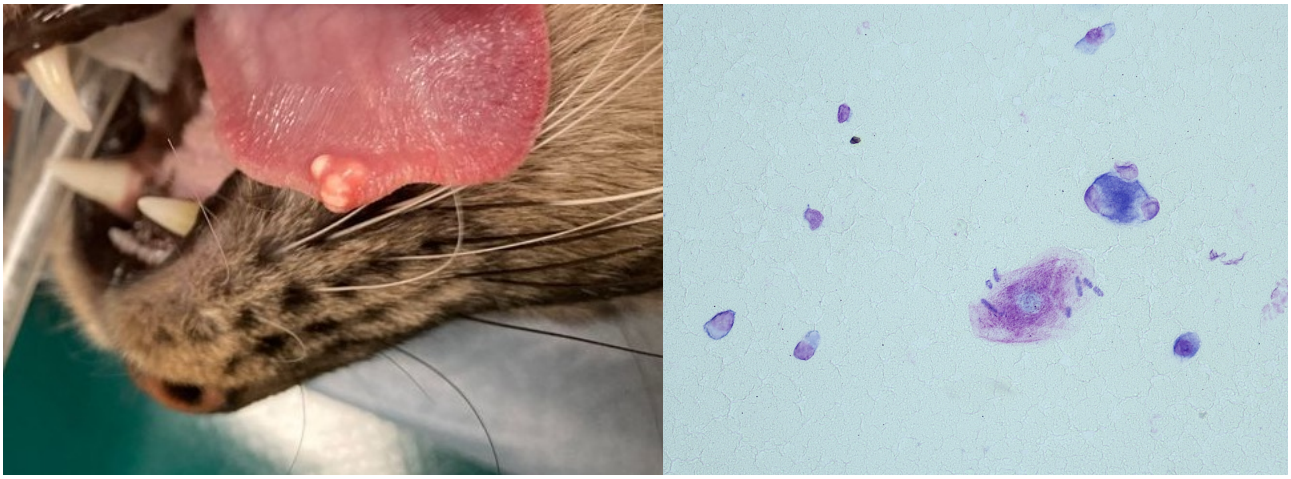

Image 2: *<u>Left:</u> White firm nodules are present on the tongue of the cat. <u>Right:</u> on the background abundant granular unstained material is seen. Cellularity is moderate and mainly represented by a mixed population of foamy macrophages and small lymphocytes. Occasionally large rod-shaped bacteria (Conchiformibius spp.) are observed on the surface of rare keratinized squamous epithelial cells (May Grünwald - Giemsa, 400X).*

Thoracic radiographs showed a scalloped appearance of the diaphragmatic line. Cardiac ultrasound revealed irregularities in the myocardial muscle of the left ventricle (suspected of infiltrative process or dystrophic calcification).

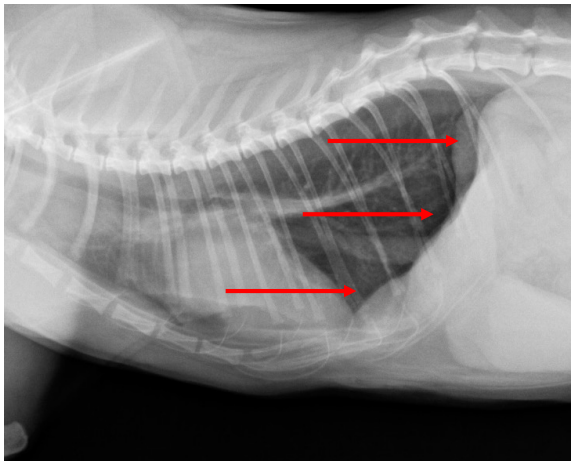

Image 3*: Radiograph of the thorax of the cat. Scalloped appearance of the diaphragmatic line is seen (red arrows).*

The cat was referred for a specialistic consultation to a board-certified neurologist; electromyography (EMG), cerebrospinal fluid (CSF) collection, and muscular biopsy were performed. CSF examination was unremarkable. In EMG, motor nerve conduction remained normal but muscular fibrillation potential was evident: these findings were most likely consistent with polymyopathy rather than polyneuropathy (muscular dystrophy, polymyositis).

Muscular biopsy was submitted to the Clinical and Comparative Neuropathology Laboratory (Institute of Veterinary Pathology, Center of Clinical Veterinary Medicine, Veterinary Faculty of München). Histopathologic and immunohistochemistry (IHC) findings were consistent with muscular dystrophy. Von Kossa stain clearly identified sarcoplasmic calcific mineralization. IHC for *Toxoplasma gondii* was negative and IHC for dystrophin did not highlight significant signal from the sarcolemma.

FINAL INTERPRETATION

Dystrophin-deficient muscular dystrophy with rhabdomyolysis and suspected secondary myoglobinuric renal injury.

TREATMENT AND FOLLOW UP

Until August 2021, the cat did not show any clinical worsening nor improvements. Unfortunately, no effective therapeutic options are available for muscular dystrophy and the prognosis is generally considered poor.

DISCUSSION AND CONCLUSION

Dystrophin-deficient muscular dystrophy, also called hypertrophic feline muscular dystrophy, is a rare recessive congenital progressive disease caused by a mutation in the dystrophin gene located on the X-chromosome (Carpenter et al., 1989; Gaschen et al., 1992). Feline dystrophin deficiency is considered one of animal models for Duchenne muscular dystrophy, a fatal hereditary neuromuscular disease characterized by generalized muscle atrophy and fibrosis (Willman et al., 2009; Nakamura and Takeda, 2010). Dystrophin is a large protein that links the internal cytoskeleton of the myofibers to the extracellular matrix; it maintains the integrity of the sarcolemma during muscular contraction and relaxation. It has also been hypothesized that dystrophin plays a role in calcium homeostasis regulation in humans (Gailly et al., 2002). Therefore, absence of dystrophin leads to muscle cell disruption due to instability of the membrane and uncontrolled influx of calcium (Ervasti et al., 2007). A presumptive diagnosis of dystrophin-deficient muscular dystrophy can be made considering signalment (young male cat), clinical presentation, biochemical data, and diagnostic imaging. The clinical presentation of affected cats is usually consistent with exercise intolerance, gait disturbance such as stiff gait and bunny hop when running. Generalized muscle hypertrophy has been reported, mostly massively affecting lingual and diaphragmatic muscles (Gaschen et al., 1992; Gaschen et al., 2004; Volk et al., 2011). Additionally, multifocal white lingual nodules (muscular calcifications) which appear and disappear spontaneously can be seen. Radiographic changes can show an unusual and typical appearance of the diaphragm line with caudal displacement and scalloping of its borders. Multifocal mineralization can be observed in the myocardium, even though these cats infrequently develop clinical features of heart failure (Gaschen et al., 1999). EMG changes could vary with predominance of myotonic discharges and fibrillation potentials, most pronounced in proximal appendicular muscles (Howard et al., 2004). A definitive diagnosis can be achieved by histopathology. On muscle biopsies, muscle degeneration associated with variable diameter of the myofibers and calcification foci within myofibers without development of endomysial and perimysial fibrosis are reported; the diagnosis is further supported

by the absence of dystrophin on the sarcolemma by IHC (Carpenter et al., 1989; Gaschen et al., 2004). No genetic tests are available to specifically identify the dystrophin gene mutation in cats. The prognosis is considered generally poor. Cats may develop lethal complications due to the muscular hypertrophy of the diaphragm and the tongue, leading to megaesophagus, respiratory distress and reduction in food and water intake (Gaschen et al., 1992). Lethal acute rhabdomyolysis in association with general anesthesia, intense physical activity, or acute stress has been reported (Gaschen et al., 1998).

Cats affected by muscular dystrophy present laboratory findings, particularly biochemical data, consistent with muscle injury. CK activity is usually persistently and markedly increased, and it also can be associated with a moderate to marked increase of ALT and AST activities (Gaschen et al., 2004). The release of these cytoplasmic enzymes from myofibers may came from both myofiber necrosis and cytoplasmic leakage due to instability of sarcolemma (Rowland, 1980). **Mgb**, a 17.5 kDa oxygen-binding protein located in skeletal and cardiac muscle sarcoplasm (Valberg, 2008), can be released secondary to myocyte necrosis or damage into interstitial fluid, lymph and finally blood. As Mgb freely passes into glomerular filtrate (Stockham and Scott, 2008) patients with severe muscle damage associated with rhabdomyolysis develop **myoglobinuria** (Shelton, 2004; Shelton, 2010). Myoglobinuria should be suspected using a urine dipstick test for heme-containing compounds; differentiation between Hgb, Mgb, and hematuria is usually archived by clinical deductive reasoning and matching different features of concurrent plasma aspect, microscopic urinary sediment evaluation, hematological and biochemical data. Other techniques can be used to evaluate myoglobinuria (e.g., precipitant test using ammonium sulfate to differentiate Mgb to Hgb in urine) but are considered unreliable (Stockham and Scott, 2008). Mgb is nephrotoxic and can cause acute tubular necrosis (Shelton, 2004).

SDS-AGE is mono-dimensional agarose gel electrophoresis used to qualitatively evaluate the proteinuria; it separates urinary proteins depending on their MW, so that proteinuria can be classified as glomerular, tubular, or mixed based on the types of bands identified (Littman et al., 2011). In human samples, myoglobinuria on SDS-PAGE is reported at 17 kDa (Rostagno et al., 2013); to our knowledge, studies about urinary Mgb migration using SDS-AGE in veterinary medicine are lacking. Bonsembiante et al. (2017) described in a striped dolphin (*Stenella coeruleoalba*) affected by rhabdomyolysis and myoglobinuric nephrosis (confirmed by histology) SDS-AGE results in which the presence of a glomerular proteinuria was hypothesized. This finding was associated with only mild increase of urea concentration. In that case, as well as in our case, 17-18 kDa bands (where Mgb is supposed to migrate) were absent. However, it is worth noting that in human medicine Mgb in urine is considered instable, and the presence of proteolytic fragments are mostly seen rather than the intact molecule, likely due to the proteolytic action of different urinary enzymes (Rostagno et al., 2013); Mgb instability is maximum in acidic urine, both *in vivo* and *in vitro* (Chen – Levy et al., 2005). In both the dolphin case report and the present case, homogenous protein traces were observed in the low MW protein region of the gel and could represent Mgb fragments. To better understand this finding, other urine sample should be sampled and processed as soon as possible after collection (even though *in vivo* denaturation can occur) or after adding bicarbonate sodium 0.1% to adjust the urine sample to a basic pH (6.5-8.8), as previously reported in humans (Chen-Levy et al., 2005).

In our case marked bands both slightly above 26.6 kDa and on albumin region (67 kDa; Maeda et al., 2015) are clearly identified suggesting a probable renal injury (both tubular and glomerular involvement; Paltrinieri et al., 2015; Giraldi et al., 2019). Although our patient does not show any clinicopathological signs consistent with renal injury (hyperazotemia, low urine specific gravity, increased SDMA concentration) except for qualitative and quantitative proteinuria, it is well known that serum creatinine and urea measurements show poor sensitivity in the early diagnosis of kidney disease (Braun, 2008).

The marked band between 66 and 150 kDa has uncertain significance. In this region, high MW proteins, such as transferrin (77 kDa; Maeda et al., 2015), and cauxin (70 kDa; Miyazaki et al., 2003) usually migrate. Recently, some high MW proteins have been also described in healthy non-proteinuric cats (Ferlizza et al., 2015). Whereas the presence of transferrin would be consistent with a glomerular damage, cauxin would not. Cauxin is a glycoprotein largely produced by epithelial cells of the distal tubules in mature intact male cats and probably involved in the synthesis of felinine pheromone (Miyazaki et al., 2003; Miyazaki et al., 2006). It can interfere with urinary protein measurement with a positive reaction to the protein pad of the dipstick test, an overestimation of UPC ratio is also hypothesized (Miyazaki et al., 2011; Mischke, 2011). In the present case, urinary *Lens culinaris* agglutinin (LCA) lectin treatment, validated to remove cauxin from feline urinary sample (Miyazaki et al., 2011), or urine resampling after castration of the cat are suggested to better elucidate the possible contribution of urinary cauxin on both qualitative and quantitative proteinuria.

The increase of UPC ratio (>0.2) is considered uncommon in cats with chronic kidney disease (CKD) (Ferlizza et al., 2015). However, previous studies observed a higher UPC ratio in cats with both tubular fibrosis and glomerular hypertrophy (as adaptative response to loss of nephrons) (Chakrabarti et al., 2013). Also, low MW bands on SDS-AGE were identified in cats in early-stage CKD, possibly indicating an early tubular involvement (Paltrinieri et al., 2015; Giraldi et al., 2019). However, it should be noted the UPC ratio may have been overestimated due to the presence of urinary cauxin and myoglobin, if the latter has been measured by pyrogallol red method.

To summarise, given the presence of tubular and albumin bands on SDS-AGE, increased UPC ratio and myoglobinuria, a mild early renal injury with tubular and glomerular involvement was suspected. Patients with degenerative muscular disorders often have recurrent myoglobinuria (Shelton, 2004) chronically causing kidney damage. Thus, monitoring renal function is highly recommended in these patients.

In conclusion, to the best of author's knowledge, this is the first case report describing a cat with dystrophin-deficient muscular dystrophy and concurrent proteinuria. Although, proteinuria is suspected to be secondary to an early renal injury due to recurrent myoglobinuria, a partial overestimation of UPC ratio due to urinary cauxin and myoglobinuria (overload pre-renal proteinuria) could not be ruled out. This case also highlights the need of further investigations to evaluate Mgb qualitative migration and stability by SDS-AGE in veterinary species, and to determine the impact of urinary cauxin on the UPC ratio particularly in adult intact male cats.

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REFERENCES

1. Bonsembiante F, Centelleghe C, Rossi G, Giglio S, Madeo E, Gelain ME, Mazzariol S. Clinico-pathological findings in a striped dolphin (*Stenella coeruleoalba*) affected by rhabdomyolysis and myoglobinuric nephrosis (capture myopathy). J Vet Med Sci. 79(6): 1013–1018. 2017.
2. Braun JP. Kidney function and damage. In: Clinical Biochemistry of Domestic Animals. Sixth ed. Elsevier, San Diego, CA. 285–298. 2008.
3. Butts DR, Langley-Hobbs SJ. Lameness generalized myopathy and myalgia in an adult cat with toxoplasmosis. Journal of Feline Medicine and Surgery Open Reports. 1–6. 2020.
4. Carpenter JL, Hoffman EP, Romanul FC, Kunkel LM, Rosales RK, Ma NSF, Dasbach JJ, Rae JF, Moore FM, McAfee MB, Peace LK. Feline muscular dystrophy with dystrophin deficiency. Am J Pathol. 135:909–919. 1989.
5. Chakrabarti S, Syme HM, Brown CA, Elliot J. Histomorphometry of feline chronic kidney disease and correlation with markers of renal dysfunction. Vet Pathol. 50: 147–155. 2013.
6. Ervasti JM. Dystrophin, its interactions with other proteins, and implications for muscular dystrophy. Biochim Biophys Acta. 1772(2):108–17. 2007.
7. Ferlizza E, Campos A, Neagu A, Cuoghi A, Bellei E, Monari E, Dondi F, Almeida AM, Isani G. The effect of chronic kidney disease on the urine proteome in the domestic cat (*Felis catus*). Vet Journal. 204: 73–81. 2015.
8. Gailly P. New aspects of calcium signaling in skeletal muscle cells: implications in Duchenne muscular dystrophy. Biochim Biophys Acta. 1600(1–2): 38–44. 2002.
9. Gaschen FP, Hoffman EP, Gorospe JR, Uhl EW, Senior DF, Cardinet GH, Pearce LK. Dystrophin deficiency causes lethal muscle hypertrophy in cats. Journal of Neurological Sciences. 110: 149–159. 2002.
10. Gaschen FP, Gaschen L, Seiler G, Welle M, Bornand Jaunin V, Gonin Jmaa D, Neiger-Aeschbacher G, Adé-Damilano M. Lethal peracute rhabdomyolysis associated with stress and general anesthesia in three dystrophin- deficient cats. Veterinary Pathology. 35: 117–123. 1998.
11. Gaschen L, Lang J, Lin S, Adé-Damilano M, Busato A, Lombard CW, Gaschen F. Cardiomyopathy in dystrophin-deficient hypertrophic feline muscular dystrophy. Journal of Veterinary Internal Medicine. 13: 346–356. 1999.
12. Gaschen F, Jaggy A, Jones B. Congenital diseases of feline muscle and neuromuscular junction. Journal of Feline Medicine and Surgery. 6: 355–366. 2004.
13. Giraldi M, Paltrinieri S, Scarpa P. Electrophoretic patterns of proteinuria in feline spontaneous chronic kidney disease. Journal of Feline Medicine and Surgery. 1–8. 2019.
14. Jepson R, Syme H, Markwell P, Miyazaki M, Yamashita T, Elliott J. Evaluation of urinary cauxin in geriatric cats with variable plasma creatinine concentration and proteinuria and use of

urine cauxin to creatinine ratio as a predictor of the development of azotemia. American Journal of Veterinary Research. 71: 982–987. 2010.
15. Howard J, Jaggy A, Busato A, Gaschen F. Electrodiagnostic evaluation in feline hypertrophic muscular dystrophy. Veterinary Journal. 168: 87–92. 2004.
16. Littman P. Protein-losing nephropathy in small animals. Vet Clin North Am Small Anim Pract. 41: 31–62. 2011.
17. Maeda H, Sogowa K, Sakaguchi K, Abe S, Sagizaka W, Mochizuki S, Horie W, Watanabe Y, Satoh M, Sanda A, Nomura F, Sozuki J. Urinary albumin and transferrin as early diagnostic markers of chronic kidney disease J Vet Med Sci. 77(8): 937–943. 2015.
18. Mischke R. Assessing proteinuria in the cat: An innovative tip. The Veterinary Journal. 189: 243–244. 2011.
19. Miyazaki M, Kamiie K, Soeta S, Taira H, Tetsuro Y. Molecular cloning and characterization of a novel carboxylesterase-like protein that is physiologically present at high concentrations in the urine of domestic cats (*Felis Catus*). Biochem. J. 370: 101–110. 2003.
20. Miyazaki M, Yamashita T,Suzuki Y, Saito Y, Soeta S, Taira H, Suzuki A. A major urinary protein of the domestic cat regulates the production of felinine, a putative pheromone precursor. Chemistry & Biology. 13: 1071–1079. 2006.
21. Miyazaki M, Soeta S, Yamagishi N, Taira H, Suzuki A, Yamashita T. Tubulointerstitial nephritis causes decreased renal expression and urinary excretion of cauxin, a major urinary protein of the domestic cat. Research in Veterinary Science. 82: 76–79. 2007.
22. Miyazaki M, Fujiwara K, Suzuta Y, Wakamatsu N, Taira H, Suzuki A, Yamashita T. Screening for proteinuria in cats using a conventional dipstick test after removal of cauxin from urine with a *Lens culinaris* agglutinin lectin tip. The Veterinary Journal. 189: 312–317. 2011.
23. Nakamura A, Takeda S. Mammalian models of Duchenne muscular dystrophy: pathological characteristics and therapeutic applications. Journal of Biomedicine and Biotechnology. 1–8. 2011.
24. Paltrinieri S, Sironi G, Giori L, Faverzani S, Longeri M. Changes in serum and urine SAA concentrations and qualitative and quantitative proteinuria in Abyssinian cats with familial amyloidosis: a five-year longitudinal study (2009–2014). J Vet Intern Med. 29:505–512. 2015.
25. Pérez-Accino J, Bernabe LF, Manzanilla EG, Puig J. The utility of combined urine dipstick analysis and specific gravity measurement to determine feline proteinuria. Journal of Small Animal Practice. 61: 541–546. 2020.
26. Rostagno A, Ghiso J. Biochemical analysis of myoglobinuria associated with rhabdomyolysis. Acta Bioquím Clín Latinoam. 47 (1): 17–24. 2013.
27. Rowland, L.P. Biochemistry of muscle membranes in Duchenne muscular dystrophy. Muscle Nerve. 3: 3–20. 1980.
28. Shelton GD. Rhabdomyolysis, myoglobinuria, and necrotizing myopathies. Vet Clin Small Anim. 34: 1469–1482. 2004.
29. Shelton D. Routine and specialized laboratory testing for the diagnosis of neuromuscular diseases in dogs and cats. Vet Clin Pathol. 39(3): 278–295. 2010.
30. Stockham L, Scott MA. Urinary system. In: Fundamentals of Veterinary Clinical Pathology. Second ed. Blackwell Publ. Ames. 466. 2008.

31. Valberg SJ. Skeletal muscle function. In: Kaneko JJ, Harvey JW, Bruss ML, Clinical Biochemistry of Domestic Animals. Sixth ed. San Diego, CA. 459–484. 2008.
32. Volk H, Shihub N, Matiasek K. Neuromuscular disorders in the cat. Clinical approach to weakness. Journal of Feline Medicine and Surgery. 13: 837–849. 2011.
33. Willmann R, Possekel S, Dubach-Powell J, Meier T, Ruegg MA. Mammalian animal models for Duchenne muscular dystrophy. Neuromuscular Disorders. 19: 241–249. 2009.