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Medical management of idiopathic chylothorax in a crossbreed cat with octreotide and rutin use: A case report

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ABSTRACT

This case report describes the diagnosis and treatment of idiopathic chylothorax in a 5-year-old female crossbreed cat who presented with respiratory distress, tachypnea, cyanosis, exercise intolerance and weight loss over a short period of time. Based on the clinical examination, blood results, radiological and echocardiographic findings, the patient was diagnosed with chylous effusion. Chylothorax was considered idiopathic because there was no underlying trauma or disease etiology. Effusion drainage was performed by thoracocentesis to reduce respiratory stress. After thoracocentesis, followed by using medical octreotide- a somatostatin analogue (Sandostatin™, 0.1 mg/ml ampoule, Novartis, USA) and rutin - a flavone benzo-γ-pyrone plant fruit extracted from the Brazilian plant Fava D'anta (Dimorphandra mollis) (Rutin - Plant-Based Bioflavonoid, 500 mg tablet, Solgar™, USA), were administered in addition to supportive treatment. Rutin and ocreotide have been used successfully in humans, dogs and cats to the treatment of pleural effusions as presented various studies. It is hoped that these drugs may also be useful for decreasing pleural effusion in cats with chylothorax. In this represented case; partial resolution of pleural effusion was observed after octreotide usage and complete resolution of pleural effusion was observed after rutin (plant-based bioflavonoid) usage. No recurrence was observed during 7 months of regular follow-up.It was determined that the use of octreotide and rutin after thoracocentesis gave successful results in the medical management of idiopathic chylothorax in cats.

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Introduction

Chylothorax is the effusion of lymph into the pleural cavity (Chinnock, 2003; Fossum, 2006). This is a complex condition and relatively rare in animals. However, it has been reported in horses, cattle, rats, dogs and cats. Chylothorax represents 2% to 3% of pleural effusions and can be classified into four different types: traumatic, malignant, idiopathic or miscellaneous (Gupta and Faith, 1977; Bichard et. al., 1995; Brink et. al., 1996; Litvin et al., 2023). Etiologies of chylothorax in cats include neoplasia (e.g. mediastinal lymphosarcoma), congenital anomalies, dirofilariasis, blastomycosis, pericardial diseases, cardiomyopathies (especially secondary to hyperthyroidism), cardiogenic disorders (e.g.

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paroxysmal atrioventricular block), thoracic duct rupture or leak, and fungal granulomas. Also rare cases reported secondary to diaphragmatic herni and lung lobe torsion. In the majority of affected cats, even after wide diagnostic examination, chylothorax is classified as idiopathic, when the underlying etiology cannot be determined. Although any condition causing increased venous pressure can cause chylothorax, a differential diagnosis should be made together with a full cardiac assessment. As the management of this condition depends on the underlying etiology and type of chylothorax, the presence of coexisting conditions should be eliminated before definitive diagnosis and treatment is administered (Fossum, 2006; Nikiphorou et al., 2016; Hambrook and Kudnig, 2012; Mclane and Buote, 2011).

Idiopatic chylothorax is a disease characterised by gradual deterioration of the cat and usually present with respiratory distress due to atelectasis of the lung caused by chylous fluid. These patients may also display symptoms such as exercise intolerance, lethargy, rapid breathing, coughing and weight loss. As the volume of the pleural fluid increases, the patient becomes more tachypneic, more dyspneic and less able to tolerate exercise (Kopko, 2005). The loss of chyle has several adverse effects; lipids, proteins, lymphocytes, electrolytes and fluids are lost. This is extremely harmful if the animal's thorax is drained regularly over weeks or months. If fluid and calorie intake is not increased, dehydration and loss of weight going to occur (Birchard and Fossum 1987; Stockdale et al., 2018).

The diagnosis of chylothorax is based on the patient's history, chest and lung sounds oscultation, and diagnostic procedure that thorax radiography, ultrasound and/or computed tomography (CT), cardiac echocardiography and Doppler imaging. Loss of cardiac silhouette, nonairated atelectatic lungs, indistinct interlobar margins, sometimes slightly dorsally elongated trachea confirm pleural effusion. Analysis of thoracocentesis fluid can be used to determine the nature of the fluid. In particular, the detection of high triglyceride levels and the identification of large numbers of lymphocytes, characteristic dencity and protein content indicate the presence of chyle (modified transudate). Its protein concentration is between 2.5-4 g/dL, with a cell count below 7000/µL and a specific gravity below 1.032. Further laboratuary test carried out to find the underlying cause (Beatty and Barrs, 2010; Spencer and Karen, 2012; Singh et al., 2012).

The management of idiopatic chylothorax in cats includes medical, surgical or both treatment modalities. Conventional medical management and palliative treatment (involving frequent thoracentesis and a low-fat diet), of idoipathic chylothorax in cats has been associated with a poor diagnosis. Therefore, limiting fluid accumulation is crucial to prevent the need for repeated thoracentesis, which can be finally lead to severe fibrosing pleuritis due to chyle - resulting in pleural thickening and impaired pulmonary expansion and increase the risk of mortality due to anesthesia-related complications post-fluid removal. Currently surgical options avaible for cat with idiopathic chylothorax, include thoracic duct ligation and mesenteric lymphangiography, post-cisterna chyli and thoracic duct glue embolization, passive and active pleuroperitoneal shunting, active pleurovenous shunting, subtotal pericardectomy, omentalization and pleurodesis. Surgical interventions such as ligation of the thoracic duct have been only limited success in relieving chylous effusions. Post-operative recurrence and death has also been reported in some of these cases (Fossum, 2001; Stockdale et al., 2018).

The primary goal of idiopathic chylothorax treatment in cats, is to achieve resolution of the chylous fluid without re-occurance. Recent studies have reported the use of octreotide (a somatostatin analogue) and rutin (a flavone benzo-γ-pyrone extracted from the Brazilian plant - Fava D'anta, Dimorphandra mollis) administration for this purpose. In medical treatment, the efficacy of octreotide has been reported in recent cases, with rutin (plant-based bioflavonoid) usage also showing effectiveness in previously reported cases (Thompson et al., 1999; Gould, 2004; Kopko, 2005). Octreotide mimics the naturally occurring hormone known as somatostatin in humans. Produces an increase in water absorption and intestinal transit and a decrease in pancreatic-duodenal secretion. More importantly, the resistance to splenic blood flow increases, and intestinal arteriolar flow decreases, in turn reducing lymphatic flow due to the inhibition of serotonin and other intestinal peptides (Esme,2019). Rutin (benzo-γ-pyrone), a bioflavonoid found in the fruit of the Brazilian fava d'Anta tree, is classified as nutraceutical and is available without a prescription. It has been used successfully to treat lymphedema in humans and it is hoped that this drug may be useful in reducing pleural effusion in cats with chylothorax (Gingirelli et al., 2016; Kopko, 2005; Thompson et al., 1999). However, the effectiveness of rutin (plant-based bioflavonoid) in reducing pleural effusion in chylothorax-afflicted cats remains uncertain. Some reports indicate complete resolution of pleural effusion in cats treated with rutin (50-100 mg/kg, po, q8h) after 2 months, although it is controversial whether this outcome is due to the drug or

spontaneous healing (Gould, 2004). In a separate study involving rutin treatment (benzo-γ-pyrone Dimorphandra mollis based bioflavonoid; 250mg or 500mg, per cat, q8h for 63 days), complete resolution was observed in a domestic cat (Kopko, 2005), and another study showed clinical improvement 3 out of 4 cats (Thompson et al., 1999). Recent findings have highlighted the efficacy of octreotide, which directly impacts lymphatic flow, in neoplastic and traumatic cases of chylothorax in humans (Esme, 2019). However, the response to octreotide treatment in cats with chylothorax varies. In one study (Yılmaz and Kocatürk, 2023), octreotide administration at 10 µg/kg subcutaneously, 3 times daily for 2-3 weeks, led to complete resolution in one case.

This case report aimed to investigate the efficacy of medical octreotide and rutin (benzo-γ-pyrone Dimorphandra mollis based bioflavonoid) usage in the treatment of idiopathic chylothorax in a cat. The researchers aim to achieve successful results with this treatment approach, reduce the necessity for surgical interventions and make significant contribution to the existing literature. This study on the treatment of this rare condition in cats, provides veterinarians with a scientifically grounded method to invastigate medical treatment options and implement healing interventions.

Case

The case was a 5 years old female crossbreed sterilised cat who was referred to the İstanbul University-Cerrahpaşa, Faculty of Veterinary Medicine, Surgery Department with complaints of respiratory difficulties, cyanosis of mucous membranes, intermittent cough, exercise intolerance and rapid weight loss in a short period of time (3.8kg to 3.2kg). During the clinical examination of the patient, it was in a sitting sternal position and moderately stressed. The patient noted dyspnea and tachypnea (44 bpm-beats per minute), along with a slight increase in body temperature (39° C). The mucosa was slightly cyanotic and the oxygen saturation (SpO2) was 92%. Heart rate was within the reference range for cats. Auscultation of the lungs revealed that breathing sounds were slightly muffled. After 30 minutes of observation in the oxygen cabinet, saturation levels increased to 95% according to the admissions. Laterolateral (LL) and ventrodorsal (VD) thorasic and abdominal radiographs of the patient were taken. Radiographs showed fluid accumulation in the interlobar cracks, significant thickening of the visceral pleura and widening of the mediastinum. Blunting and rounding of the costophrenic and lumbodiaphragmatic angles of the lung lobes was observed, along with border effacement with the cardiac silhouette and diaphragm. Interlobar fissure lines and cranial lung lobes atelectasis were noted, with dorsal elevation of caudal lung lobes. In addition to these findings, thoracic radiography (VD) showed the cardiac silhouette was almost completely absent, especially on the right side (Figure 1, Figure 2).

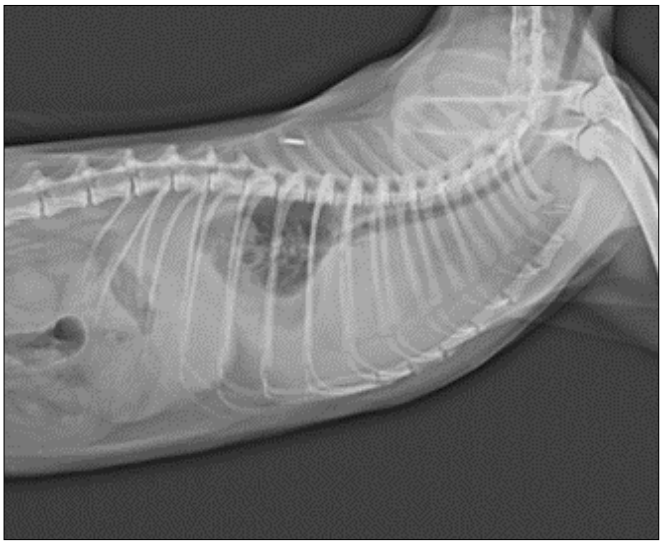

Figure 1. Thorax LL (laterolateral) radiography.

Figure 2. Thorax VD (ventrodorsal) radiography

Thoracic and abdominal ultrasound, examinations, along with color Doppler echocardiography (Mindray Vetus 8, Shenzhen Mindray Animal Medical Technology Co., LTD.; China), were performed. Pleural fluid was anechoic on thoracic ultrasonography (USG), with intact diaphragmatic integrity. Other ultrasound findings were unremarkable. In 2D, M-mode echocardiography the systolic and diastolic diameters of the left ventricular free wall (LVFW) and interventricular septum (IVS) were within normal

range (<6mm), along with normal left ventricular systolic function, indicated by fractional percentages (FS & EF), and a Sphericity index of 1.42 (normal: 1.43 ±0.12). No evidence of pericardial effusion or cardiac neoplasm was found. However, there was generalized bilateral pleural effusion. Sinus tachycardia (212 bpm) with normal QRS morphology on ECG was considered to be stress-related.

The drainage of pleural effusion was decided upon to regulate dyspneic respiration, reduce compression on the lungs, and determine the character of the effusion. For the purpose of prevent to triggering stress, mild sedation was administered with butorphanol (Butomidor, 10mg/ml, Richter Farma, Wels-Austria) at a dose of 0.2mg/kg intramuscularly (im), before 10 minutes of thoracosenthesis. During administration, to achieve stabilization, sedation depth was increased with propofol (Propofol-PF, 10 mg/ml, Polifarma, Turkey) at a dose of 1-4mg/kg intraveneously (iv) and local anesthesia was applied to the intercostal muscles and skin with lidocaine HCl (Jetokain Simplex, 20mg/2ml, ampoule, ADEKA Pharmaceutical Industry and Trade Inc., Turkey; im infiltration applied until desensitization is achieved) while the patient was conscious and in sternal position. Bilateral thoracentesis was performed using 23 gauge butterfly cannula and 3-way stopcock. The fluid obtained from thoracentesis was creamy in color, had an oily consistency, milk-like character and was odorless, costent with chylothorax (Figure 3).

No alteration in the color of the fluid was observed post-centrifugation. The milky fluid had a specific gravity of 1.025 (reference range for chylous fluid, 1.010 to 1.050) and total protein content of 373g/dL (reference range 6.0-7.9g/dL) was very high. The Rivalta test was negative and rapid biogram (Speed Biogram, Virbac, England) yielded no microbial growth from chylous fluid.

Figure 3. Milky pleural aspirate.

Post- thoracentesis radiograhic imaging of thorax revealed consolidation of lung lobes with boundaries marked. Cranial lung lobes exhibited atelectasis, while aerated lung was present only in the caudal 1/3 of thorax. Further investigations through thoracic and abdominal computed tomography (SOMATOM go.Now, Simens, Germany) revealed findings

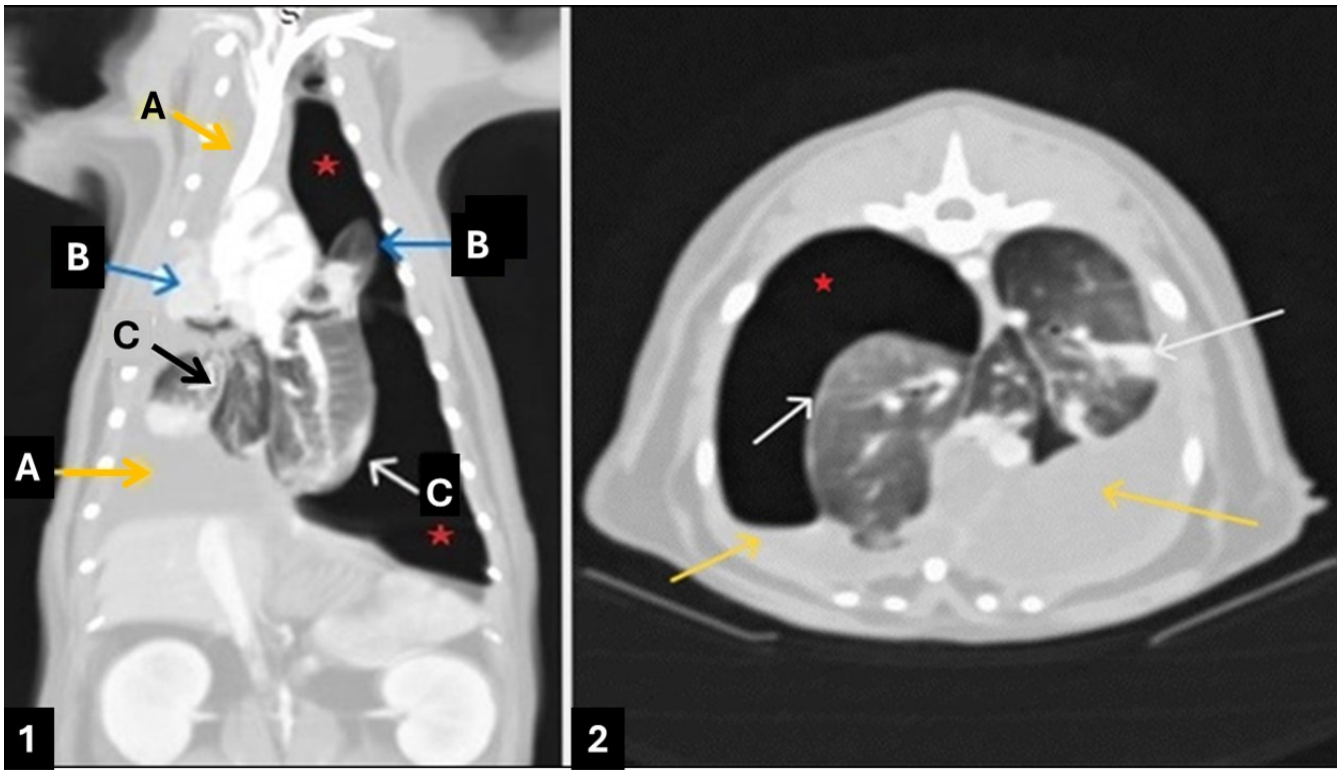

Figure 4. Computed Tomography Dorsal Plan (1) and Transversal Plan(2) Thorax Images. Pleural effusion - yellow arrows (A), lung athelactesis - blue arrows (B), visseral pleura dencity incraese - white arrows (C), left sided pneumothorax red stars represented.

pleural efusion reaching a thickness of 12 mm on the right and 38 mm on the left; was observed. Increased soft tissue density in a thick band-like pattern on the right lung suggests compression atelectasis. Retrosternal localization lymph nodes were enhanced in the cranial mediastinum (Figure 4).

The biochemical profile (Fuji DRI-CHEM NX600V, Fujifilm, Japan) was normal (alkaline phosphatase - ALP, gamma glutamyl transferase- GGT, glucose, total bilirubin - TBIL, creatinine - CRE, blood urea nitrogen - BUN, albumine - ALB, phosphor, total cholesterol, triglyceride, calcium) except alanine aminotransferase - ALT 151 u/L (reference ranges 22-84 u/L) total protein - TP 8.4 g/dL (reference ranges 5.7-7.8 g/dL), ammonia - NH_3 93 µg/L (23-78 µg/L) which were increased. Hemogram (BC60R Vet, Mindray China) analysis abnormalities noted were mild lymphopenia (0.298 x10^9/L, referance range 0.7-7.4 x10^9/L) and low PCT (0.25ml/L, reference range 0.9-7 ml/L). Feline NT-ProBNP <50pmol/L (referece range <100pmol/L:normal; 100pmol/L and >100pmol/L: abnormal,V-Check, Bionote Inc., Korea) ve feline troponin I, 0.12ng/ml (referece ranges, <0.14 ng/ml:normal; 0.14-0.22ng/ml equivo and > 0.22ng/ml abnormal, V-Check, Bionote Inc., Korea) founded. Feline immunodeficiency virus (FIV Ab), feline leukemia virus (FeLV Ag) and feline heartworm (FHW Ab) tests performed on the patient (Anigen Rapid FIV Ab/FeLV Ag Test Kit and Anigen FHW Ab; Anigen Animal Genetics Inc., Korea) also gave negative results.

Based on laboratory results, clinical, radiological and echocardiographic findings, the patient was diagnosed with chylous effusion. Since there was no underlying trauma or disease etiology, diagnosis was considered idiopathic chylothorax.

Octreotide (Sandostatin®, 0.1 mg/ml ampoule, Novartis, USA; 10 µg/kg, q8h, sc, 21 days) was used for the resolution of chylous effusion. Salbutamole (Ventolin® Nebules®, 2,5 mg/2,5 ml nebule, GlaxoSmithKline, Australia Pty. Ltd., Australia; 0.5mg per cat, q12h, nebule) and fluticasone propionate (Flixair 500 µg /2 ml, aerosol, VEM Pharmaceutical Ind. and Trade Inc, Ankara; 110 µg per cat, q12h, nebule) were added to the treatment for the first 3 days as supportive therapy. After 21 days, the chylous fluid had slightly decreased but not completely resolved. Subsequently of these finding, a second thoracentesis was performed. Following this procedure, rutin (Rutin - Plant-Based Bioflavonoid, 500 mg tablet, Solgar®, USA; 250mg/per cat, q8h, 63 days) was initiated. Two weeks later respiratory findings had normalised and the pleural effusion had significantly decreased. Haematological parameters were found to non-specific. Biochemical analysis showed that ALT returned to normal reference range whereas glucose and TP were slightly increased. The patient, who was noted to have a normal mental status and appetite, was noted to have gained weight (4.3 kg) after treatment. No clinical signs were observed at the 4th, 8th and 12th week examinations. It was observed that atelectatic cranial lobes stayed non-aerated and did not return to normal localization on radiography (Figure 5). Rounded lung lobes and findings consistent with pleural fibrosis were observed on radiography. It was determined that the chylous effusion was completely resolved.

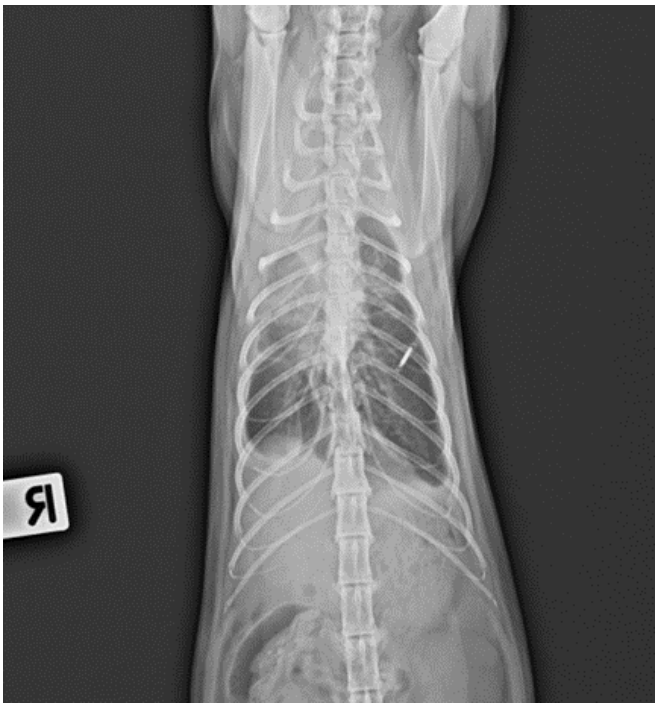

Figure 5. Thorax VD radiography – after two weeks of rutin (plant-based bioflavonoid) treatment.

Disscussion

Chylothorax is a rare type of pleural effusion in animals and has been reported in many different species. In cats, it is expressed that it is mostly seen in pure breeds such as Siamese and mostly affects aged cats (Fossum, 1991; Beatty and Barrs 2010). In this case, the patient was a crossbreed and a 5-year-old middle aged cat. The study presented (Gould, 2004) is supported by the case being neither purebred nor aged. Various factors such as neoplasia, cardiogenic disorders, diaphragmatic hernias and trauma play a role in the formation of chylothorax in cats (Fossum 2006; Nikiphorou et al., 2016; Hambrook and Kudnig,2012; Mclane and Buote, 2011). Clinical examination, radiological and echocardiographic evaluation of this case revealed no findings of any disease that could lead to chylothorax formation. Thoracic and abdominal ultrasound imaging along with color Doppler echocardiography represented that the

masses (Gould, 2004) and computed tomography findings consist with that findings (McGrath, 2011). As there was no underlying trauma or disease etiology (Fossum 2006), based on the radiographic findings of pleural effusion as well as the appearance and analysis of pleural fluid, the diagnosis was considered to be idiopathic chylothorax. The milky apperiance, protein concentration and density of the chylous fluid also found to confirm the diagnosis. (Beatty and Barrs, 2010; Spencer & Karen, 2012; Singh et al., 2012).

Idiopathic chylothorax is a disease characterised by gradual progressive detorioration of the cat's clinic condition which usually present with respiratory difficulty, rapid breathing and coughing due to atelectatic lung caused by chylous fluid (Kopko, 2005). In this presented case, significant dyspnea, increased respiratory rate and intermittent cough were observed. In addition to respiratory symptoms, a poor appetite and weight loss (Gould, 2004; Beatty and Bars, 2010) have been observed to accompany the clinical presentation. The fast decrease in body weight in this patient history, was presumed to originate from the energy deficit occurring during respiratory effort and the loss of chyle fluid as reported in the literatures (Kopko 2005; Bitchard at all., 1998).

Also dsypnea and coughing findings (Gould, 2004; Yılmaz and Kocatürk, 2023) consistent with radiological findings (USG, thoracic radiography and CT) which presented of a bilateral diffuse pleural effusion and a large area of atelectasis. The presence of pneumothorax on CT images was considered as an air-filled area remaining from the unventilated atelectic lungs remaining from the chylous fluid formed after thoracocentesis. The cardiac silhouette in the VD radiograph is indistinct compared to that in the LL radiograph which was thought to be due to the displacement of the chylous fluid in the mediastinal apertures according to the patient position (Beatty and Barrs, 2010).

There was no spesific medical treatment of idiopathic chylothorax as known. The management of idiopathic chylothorax in cats poses a challenge, with the primary goal being the resolution of chylous fluid accumulation without recurrence (Thompshon, 1999). Recent studies have explored various treatment modalities, including the use of octreotide and rutin. Octreotide has garnered attention for its potential effectiveness in preventing chyle formation, as evidenced by recent cases (Ghiringhelli, 2016; Yılmaz & Kocatürk, 2023; Bichard, 2012; Esme,2019). However, the response to octreotide treatment in cats with chylothorax appears to variable; some cases achieving complete resolution with prolonged administration (Yılmaz & Kocatürk, 2023), while others may require additional interventions (Fossum 1991; Singh at all,2012; Reeves et al., 2020).

In our case, octreotide administration post-thoracentesis resulted in a partial reduction in chyle fluid volume by the 21st day of treatment initiation, although complete resolution was not achieved. Subsequently, rutin (plat-based bioflavonoid) was introduced, which has been reported to aid in the dissolution of chyle (Gould, 2004; Kopko, 2005; Thompson et al., 1999). After two weeks of rutin (plant -based bioflavonoid) administration, complete resolution of chyle fluid was observed during the initial follow-up. This outcome prompts discussion regarding the mechanisms underlying treatment success. While some literature suggests that the resolution may be attributed to time-dependent healing processes, others argue for the efficacy of medication. Despite octreotide usage not achieved complete response within 21 days; after two week rutin (plant-based bioflavonoid) usage, the resolution of chyle observed. This indicated the potential effects of rutin, which contribute to the resolution of chyle accumulation in idiopathic chylothorax.

The findings from the 4th, 8th, and 12th-week examinations indicated that the patient was able to breathe comfortably without respiratory distress, exhibited normal appetite, and even gained weight compared to admission. However, the cranial atelectatic lung lobes remained non-aerated bilaterally, and radiographic evidence consistent with pleural fibrosis manifested as rounded, consolidated lung lobes and accentuated interlobar pleural lines (McGrath 2011, Beatty and Barrs 2012, Sack et al., 2022) was observed. Nevertheless, there was no recurrence of chylous fluid.

Surgical treatment is considered in cases where medical treatment cannot be performed or unsuccessful (Fossum 2001). However, no further surgical intervention was required in this case diagnosed as idiopathic chylothorax because the patient responded positively to medical octreotide and a specially rutin (plant based bioflavonoid) treatment.

This synthesis highlights the ongoing discussions about the optimal management of idiopathic chylothorax in cats and underlines the need for further research to explore the mechanisms of its possible effects and to optimise treatment strategies (Reeves et al., 2020).

In conclusion, our study demonstrated that administration of octreotide and rutin (plant-based bioflavonoid) treatment following thoracocentesis yields favorable results in the medical management of idiopathic chylothorax in cats. The utilization of these treatments before considering invasive surgical interventions may offer a beneficial therapeutic approach.

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