CASE REPORT

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Iodine is One of The Odds for Therapeutic Armamentarium Against Feline Polycystic Renal Disease

Kerem Ural[1,a], Hande Mutlu[2,b], Hasan Erdogan[1,c], Songul Erdogan[1,d,*]

[1] Aydin Adnan Menderes University, Veterinary Faculty, Department of Internal Medicine, Aydin, Turkey
[2] Pasteur Veterinary Clinic, Kadıköy, Istanbul, Turkey

[a]ORCID: 0000-0003-1867-7143; [b]ORCID: 0000-0003-0879-3626;
[c]ORCID: 0000-0001-5141-5108; [d]ORCID: 0000-0001-5141-5108

*Corresponding Author
E-mail: songul.toplu@adu.edu.tr

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Abstract

A cat was referred to clinics with a history of loss of appetite, deterioration in general condition, weight loss, vomiting, and mass-like swelling in the abdomen at the level of the vertebrae. On physical examination, the cat had a swelling in the abdomen palpated in the localization of the kidney. Multiple cysts in both kidneys were determined with abdominal ultrasonography. The treatment was initiated with iodine drop, broccoli powder, EPA/DHA, vitamin D3 and K2 and Chlorella capsule for 5 weeks along with pre- and probiotic supplementation, low glycemic index cat food. Following natural and nutraceutical intervention renal cysts and abdominal swelling were disappeared. This report suggests that multiple renal cysts may be successfully managed with oral iodine as one of the therapeutical odds along with supportive nutraceuticals.

Keywords: Cat, renal cyst, iodine.

INTRODUCTION

The polycystic kidney disease (PKD) as most common in domestic cats especially Persian/Persian related breeds is typical by cysts formation in the renal parenchyma (Sato et al., 2019; Bilgen et al., 2020; Guerra et al., 2020). Although it is generally hereditary autosomal disease and caused by mutation of polycystin 1 genes (Sato et al., 2019; Bilgen et al., 2020; Guerra et al., 2020), in a study performed in purebred Maine Coon cats reported that cats with renal cysts were negative for genetic mutation (Gendron et al., 2013).

Clinical signs are mostly variable and may occur in middle or older age (Barrs et al., 2001) related to renal failure and due to the disease is usually subclinical (Barrs et al., 2001). The main signs are compatible with chronic kidney failure including lethargy, anorexia, loss in weight, vomiting, polyuria, polydipsia (Domanjko-Petrič et al., 2008).

Recognized of disease is primarily based on renal ultrasonography (Wills et al., 2009; Vučićević et al., 2016; Guerra et al., 2019), genetic testing revealed of polycystin 1 variation (Vučićević et al., 2016; Sato et al., 2019; Bilgen et al., 2020; Guerra et al., 2020) or post-mortem examination (Benetido et al., 2020).

The classically accepted medical theory is that there is no known treatment of the PKD. Only control of the clinical findings and outcome of chronic kidney disease are performed (Polzin, 2013). As like veterinary science, in human medicine, there are no effective treatment and generally it includes increased water conception, excessive water intake, restricted sodium and protein intake, and there are several drug trials (Tesar et al., 2017; Torres et al., 2018; Zhao et al., 2019).

The aim of this case report was to be sharing of the possible treatment trial with iodine of one cat with unilateral renal cysts diagnosed by abdominal ultrasonography attendant with the clinical and laboratory findings. In this way, we aimed to help to the veterinarians referencing cases with similar findings, and to clarify the research to be performed for the use of iodine as the headliner with supportive nutraceuticals including pre/probiotic supplementation, low glycemic index cat food and broccoli powder in the treatment of PDK.

CASE HISTORY

A 4-year-old, female, Sarman cat named Mia was referred to veterinary clinic with a history of loss of appetite, deterioration in general condition, weight loss, vomiting, and mass-like swelling in the abdomen at the level of the vertebrae. According to physical examination of Mia, swelling was palpated in the area where the kidney was located in the right upper abdomen, fossa paralumbal region (Figure 1a).

At presentation to the clinic, routine complete blood count (CBC) and biochemical profile were analyzed with abdominal radiography (Figure 2) and ultrasonography (Figure 3).

The cat was monitorized by weekly for first month after the treatment and then controls were performed monthly to be twice. Abdominal ultrasonography at third week and biochemical analysis at first week and 2nd months of the treatment were repeated. Post-treatment CBC could not be performed at time of writing the manuscript.

Following tentative diagnosis, the treatment was initiated with iodine drop (Venatura Iyot, VEFA

pharmaceuticals, Turkey) adminestered orally after dilution of 1 drop iodine in 10 drops of clean water and 1/3 of prepared solution was given once a day for first 10 days and then iodine solution was to be continued every other day for 2 months. At the same time, probiotic drop (Lactocol liquid probiotic supplementation, Orthogen, Turkey) with 9 drop/cat once a day and probiotic/prebiotic combination (Gutfeel powder, ASSOS pharmaceuticals, Turkey) given twice a day mixed with liquid (water) were administered for three weeks. For ceasing of the carbohydrate-containing diet completely, it was recommended to prescribe low glycemic index cat food added three grams of broccoli powder (Proteinocean Broccoli Powder, Proteinocean Pharmaceuticals, Turkey) twice a day.

Figure 1. Swelling on the abdomen before treatment (a). Abdominal appearance on 3th week (b) and 2nd month (c, d) of treatment.

After the 3rd week, the treatment was continued as with iodine drop, nutraceutical for kidney function (Nefropiu pasta, Aurora Licensing, Italy), vitamin D3 and K2 (Venatura Vitamin D3 K2 oral drop, VEFA pharmaceuticals, Turkey), Chlorella capsule with once a day (Solgar chlorella dietary supplement, Turkey) for 5 weeks and also fluid therapy icluded Mannitol and Voluven intravenously at a dose of 15 ml/kg over 15 to 20 minutes for 4 days and Dipeptiven® (Fresenius Kabi, Turkey) rectally at a dose of 2 ml/kg for 4 days.

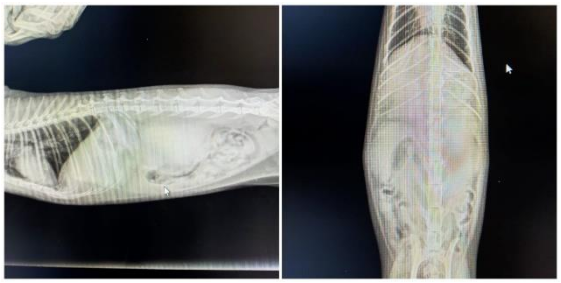

Figure 2. Abdominal radiography of the cat when presence to clinic.

RESULTS

Increased kidney size covering hypogastric and mesogastric area removing colon to more medial and ventral towards than normal location was observed in the abdominal radiography (Figure 2).

Abdominal ultrasonography demonstrated that multiple renal cysts with anechoic, round and distinct border structures were observed in both kidneys (Figure 3a, b). Ultrasonographic findings of kidney dimensions were observed as follows: right renal height was 52.4 mm, left renal height 63.1 mm, right renal width 35,3 mm, and left renal width 39.3 mm (Figure 4a, b).

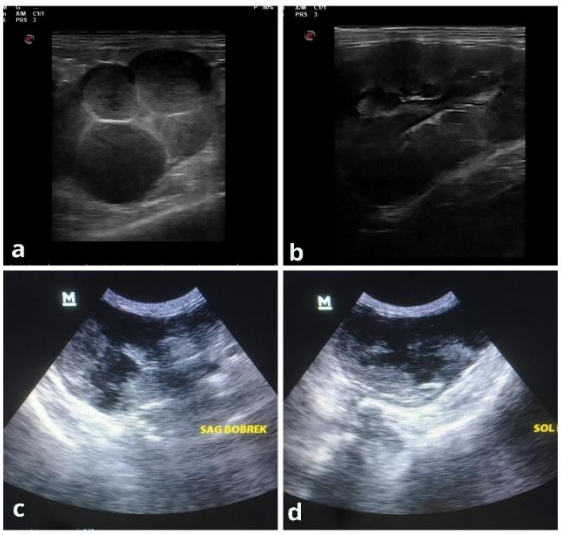

Figure 3. Images of abdominal ultrasonography; multiple renal cyst in both kidney (a, b) and disappearance of cysts on the 3th week of treatment (c, d).

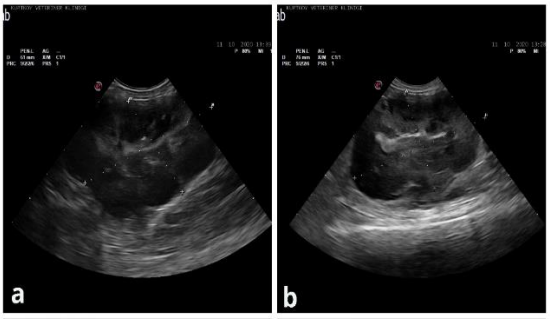

Figure 4. Ultrasonography findings of kidney dimensions of both kidney before treatment.

Two weeks after the treatment, it was observed that the swelling in the right side of abdomen decreased morphologically. The case presented better general condition with a slight increase in appetite.

At the control examination performed in the third week after the treatment, ultrasonography was repeated where right renal height was 24.7 cm, left renal height 22.2 cm, right renal width 42.2 cm, and left renal width 29.4 cm and also the cysts in the kidneys disappeared (Figure 3c, d). Appetite of the cat, Mia, increased, vomiting ceased, and had clinically healthy appearance and the swelling in the right side of abdomen disappeared (Figure 1b-d). Furthermore, the treatment of the patient was continued.

The results of the CBC and biochemical analysis were presented in Table 1. According to blood analysis leukocytosis, mildly increased globulinemia and creatinine level (1.8 mg/dL) were initially recorded. After treatment it was found that only BUN value increased to 54 U/L and there was any increase of biochemical parameters. Furtherly, creatinine levels decreased from 1.8 mg/dl to 1.52 mg/dl 7th day and 2nd month of the treatment.

Table 1 The results of the CBC and biochemical analysis related to treatment

Before treatment						**After treatment**			
CBC			**Biochemical analysis**			**Biochemical analysis**			
Results		References range	Results		References range	Results	7th day of the treatment	2nd month of the treatment	References range
WBC (10^9/L)	**14.1**↑	1.0 - 7.0	GLU mg/dl	146	74 - 159	TP g/dL	**8.4**↑	7.4	5.7 - 7.8
LYM (10^9/L)	1.0	0.2 - 1.0	CREA mg/dl	1,8	0.8 - 2.4	ALB g/dL	3.2	2.9	2.3 - 3.5
MONO (10^9/L)	0.9	2.8 - 13.0	BUN mg/dl	34	16 - 36	ALP U/L	19	-	9 - 35
NEU (10^9/L)	12.0	3-12	BUN/ CREA	19	-	GLU mg/dl	123	-	71 - 148
EOS (10^9/L)	0.2	0.1-1	PHOS mg/dl	5,2	3.1 - 7.5	TBIL mg/dl	0.2	-	0.1 - 0.4
LYM%	**7.3** ↓	12-30	CA mg/dl	9,3	7.8 - 11.3	IP mg/dl	5.1	5.2	2.6 - 6.0
MON%	**6.2**↑	2-4	TP g/dl	8,8	5.7 - 8.9	TCHO mg/dl	126	-	89 - 176
NEU%	85.0	62-87	ALB g/dl	2,9	2.2 - 4.0	GGT U/L	10	-	1 - 10
EOS%	1.5	5.00 - 11.00	GLOB g/dl	**5.9**↑	2.8 - 5.1	ALT U/L	39	-	22 - 84
RBC (10^{12}/L)	**7.31**↓	8.0 - 15.0	ALB/G LOB	0,5	-	Ca mg/dl	**16.0**↑	**12.0**↑	8.8 - 11.9
HGB (g/dL)	**11.5**↓	25.0 - 45.0	ALT U/L	**11**↓	12 - 130	CRE mg/dl	1.52	1.05	0.80 - 1.80
HCT	33.4	32.0 - 60.0	ALKP U/L	**<10**↓	14 - 111	BUN mg/dl	**54.1**↑	32	17.6 - 32.8
MCV	**45.7**↑	12.5 - 17.5	GGT U/L	0	0 - 4	GLOB g/dl	**5.2**2	4.5	2.8 - 5.1
MCH	**15.8**↓	28.0 - 45.0	TBIL mg/dl	0,5	0.0 - 0.9	ALB/GL OB	0.6	0.6	-
MCHC	34.6	20.0 - 43.0	CHOL mg/dL	128	65 - 225	BUN/CR E mg/dl	35.6	30.5	-
RDWa	**29.5**↑	14.0 - 18.5	AMYL U/L	1275	500 - 1500				
RDW%	345	200 - 500	LIPA U/L	576	100 - 1400				
PLT	**17.0**↑	8.0 - 12.0							
MPV	6.4	1.0 - 7.0							

CBC: complete blood count, WBC: white blood cell, LYM: lymphocyte, MONO: monocyte, NEUT: neutrophils, EOS: eosinophil, GLU: glucose, CREA: creatinine, BUN:blood urea nitrogen, PHOS: phosphor, CA: calcium, TP: total protein, ALB: albumin, ALP: alkaline phosphatase, TBIL: total bilirubin, IP: inorganic phosphor, TCHO: total cholesterol, GGT: Gamma-glutamyl transferase, ALT: alanine aminotransferase, RBC: red blood cell, HGB: hemoglobin, HCT: hematocrit, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, RDW: red cell distribution width, PLT: platelet, MPV: mean platelet volume, AMYL: amylase, LIPA: lipase, GLOB: globulin

DISCUSSION AND CONCLUSION

This is the first study investigating the effects of iodine attended with nutraceuticals including supportive treatment with pre/probiotic supplementation, low glycemic index cat food and broccoli powder in a cat with PKD. The study researched the therapeutic efficacy of oral iodine reducing cyst progression in a cat with PKD diagnosed by ultrasonography. This study proved that oral iodine as the headliner attended with nutraceuticals significantly regulated renal cyst progression ultrasonographically revealed after the treatment.

Polycystic kidney disease is characterized with multiple cysts formation that differentiated renal parenchyma and it may be occurred unilaterally due to hereditary nature (Domanjko-Petriĉ et al., 2008). Although genetically Persian and related cats are predispose to the disease due to PKD1 gene mutation (Cannon et al., 2001; Bonazzi et al., 2009) in which it has also been reported in different breeds (Kappe et al., 2005; Helps et al., 2007). Renal cysts mostly are not detected until they have cause clinical findings related to renal failure or abdominal enlargement as size and number of cysts develop with age (Guerra et al., 2019). For these reasons, especially in young cats, genetic analysis based to detection of PDK1 mutation are recommended (Bonazzi et al., 2009). In a different study, it has been reported that a certain number of cysts should be seen in certain age ranges for diagnosis, and it is sufficient to be imaged at least one renal cyst till fifteen-month age (Guerra et al., 2019). Considering to studies stated that it is sufficient to reveal the presence of at least one cyst in at least one kidney for the diagnosis of PKD (Beck et al., 2000; Guerra et al., 2019). The genetic analysis was not performed in our study due to age of cats and imaged multiple renal cysts with ultrasonography was found sufficient for diagnosis. On the other hand, absence of the genetic analysis does not reduce the prominence of this report due to the focus of the study is the disappearance of the cysts with the treatment attempt.

Treatment of PDK is limited with control of clinical findings, outcome of chronic kidney disease and reducing growth of cysts due that it is believe to renal cysts are not eliminated in both medicine (Polzin, 2013). Even so, there are some treatment trials including novel drugs in human medicine (Tesar et al., 2017; Torres et al., 2018; Zhao et

al., 2019) or invasive intervention in veterinary science (Gonzalez et al., 2009). At this point, the striking part of our study is the disappearance of the cysts and the recovery of the cat with the use of iodine for PKD treatment.

Povidone iodine solution is reported as a safe sclerotherapy agent, especially used in the treatment of cystic structures covered with fluid and surrounded by epithelium, therefore it is used in the treatment of lymphocele, pleural effusion, empyema, pericardial effusion, thyroid cysts, hydrocele, echinococcosis and ovarian cysts (Polat et al., 2009; Cheng et al., 2012; Alago et al., 2013; Atilgan et al., 2019). Similarly, in a study conducted on dogs with idiopathic renal hematuria, it was reported that povidone can be used to provide renal protection in sclerotherapy with iodine (Adelman et al., 2017). In addition to these, in a similar study conducted on renal cysts, while in one stated that povidone iodine was effective (Phelan et al., 1999), the more recent study indicated that relapses were observed, and it was not effective in sclerotherapy (Madeb et al., 2006). It was reported that povidone iodine applied into the cyst as a sclerotherapeutic agent is effective by causing damage to the cyst wall and surrounding tissues indicated by histopathology (Atilgan et al., 2019).

The evidence shows us that iodine has an antioxidant, antiproliferative effect and it helps to maintaining integrity of organs by taking iodine besides thyroid function (Aceves et al., 2013). It inhibits to progression of both benign and malign neoplasia by several mechanism. So, antiproliferative effect of iodine on neoplasia occurs by two different pathway directly and indirectly in which first one, oxidized form of iodine has triggered apoptosis with breaking the mitochondrial membrane potential by antioxidant activity to be caused depletion of total cellular thiol content (Shrivastava et al., 2006) or to be removing free oxygen radicals (Smyth, 2003) and latter, its coadjuvant formation activates to peroxisome proliferator–activated receptors that indirectly trigger apoptosis and causes cell death as like to direct effect (Nava-Villalba and Aceves, 2014). Although genetic effect is known about the pathophysiology of PKD (Sato et al., 2019), there is no study about cellular/intracellular mechanisms triggering progressive enlargement of cyst formation unlike human medicine (Riwanto et al., 2016; Chumley et al., 2019). Furthermore, it is known that the resulting genetic mutation in PKD also impairs mitochondrial and energy metabolism (Chumley et al., 2019) and it has been observed that cyst growth decreases with the inhibition of glycolysis (Riwanto et al., 2016). In a recent study performed in rats, ketogenic diet (time-restricted feeding/intermittent fasting) lead to amelioration of renal cyst growth as regulation metabolic changing with intermittently decreased blood glucose levels and increased ketogenesis (Torres et al., 2019). The low glycemic index diet on energy metabolism are considered as secondary mechanisms in the elimination of the cysts in this study. Therefore, in the light of all the mentioned mechanisms of iodine, it may be shaped by the loss of the renal cysts as a result of iodine treatment with the development of the cyst wall damage, and the loss of cellular energy. Interestingly a low glycemic diet was prescribed to the present case, in which should have ameloriated possible low grade systemic inflammation background.

Apart from aforementioned and discussed data, mandatory but not brief explanation is necessary. Given the bioactive lipids participate in systematic homeostasis, atherosclerosis, and renal-vascular alterations (Dailey and Imming, 1999; Zhao and Funk, 2004), autosomal dominant polycystic kidney disease has been associated with dysregulated metabolism of bioactive lipids (Klawitter et al., 2014). Related data in mice with PKD claimed that inflammatoric and secretoric lipids both were overrepresented. A lipid detected within the cyst fluid in DBA/2FG pcy-pcy mice caused fluid secretion and proliferation by MDCK cells (Yamaguchi et al., 1995). It was previously described that human cyst fluids retain chemotactic and secretagogue lipids significantly participating within the autosomal dominant PKD. Given those lipids could present unique structure, might be existed by renal epithelial cells (Grantham et al., 1997), their presence in cyst fluid accompany cell proliferation, fluid secretion and chemotaxis, as cyst activating factor (Sullivan et al., 1998). Aforementioned lipids present pro-inflammatoric characterization enrolled in cell proliferation pathways (Klawitter et al., 2014)

Regarding the process of organ formation for iodine, secondary pathway comprised iodine incorporation into lipid molecules. The latter iodolipids were secluded to those of thyroidal tissue, in which denoted as clue governor of thyroid cell metabolism and proliferation (Dugrillon, 1996). The iodination of lipids has been related to iodide peroxidases catalyzation (Boeynaems et al., 1981). A composite derived from arachidonic acid, namely d-iodolactone, detected to inhibit human thyroid follicular cell proliferation (Dugrillon et al., 1994) and to cause goiter regression in rats (Pisarev et al., 1984), both in vivo. Therefore, in addition to its embodiment into thyroid hormones, it is corporated into anti-proliferative iodolipids within the thyroidal tissue; briefly addicted to its probable participation for anti- proliferative efficacy of extrathyroidal tissues (Cann et al., 2000). Given lipid existence in cyst fluid as aforementioned above, iodination of lipids along with anti-proliferative efficacy might cause cyst regression in the present case.

In this case report, it was proved to be sharing of the possible treatment trial for the cyst regression with iodine of one cat with unilateral renal cysts diagnosed by abdominal ultrasonography. In this way, we aimed to help to the veterinarians referencing cases with similar findings, and to clarify the research to be performed for the use of iodine as the headliner with nutraceuticals including pre/probiotic supplementation, low glycemic index cat food and broccoli powder in the treatment of PDK. It should not be unwise to draw preliminary conclusion that iodine, as a simple essential mineral, should prevail immunosuppressive drug choices with unknows results and parts.

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Conflict of Interest
The authors declared that there is no conflict of interest.

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