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Intrahepatic portosystemic shunt with a second degree atrioventricular block fixed by transvenous coil embolization in a dog

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Abstract : A 2-year-old female Pekingese dog was presented with primary complaints including exercise intolerance and neurological sign associated with hepatic encephalopathy. The major findings in clinical examination included an intermittent seizure, a slow heart rate with pulse deficit, leukocytosis and anemia in hemogram, elevated pre- and post-prandial serum bile acid and hepatic enzymes, hypoproteinemia, coagulopathy, ammonium urate crystaluria and bilirubinuria. Diagnostic tests revealed an intrahepatic portosystemic shunt complicated with a second degree atrioventricular block and QT prolongation. The case was successfully treated with a transvenous coil embolization. Clinical signs were gradually improved and cardiac bradyarrhythmia disappeared. This case is a rare case of intrahepatic portosystemic shunts complicated with a cardiac bradyarrhythmia in a small breed dog fixed by a transvenous coil embolization.

Keywords : atrioventricular block, IPSS, portosystemic shunt, transvenous coil embolization

Introduction

A portosystemic shunt (PSS) is an abnormal connection between the portal vein and the systemic circulation. The PSS can be subdivided into extraheptic (shunts located outside the liver) and intrahepatic (shunts located inside the liver) PSS, depending on the location of the shunted vessel. The PSS can be also subdivided into congenital and acquired, depending on the etiology. Either incomplete or botched closure of patent ductus venosus after birth is the main cause of PSS in dogs [17]. In the small breed dogs, extrahepatic portosystemic shunts (EPSS) are more common, while intrahepatic portosystemic shunts (IPSS) are more common in large breed dogs. To date, the exact mode of inheritance for this disorder has not been determined, although PSS is over-presented in certain dog breeds such as Havanese, Yorkshire Terriers, Miniature Schnauzers, and Maltese [11, 24].

Most dogs with PSS will develop clinical signs early in life. The common clinical presentations associated with PSS are a history of doing poorly, the smallest size in littermates, waxing and waning neurologic signs, polyuria/polydipsia, microhepatica and urate urolithiasis [17]. The characteristic hemogram is a microcytic, normochromic nonregenerative anemia with target cells and poikilocytes, resulted from abnormal lipid metabolism, iron sequestration, or iron deficiency [3, 10, 27].

Liver enzymes are often not significantly elevated in dogs with PSS. The more common biochemical changes in PSS include hypoalbuminemia, hypocholesterolemia, hypoglycemia (especially after fasting), and decreased BUN. Low urine specific gravity and ammonium biurate crystals are the most common abnormalities observed in urinalysis of dogs with PSS. Coagulation abnormalities are gradually apparent, when the disease progresses. Both serum bile acids (fasting and 2-h postprandial) and ammonia tolerance tests are more accurate method for diagnosing PSS in dogs, although they may be increased by other causes of hepatic dysfunction.

For definitive diagnosis, a visualization of shunting vessel is required using an exploratory laparotomy, contrast radiography (portography), computed tomography, ultrasound, or nuclear scintigraphy. Medical manage-

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ment for PSS predominantly aims to control signs of hepatic encephalopathy using a low-protein diet and oral ammonia absorption blockers. However, the medical management alone is usually not very successful and most animals are euthanized because of inability to adequately control signs.

Ultimately, all dogs with PSS are required either surgical or non-surgical occlusion of shunted vessel(s). Many different surgical procedures of PSS have been described in veterinary literatures [6, 24, 26]. Gradual ligation (for preventing portal hypertension) using cellophane tape and ameroid constrictors is the most commonly used method for EPSS. However, for IPSS, this surgical ligation alone is often difficult to occlude this shunt. Transvenous coil embolization (TCE) has been recently developed and successfully applied to occlude the shunted vessel located inside the liver [5, 22]. However, overzealous occlusion of a shunt vessel can result in acute portal hypertension, which can cause ascites, bowel ischemia, and endotoxemic shock [17].

Cirrhotic cardiomyopathy (CC) is a relatively new clinical entity characterized by inconstant and often subclinical series of heart abnormalities induced by chronic hepatic failure (e.g. hepatic cirrhosis) [18]. In humans with CC, a significant prolongation of QT interval on basal ECG has been well recognized [13, 15, 16], presumably due to an impaired electrical ventricular recovery. The abnormally prolonged QT is associated with sudden cardiac arrest in dogs and humans [7, 8, 20]. In humans, about 30-60% of cirrhotic patients have prolonged QT interval [1, 2]. Furthermore, the extent and magnitude of long QT were closely correlated with the severity of liver disease [1, 2]. Although the long QT disappeared in most human patients after liver transplantation, the clinical relation between QT prolongation and hepatic cirrhosis is still debatable [4].

This case study described a rare case of IPSS complicated with a cardiac bradyarrhythmia and long QT in a small breed dog fixed by a TCE.

Case history

A 2-year-old female Pekingese dog (body weight 4.1 kg) was referred to the Veterinary Teaching Hospital, Kangwon National University with primary

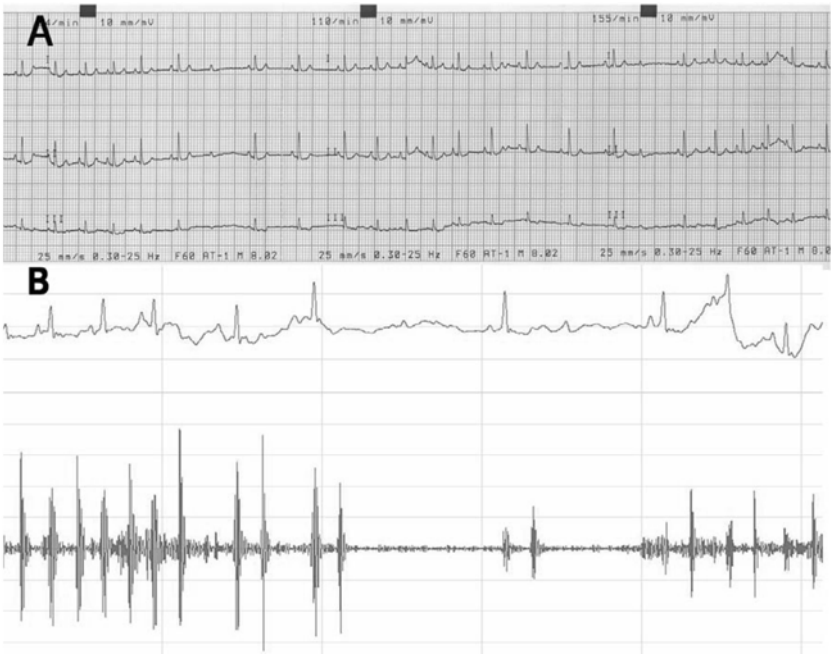

Fig. 1. The electrocardiogram (A) and phonocardiogram (B) of this case. The electrocardiogram showed a second degree atrioventricular heart block (atrial rate: 125 bpm, ventricular rate 120 bpm) with QT prolongation (QTc = 269 × 10.8 msec). The phonocardiogram showed an irregular interval and intensity of heart sound. There is also intermittent absence of heart sound.

complaints including exercise intolerance and neurological sign associated with hepatic encephalopathy. Before the presentation, the dog was received mediations to reduce the absorption and production of ammonia (i.e. metronidazol, 7.5 mg/kg PO q 8 h; lactulose, 0.5 ml/kg PO q 8 h with a protein-restricted diet).

In physical examination, the dog was anorexic and lethargic. Femoral pulsation was intermittently deficient with slow heart rate. Pulse deficit was more obvious in the phonocardiogram and electrocardiogram (ECG; Fig. 1). The 12 lead- surface ECG and digital ECG recordings revealed a second degree atrioventricular (AV) heart block with QT prolongation (269 ± 10.8 msec; Fig. 1A). A subsequent atropine response test revealed second degree Mobitz type I-AV block.

Complete blood count revealed a leukocytosis (23.78 $\times 10^3/\mu l$; reference range: 6-17 $\times 10^3/\mu l$) with neutrophilia (13.30 $\times 10^3/\mu l$; reference range: 3.0-11.8 $\times 10^3/\mu l$) and mild anemia (5.1 $\times 10^{12}/\mu l$; reference range: 5.5-7.5 $\times 10^{12}/\mu l$). Serum biochemistry revealed reduced hepatic function with an increased pre- and post-prandial serum bile acid levels (Table 1). Blood coagulation profiles were also prolonged (Table 1). Urinalysis revealed ammonium urate crystaluria and bilirubinuria.

Diagnostic imaging studies revealed a cranial gastric axis deviation indicating small size liver, abdominal fluid accumulation, decreased number of portal veins in the liver and generalized enhancement of the hepatic echogenicity (Fig. 2). The portal vein was not tapered in the hepatic parenchyma (Fig. 2). The portography clearly visualized a single straight shunted portal vein to the caudal vena cava (Fig. 3). The ultrasonography revealed the maximal diameter of the shunted vessel was 5.0 mm in diameter.

Based on diagnostic findings, the case was diagnosed as IPSS complicated with second degree atrioventricular (AV) block and QT prolongation. With the consent of owner, we decided to occlude IPSS by lodging transvenous embolization coils. Since the shunt diameter was 5 mm, we decided to initially lodge a

Table 1. Hemogram and blood chemistry of this case

	Reference range	3 day before	Day 0 (Occlusion)	1 day after	2 day after	3 day after	1 month after	2 month after
WBC ($\times 10^3/\mu l$)	6-17	19.54	26.58	26.82	24.78	23.78	17.6	16.4
Hemoglobin (g/dl)	12-18	12.4	9.5	6.17	8.1	8.6	11.1	11.4
HCT (%)	37-55	46	39.8	35.4	30.5	27.5	34.4	29
MCV (fl)	60-77	56.5	54.8	57.3	56.6	55.2	54	53
MCHC (g/dl)	33-36	27	23.9	29.9	26.6	31.3	32.3	33.7
RBC (1,012/μl)	5.5-7.5	8.14	7.26	6.17	5.38	4.99	6.37	6.36
Platelets (103/μl)	150-500	712	836	503	471	466	317	311
Total protein (g/dl)	5.5-7.5	3.9	3.7	4.6	4	4	4.7	5.3
AST (U/l)	1-50	43	56	58	52	56	48	44
Creatinine (mg/dl)	0.9-1.7	0.6	0.3	0.4	0.4	0.7	0.8	0.6
Albumin (g/dl)	2.7-3.5	1.2	1.1	1.4	1.3	1.2	1.2	2.7
ALP (U/l)	20-300	428	440	414	283	204		67
ALT (U/l)	3-100	41	54	32	38	26	40	57
BUN (mg/dl)	7-28	<5	5	5	2	3	20	20
APTT (sec)	22-40	48	39	ND	ND	ND	ND	29
PT (sec)	10-14	11	14	ND	ND	ND	ND	11
Cholesterol (mg/dl)	126-350	52	ND*	52	ND	ND	ND	51
Pre-prandial bile acid (μmol/l)	0-10	100	ND	70	ND	25	12	15
Post-prandial bile acid (μmol/l)	0-25	118	ND	95	ND	50	30	45

WBC, white blood cell; HCT, hematocrit; MCV, mean corpuscular volume; MCHC, mean corpuscular hemoglobin concentration, RBC, red blood cell; AST, aspirate transaminase; ALP, alkaline phosphatase; ALT, alanine transaminase; BUN, blood urea nitrogen; APTT, activated partial thrombin time; PT, prothrombin time.
*ND: Not done.

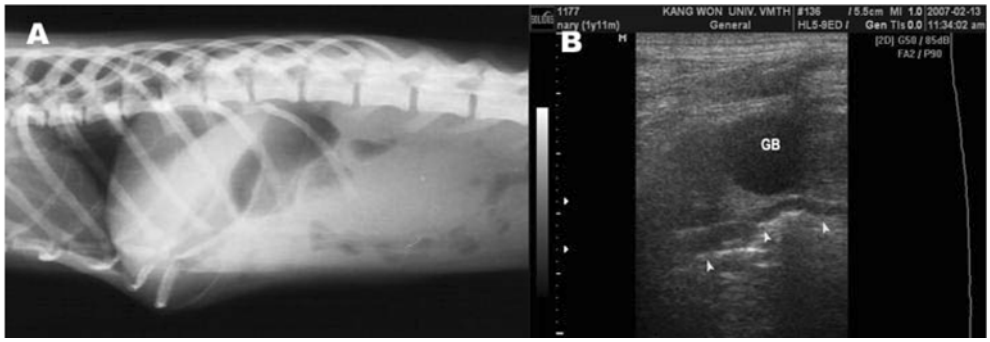

Fig. 2. Abdominal radiography (A) and ultrasonography (B) of this case. Abdominal radiography revealed a cranial gastric axis deviation indicating small size liver and abdominal fluid accumulation. Ultrasonography revealed decreased number of portal veins in the liver and generalized enhancement of the hepatic echogenicity. The portal vein (arrowheads) was not tapered in the hepatic parenchyma.

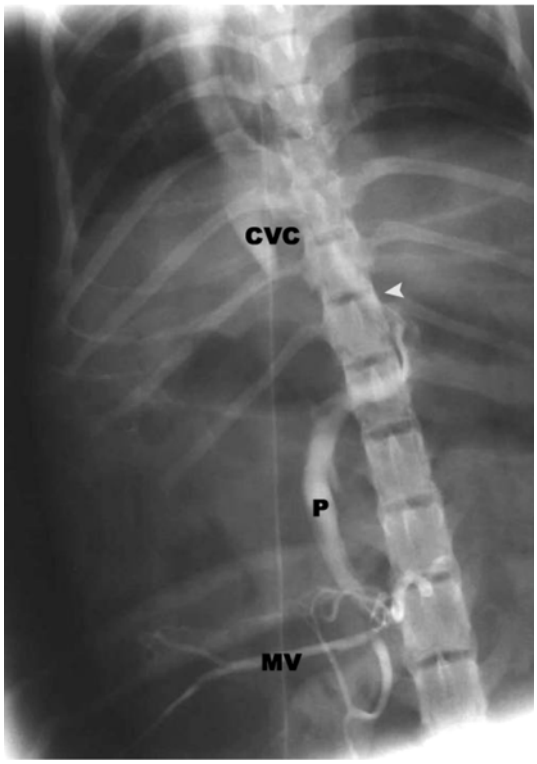

Fig. 3. The portography of this case. A contrast media was infused from the mesentery vein (MV) to visualize the portal vasculature (P). There was a single straight shunt (arrowhead) between the portal vein and caudal vena cava (CVC).

6.5 mm (4 loops) coil (Flipper detachable embolization coils; COOK, USA). We also decided to lodge a second coil, if necessary.

Since the dog was hypoalbuminemic and had coagulopathy, we transfused a fresh blood (6-10 ml/kg) with medication of preventive antibiotics (cephazolin, 15 mg/kg orally q 8 h), before the TCE. For general anesthesia, the dog were premedicated with an atropine (0.05 mg/kg, SC) and nalbuphine (0.5 mg/kg) followed by a propofol induction (5 mg/kg) and isoflurane maintenance. Heart rhythm, blood pressure, SpO_2, pCO_2 and rectal temperature were closely scrutinized using a patient monitor (VETSPEC VSM7; VetSpecs, USA).

After achieving surgical anesthesia, the venipuncture was performed at right jugular vein with an 18 G needle. A guide-wire (Fixed Core Wire Guides; Cook, USA) was inserted into the needle and located at the caudal vena cava. A 6F introducer sheath (13 cm in length, Check-Flo Performer Introducer; Cook, USA), was then placed into the jugular vein along with the guide-wire. A 5F angiocatheter (120 cm in length, Slip-Cath Beacon Tip Catheters; Cook, USA), was then inserted into the introducer sheath and located at the shunt with the guidance of fluoroscopy (Fig. 4). A 6.5 mm embolization coil (4 loops, Flipper detachable embolization coils; Cook, USA; Fig. 5A) was attached to a coil delivery system (Flipper Delivery Systems; Cook, USA; Fig. 5B) and inserted into the angiocatheter, which was pre-placed at the shunt (Fig. 4). After the coil was released at the shunt, the pre-place catheter and introducer were removed from the jugular vein (Fig. 4).

On the clinical examination at the first day after the TCE, the dog showed mild ascites (transudate). However, no other serious complications associated with sudden increase of portal venous pressure were observed. Nitroglycerine patch (0.25 mg/kg, every

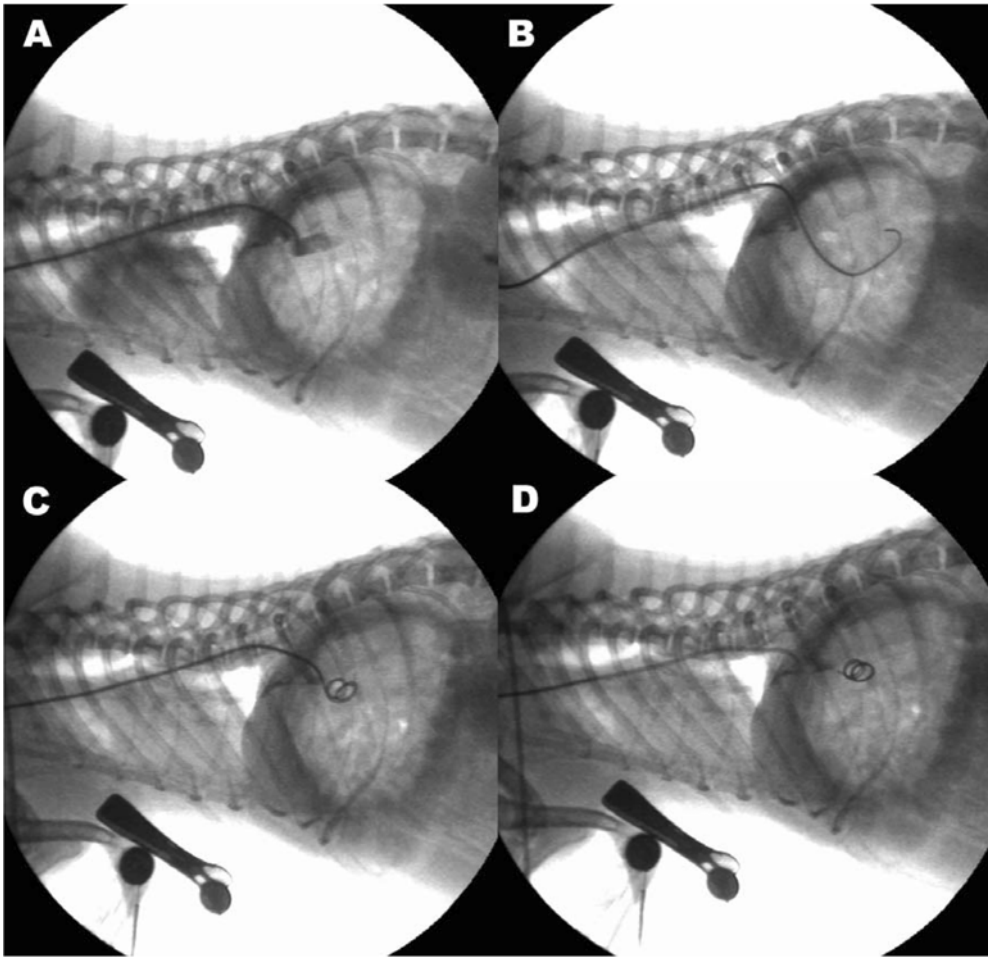

Fig. 4. Transvenous coil embolization of this case. (A) A 5F angiocatheter was inserted through jugular vein to visualize the shunted area. (B) A guide-wire was then located at the shunt with the guidance of fluoroscopy. (C) A 6.5 mm embolization coil (4 loops) was attached to a coil delivery system and then inserted into the angiocatheter. After locating at the shunt, the coil was released. (D) After the release of coil, the pre-place catheter and introducer were removed from the jugular vein.

other 12 h) was applied to the abdominal skin. From the third day of the TCE, the ascites was no longer existed. Pre- and post-prandial serum bile acid levels were reduced to 25 μmol/l and 50 μmol/l, respectively at the 1 week after the TCE. Interestingly, the dog did not show AV block (Fig. 7). The dog was released with a prescription (lactulose, metronidazole, neomycin, Hill's l/d) for a month. On the clinical examination performed a month after the TCE, the clinical condition was much improved. Pre- and post-prandial serum bile acid levels were remarkably reduced to 12 μmol/l and 30 μmol/l, respectively. In addition, the 1 h-digital ECG recording could not detect any rhythm abnormalities in this dog. We gradually removed medication and changed to normal diet (Science diet maintenance; Hill's, USA), since the dog was still hypoproteinemic. On the clinical examination performed 2 month after the TCE, pre- and post-prandial serum bile acid levels were slightly increased to 15 μmol/l and 45 μmol/l, respectively, although the serum albumin concentration returned to normal range (2.7 g/dl). The dog is currently fed with 60% prescription diet (Hill's l/d) and 40% normal maintenance diet and is re-medicated with lactulose (0.5 ml/kg PO q 12 h) and S-adenyl methionine (20 ml/kg PO q 12 h).

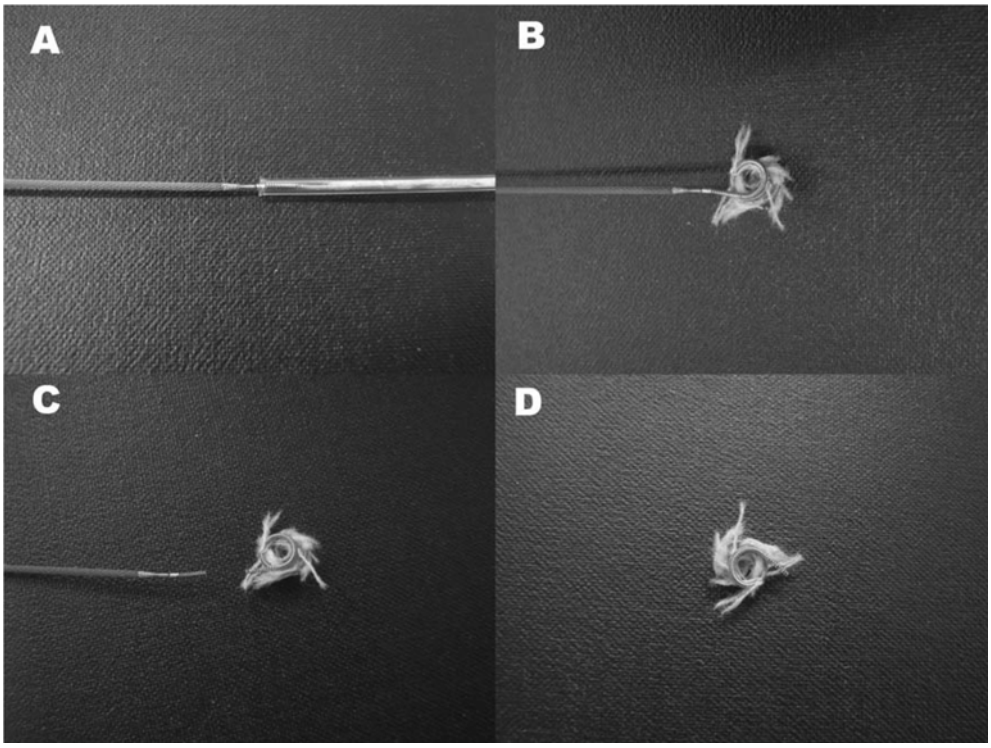

Fig. 5. The transvenous embolization coil and delivery system used in this case. (A) A coil delivery system. (B) The coil delivery system attached with an embolization coil. (C) The embolization coils after release from the delivery system. (D) The embolization coil used in this study (6.5 mm in diameter, 4 loops).

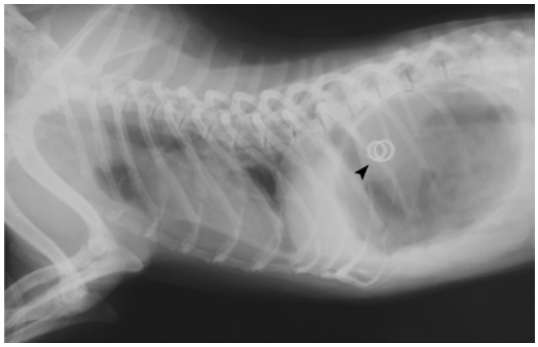

Fig. 6. The abdominal radiography taken at 1 week after the transvenous coil embolization. The coil was still located at the same position where the coil was released.

Discussion

TCE has been well described in humans since 1975 [19, 21, 25]. Because of the difficult surgical approach and high risk of complications after surgery, the surgical fixation is not generally recommended for IPSS in dogs [5, 6, 17]. However TCE is a relatively new technique in veterinary medicine and only a few case studies have been published in veterinary literature [5, 14, 22]. Despite the promising results of those studies, more studies (e.g. complications related to TCE, long-term management skills related to the staged occlusion by TCE and long term prognosis) are still required.

CC or cardiac arrhythmias related to hepatic disease has never been reported in veterinary literature, although the average corrected QT interval was significantly prolonged in dogs with hepatic failure (unpublished data). In this case of dog, two cardiac rhythm abnormalities (i.e. QT prolongation and 2nd degree AV block) were observed, probably due to hepatic failure by IPSS. Since those cardiac rhythm abnormalities were disappeared after the shunt occlusion, those abnormalities seemed to be associated with hepatic failure. In general, AV block in adult dogs is almost always abnormal and is usually produced by

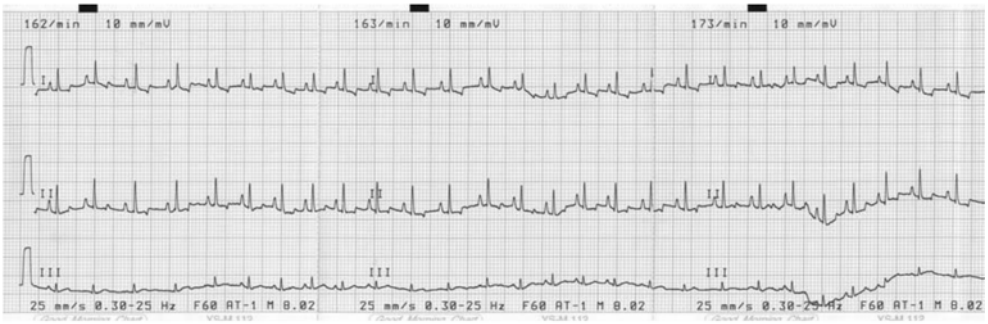

Fig. 7. Electrocardiogram taken at 1 week after the transvenous coil embolization. The heart rate and rhythm were normalized and the atrioventricular block and QT prolongation disappeared (Heart rate = 162-173 bpm; QTc = 228 ± 7.1).

conditions associated with increased vagal tone (e.g. chronic respiratory disease, digitalis intoxication) [12]. Although autonomic dysfunction and β-adrenergic down regulation on the heart have been demonstrated in humans with CC, no studies have found the abnormal overactivity of the parasympathetic system in humans with CC [18]. Instead, recent rat study found the muscarinic receptor function was blunted in the myocardium of cirrhotic rats [9]. Although a high grade AV block has been reported in cirrhotic humans having a transjugular intrahepatic portosystemic shunt to treat refractory ascites or intractable esophageal varices, no studies have found AV block associated with hepatic cirrhosis in humans and dogs, to date. We are still uncertain whether the incidence of AV block is directly associated with hepatic cirrhosis in this case. Reversible AV block in this case suggests that AV block may not be originated from the substantial conductive cellular damage but from harmful metabolites from hepatic dysfunction due to IPSS. Increased bile acid concentration in cirrhotic human patients has found to be associated with the prolongation of QT interval [2, 23]. Further study is warranted to clarify the association of bradyarrhythmia and hepatic cirrhosis in dogs.

In conclusion, the case presented is a rare case of IPSS in a small breed of dog. Although the dog was complicated with subclinical cardiac arrhythmias (i.e. second degree AV block and QT prolongation), the dog was successfully treated with a TCE.

Acknowledgments

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