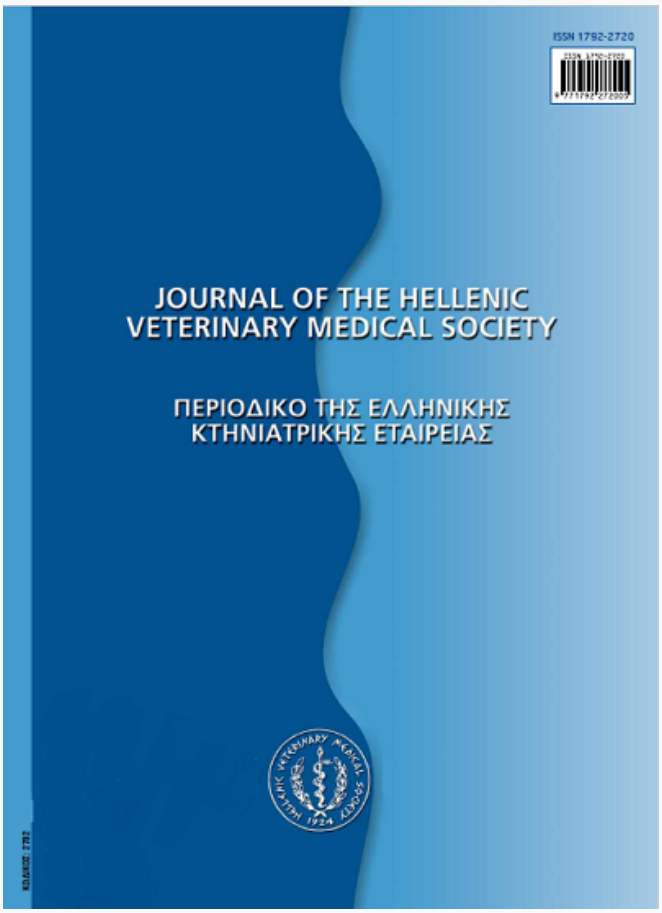
Journal of the Hellenic Veterinary Medical Society

Vol 65, No 4 (2014)



Primary portal vein hypoplasia with portal hypertension in a young dog

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doi: 10.12681/jhvms.15574

J HELLENIC VET MED SOC 2014, 65(4): 257-264
ΠΕΚΕ 2014, 65(4): 257-264

Research article
Ερευνητικό άρθρο

Primary portal vein hypoplasia with portal hypertension in a young dog

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Υποπλασία της πυλαίας φλέβας και πυλαία υπέρταση σε νεαρό σκύλο

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ABSTRACT. A 5-month old Caucasian dog was presented with a 20-day history of abdominal distention along with inappetance, depression and vomiting of 24-hour duration. Physical examination findings included depression, ascites, mild inspiratory dyspnea and dehydration. Clinicopathological evaluation revealed hyperammonemia, hypoalbuminemia, hyperbilirubinemia, hypoglycemia and hyponatremia. Microhepatia and free abdominal fluid was detected with abdominal ultrasonography. During exploratory laparotomy, multiple acquired portosystemic collateral vessels were found, indicative of portal hypertension, along with a small liver of normal color and texture. Liver histopathology included features consistent with liver hypoperfusion. These findings supported the diagnosis of primary portal vein hypoplasia with portal hypertension. The animal recovered uneventfully postoperatively and was discharged with diuretics, hepatoprotectants and a low-protein diet and remains healthy two years after diagnosis. This case underscores that a favorable prognosis may be anticipated in cases of primary portal vein hypoplasia with portal hypertension, thus, justifying the long-term conservative management instead of considering euthanasia.

***Keywords*:** ascites, dog, portal hypertension, portal vein hypoplasia.

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Date of initial submission: 23 September 2013
Date of acceptance: 22 December 2013

Ημερομηνία αρχικής υποβολής: 23 Σεπτεμβρίου 2013
Ημερομηνία αποδοχής: 22 Δεκεμβρίου 2013

ΠΕΡΙΛΗΨΗ. Σκύλος φυλής Καυκάσου, ηλικίας 5 μηνών, προσκομίστηκε με ιστορικό διόγκωσης της κοιλίας διάρκειας 20 ημερών και ανορεξίας, κατάπτωσης και εμέτων κατά το τελευταίο 24ωρο. Στην κλινική εξέταση παρατηρήθηκαν κατάπτωση, ασκίτης, ήπια εισπνευστική δύσπνοια και αφυδάτωση. Κατά την εργαστηριακή διερεύνηση διαπιστώθηκαν υπεραμμωνιαιμία, υπολευκωματιναιμία, υπερχολερυθριναιμία, υπογλυκαιμία και υπονατριαιμία. Τα ευρήματα της υπερηχοτομογραφικής διερεύνησης της κοιλίας ήταν μικροηπατία και ελεύθερο περιτοναϊκό υγρό. Στην ερευνητική λαπαροτομή διαπιστώθηκαν πολλαπλές επίκτητες εξωηπατικές αναστομώσεις της πυλαίας φλέβας, συμβατές με πυλαία υπέρταση, ενώ το ήπαρ ήταν μικρό σε μέγεθος και φυσιολογικής υφής και χρώματος. Η ιστοπαθολογική εξέταση του ήπατος ήταν συμβατή με υποαιμάτωση του οργάνου. Με βάση τα παραπάνω αποτελέσματα τέθηκε η διάγνωση της πρωτογενούς υποπλασίας της πυλαίας φλέβας με πυλαία υπέρταση. Η αγωγή που ακολουθήθηκε συμπεριλάμβανε διουρητικά, ηπατοπροστατευτικά και διατροφή χαμηλή σε πρωτεΐνες. Ο σκύλος παραμένει υγιής δύο χρόνια μετά τη διάγνωση. Το περιστατικό αυτό, αναδεικνύει την καλή μακροχρόνια πρόγνωση που έχουν τα περιστατικά με πρωτογενή υποπλασία της πυλαίας φλέβας και πυλαία υπέρταση στο σκύλο, γεγονός που δικαιολογεί την συντηρητική θεραπευτική αντιμετώπιση και την αποθάρρυνση της διενέργειας ευθανασίας.

Λέξεις ευρετηρίασης: ασκίτης, πυλαία υπέρταση, σκύλος, υποπλασία πυλαίας φλέβας.

INTRODUCTION

Congenital hepatic vascular anomalies described in the dog include primary portal vein hypoplasia (PPVH), hepatic arteriovenous malformations, portal vein atresia and congenital portosystemic shunts (CPSS) (Berent and Tobias, 2009). Based on the latest nomeclature proposed by the WSAVA Study Liver Group, PPVH is the preferred term to describe a number of conditions with clinical, clinicopathological, and histopathological similarities such as non-cirrhotic portal hypertension, hepatoportal fibrosis, idiopathic hepatic fibrosis, veno-occlusive disease, idiopathic liver disease, non-fibrosing liver disease and hepatic microvascular dysplasia (Cullen, 2009). In PPVH the intrahepatic and occasionally the extrahepatic portal vein are abnormally small or absent, resulting in hepatic hypoperfusion and microhepatia without evidence of cirrhosis. The subsequent resistance in hepatic blood flow can lead, although not invariably, to the development of portal hypertension and peritoneal effusion (Berent and Weisse, 2010). The purpose of our study is to describe the clinical presentation, clinicopathological abnormalities, diagnosis and treatment of a dog with PPVH and portal hypertension.

CASE DESCRIPTION

A 5-month-old, intact female, Caucasian dog was presented with a 20-day history of abdominal enlargement. During the last 24 hours the animal had displayed inappetence, depression and vomiting. Physical examination revealed mild inspiratory dyspnea, dehydration and abdominal distention consistent with peritoneal effusion (Fig. 1). Complete blood count was unremarkable, while biochemical abnormalities included hyperammonemia, hypoalbuminemia, hyperbilirubinemia, hyponatremia, and mild hypoglycemia (Table 1). Thoracic radiography was normal, while abdominal ultrasonography revealed large amounts of free abdominal fluid and microhepatia. No evidence of intrahepatic or extrahepatic vascular anomalies was detected. Peritoneal fluid obtained with a butterfly-assisted abdominocentesis was analyzed and classified as a pure transudate based on the low total protein concentration (0.5 g dL^{-1}) and nucleated cell count (0 cells μL^{-1}) on an automated analyzer. Cytologic examination of a buffy coat blood smear for *Babesia* sp. organisms and serology for *Dirofilaria immitis* antigens (dot-ELISA Heartworm Snap test®, IDEXX) were negative.

Since a hepatic vascular anomaly was the pri-

Table 1. Biochemical findings on admission in a dog with primary portal vein hypoplasia and portal hypertension

Serum biochemistry	Value	Reference intervals
Total Protein	6.4	6.0-7.8 g dL^{-1}
Albumin	2	2.6-4.0 mg dL^{-1}
Creatinine	0.3	0.4-1.4 mg dL^{-1}
BUN	15.7	9.2-22.9 mg dL^{-1}
Glucose	60	76-128 mg dL^{-1}
Total billirubin	0.6	0.1-0.5 mg dL^{-1}
Alkaline phosphatase	186	69-333 U L^{-1}
Alanino amino transferase	64	17-78 U L^{-1}
Cholosterol	95	111-312 mg dL^{-1}
Triglyceride	32	30-133 mg dL^{-1}
Ammonia	240	16-75 μg dL^{-1}
Phosphorus	6.4	1.9-5.0 mg dL^{-1}
Calcium	10.2	9.3-12.1
Potassium	4.8	3.8-5.0 mEq dL^{-1}
Sodium	137	141-152 mEq dL^{-1}

Figure 1. Abdominal distention compatible with ascites in a young Caucasian dog with primary portal vein hypoplasia and portal hypertension.

mary differential, exploratory laparotomy was recommended in order to visualize the hepatic vasculature, ligate any shunting vessel if possible and obtain liver biopsies. Pending the owner's decision the dog, was hospitalized and given intravenous crystalloids (NS 0.9%) along with lactulose (3.35 g kg^{-1} bw, every 12 hours, per os) (Duphalac, Solvay), ranitidine (2.5 mg kg^{-1} bw, every 12 hours, intravenously) (Zantac, Glaxo Smith Kline), metoclopramide (0.5 mg kg^{-1} bw, every 8 hours, intravenously) (Primperan, Sanofi-Aventis), sucralfate (1 g 30 kg^{-1} bw, every 8 hours, per os) (Peptonorm, Unifarma) and furosemide (2 mg kg^{-1} bw, every 12 hours, intravenously) (Lasix, Sanofi-Aventis). Abdominocentesis was performed once a day for the first two days to relieve dyspnea, with a total volume of 3 liters of abdominal fluid being gradually removed. On the 3rd day, spironolactone (1 mg kg^{-1} bw, every 12 hours, intravenously) (Aldactone, Pfizer) was added to further mobilize the ascitic fluid. Additionally, a therapeutic trial with imidocarb dipropionate (3 mg kg^{-1} bw, subcutaneously) was commenced (Imizol, Schering-Plough). The dog's appetite and demeanor returned to normal on the 9th day of hospitalization.

Exploratory laparotomy was performed on the 10th day of hospitalization after administering one unit of fresh cross-matched and blood-typed whole blood. A small liver with normal texture and multiple tortuous acquired portosystemic collaterals (APSC) located near the kidneys were seen (Fig. 2). No gross lesions of neoplastic or inflammatory nature were identified and the portal vein appeared patent and of presumed normal size. A liver biopsy was obtained

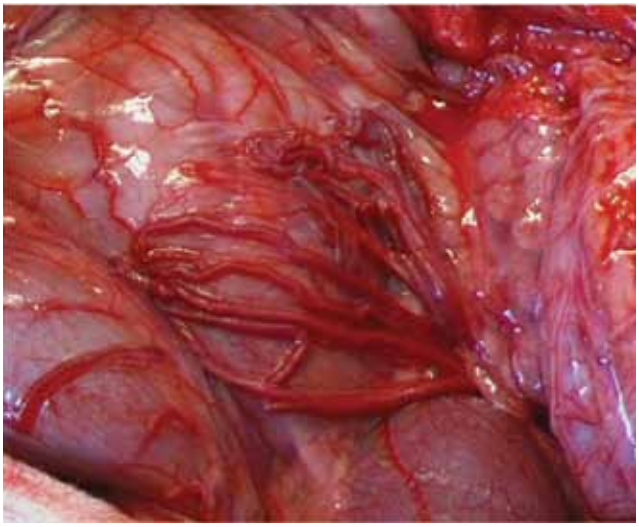

Figure 2. Multiple extrahepatic acquired portosystemic collaterals (arrows) causal to the left kidney (asterisk).

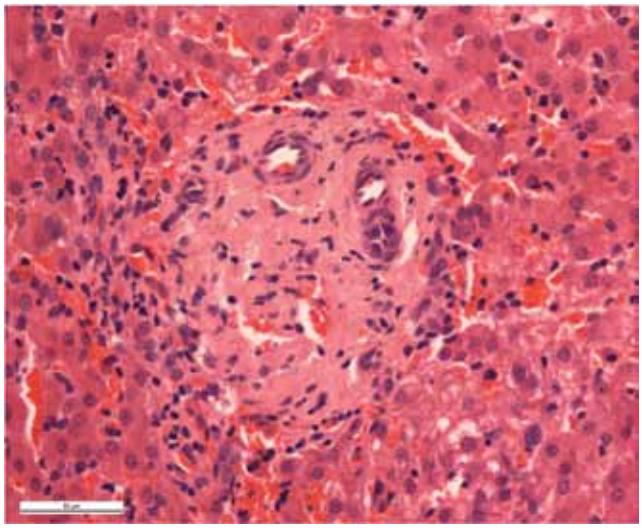

Figure 3. Portal region with multiple arteriolar profiles and increased portal fibrous connective tissue. The portal vein is not apparent. There is minimal to mild portal and periportal population of lymphocytes and fewer neutrophils (Hematoxylin-Eosin, Bar: 50μm)

and submitted for routine histopathology. The histopathological findings included diminished portal vein profiles, portal arteriolar and bile duct proliferation along with portal fibrosis, consistent with a hepatic circulatory disorder associated with portal vein hypoperfusion (Fig. 3). Additional features included mild hepatitis with a mixed inflammatory cell infiltrate; multifocal capsular and patchy subcapsular mild perisinusoidal fibrosis with vascular proliferation and sinusoidal dilation and congestion. However these latter findings were not considered to be supportive of an underlying primary hepatic disease with advanced fibrosis as the cause of portal hupertension. Based on the clinical, clinicopathological and histopathological findings, a diagnosis of PPVH with portal hypertension was reached.

Following surgery the dog was discharged on lactulose (3.35 g kg^{-1} bw, every 12 hours, per os) (Duphalac, Solvay), spironolactone (1 mg kg^{-1} bw, every 12 hours, per os) (Aldactone, Pfizer), furosemide (1 mg kg^{-1} bw, every 12 hours, per os) (Lasix, Sanofi-Aventis), S-adenyl-methionine (20 mg kg^{-1} bw, every 24 hours, per os) (Denosyl, Nutramax), ursodeoxicholic acid (15 mg kg^{-1} bw, every 24 hours, per os) (Ursofalk, Galenika) and famotidine (0.5 mg kg^{-1} bw, every 24 hours, per os) (Peptan, Vianex), along with a protein and sodium restricted diet. One week later the dog was bright and alert with a normal appetite. A small amount of abdominal fluid was detected on physical examination. Upon reexamination, seven months after surgery, no clinical abnormalities were noticed other than a degree of stunted growth (Fig. 4), while complete blood count and blood biochemisrty where within normal limits with the exception of a mildly elevated ammonia concentration (104 μg dL^{-1}, reference intervals, 16-75 μg dL^{-1}). The owners were satisfied with their dog's quality of life.

DISCUSSION

PPVH with portal hypertension has been described in a wide variety of breeds, with Dobermans being overrepresented. Age of presentation ranges from 3 months to 8 years, with the majority of dogs being less than 4 year-old at the time of diagnosis, similar to the present case (de Marco et al., 1998; Bunch et al., 2001). Abdominal distention, intermittent gastrointestinal signs, polydipsia, small stature and central nervous system signs related to

Figure 4. The same dog as in figure 1, seven months after diagnosis displaying retarded growth.

hepatic encephalopathy are common historical and clinical manifestations in dogs with PPVH and portal hypertension (van den Ingh et al., 1995; de Marco et al., 1998; Bunch et al., 2001). In the absence of overt neurologic signs (eg cortical blindness, seizures, coma) the diagnosis of hepatic encephalopathy can be elusive. The presence of depression in conjunction with the persistent hyperammonemia is an early indicator of hepatic encephalopathy (Adam et al., 2012). The majority of the typical manifestations of the disease were witnessed in the present case.

Clinicopathological abnormalities in dogs with PPVH and portal hypertension are the result of hepatic hypoperfusion, increased portal pressure and failure to metabolize ammonia (Buob et al., 2011). Typically, hypoalbuminemia, moderate to severe increases in liver enzyme activities, hyperbilirubinemia, hyponatremia, increased fasting serum ammonia and total serum bile acid concentrations are seen. Less commonly, low BUN concentration and hypoglycemia are documented (van den Ingh et al., 1995; de Marco et al., 1998; Bunch et al., 2001; James et al., 2008). Several of the expected biochemical alterations were seen in this case. These findings, however, are nonspecific and may be seen in all hepatic vascular anomalies, thus, they cannot be used to differentiate them (Berent and Tobias, 2009).

Ascitic fluid in portal hypertension is classified either as a pure or a modified transudate. In the absence of severe hypoalbuminemia, protein concentration can be helpful in determining the anatomic location of portal hypertension (Johnson, 1987). Prehepatic and presinusoidal causes of increased portal pressures, like PPVH, invariably lead to the development of a low-protein fluid accumulation (pure transudate), as was the case in the present report. In contrast, ascitic fluid in postsinusoidal and posthepatic diseases has high protein concentration (modified transudate) (Buob et al., 2011). The protein concentration of ascitic fluid associated with sinusoidal causes of portal hypertension (e.g., liver cirrhosis) is unpredictable, because, even though a high protein ascitic fluid is anticipated, hypoalbuminemia and sinusoid capilarization may result in a pure transudate formation (Johnson, 1987).

The suspicion of a liver vascular anomaly in the current case was based on the increased fasting plasma ammonia concentration. The differential diagnosis of increased fasting plasma ammonia concentration further include loss of >70% of functional liver parenchyma, urea cycle enzyme deficiencies (Szatmary et al., 2004) and physiologic hyperammoniema (Irish Wolfhounds) (Meyer et al., 1996). The overall sensitivity and specificity of fasting plasma ammonia for the detection of hepatic vascular anomalies range from 68%-100% and 86-89%, respectively. (Meyer, 1986; Walker et al., 2001; Gerritzen-Bruning et al., 2006; Ruland et al., 2010). Even though, measurement of pre- and postprandial bile acids seems to be a more sensitive indicator of liver vascular anomalies, there is no apparent benefit in performing both when one value is abnormal (Meyer et al., 1986; Winkler et al., 2003). In the current case, since there was marked hyperammonemia measurement of bile acids was not deemed necessary.

Abdominal ultrasonography findings in animals

with PPVH include alterations in liver size and echogenicity, abdominal effusion, APSC, renomegaly, splenomegaly, enlarged portal vein and caudal vena cava (Bunch et al., 2001; de Marco et al., 1996). In our case, besides abdominal effusion and microhepatia, ultrasonography was unremarkable. Regarding the detection of CPSS and APCS the sensitivity and specificity of abdominal ultrasonography ranges from 80.5% to 98% and 66.7% to 98% respectively but it is considered a very operator dependent examination (Lamb, 1996). Even though it is a very important tool, not only in detecting liver vascular anomalies but also for investigating other causes of abdominal distention in the dog, it should not be used alone to rule out the presence of CPSS and APCS (Winkler et al., 2003).

Gross pathological findings during exploratory laparotomy include small liver with various coloration and texture, portosystemic collateral vessels and free abdominal fluid. The extrahepatic portion of the portal vein is apparently normal in the majority of cases, similar to the current case, and no correlation exists between the presence or not of gross hypoplasia and the histological pattern within the portal area (van den Ingh et al., 1982; Rutgers et al., 1990; Hunt et al., 1993; van den Ingh et al., 1995; de Marco et al., 1998). APSC develop secondary to chronic portal hypertension of pre- or intrahepatic, but not of posthepatic origin, and they are usually detected in the omentum just caudal to the left kidney as was documented in the present case (Fig. 3) (Rothuizen, 2009).

The histopathological features observed in PPVH reflect stereotypical changes that arise as a consequence of hepatic hypoperfusion and may include loss or diminution of portal vein profiles, increased arterioral profiles in the portal tract and hepatocellular atrophy with varying degrees of fibrosis within and between the portal tracts (Buob et al., 2011). The histopathological pattern in PPVH overlaps considerably with that of CPSS, hepatic arteriovenous malformations and portal vein thrombosis (Bunch et al., 2001). The importance of acquiring hepatic biopsies in such cases relies in documenting a pattern of hepatic hypoperfusion and most importantly, excluding severe diffuse hepatobilliary disease as the cause of portal hypertension (van den Ingh et al., 1995).

Diagnosis of PPVH in the current case was based on the clinical manifestations suggestive of portal hypertension along with histopathological findings consistent with hepatic hypoperfusion. Even though portal pressures were not directly measured, the diagnosis of portal hypertension can be reliably based on the presence of ascites (in the absence of severe hypoalbuminemia) and numerous APSC (van den Ingh et al., 1995; Rohuizen, 2009). Other differentials included portal vein obstruction and hepatic artiriovenous malformations. Portal vein obstruction was excluded based on the absence of visible thrombi, local neoplastic and inflammatory conditions during laparotomy and lack of predisposing factors (abdominal surgery, steroid administration) or clinicopathological evidence of concurrent disease that can lead to a hypercoagulable state (pancreatits, peritonitis, protein loosing nephropathy and enteropathy) (Winkler and Bruce, 1993). Hepatic arteriovenous malformations were excluded on the basis of absent compatible ultrasonographicc and macroscopic findings during laparotomy (Chanoit et al., 2007). Although advanced imaging was not undertaken, CPSS was excluded since they are not accompanied by portal hypertension (Winkler et al., 2003).

Therapeutic recommendations in PPVH aim to alleviate symptoms and prevent lethal complications of sustained chronic portal hypertension. To this end, treatment in the present case targeted to mobilize the ascitic fluid, reduce ammonia concentration, ameliorate gastrointestinal signs, and prevent further liver damage. The use of a protein- and sodium restricted diet is sufficient to control ascites in most of the cases (Bunch et al., 2001). When diuretics are

needed, the aldosterone antagonist spironolactone is preferred. Because fluid mobilization is slow with spironolactone, low dose furosemide can be added to enhance initial natriuresis (Buob et al., 2011). Abdominocentesis is recommended when respiratory compromise develops due to abdominal distention. Fluid removal must be gradual as in the present case, since circulatory collapse and renal function deterioration may occur (Rothuizen, 2009). The most common and potentially lethal consequence of chronic portal hypertension is the development of gastroduodenal ulcers (Buob et al., 2009). Thus, the continuous use of antiulcer medication, such as histamine type-2 receptor antagonists, is essential for long term management (Bunch et al., 2001).

Antifibrotic therapy (colchicine, glucocorticoids) has been suggested by some authors since there is evidence for a gradually increasing fibrosis in animals subject to serial liver biopsies (Rutgers et al., 1990; 1993). However, there are currently no evidence-based suggestions to support its efficacy in PPVH. Nonetheless, colchicine may be considered when significant fibrosis exists in liver histopathology at the time of diagnosis (Bunch et al., 2001).

The prognosis of PPVH with portal hypertension depends upon the severity of clinical signs and the response to initial treatment but it is generally considered favourable (Buob et al., 2011). In a retrospective study of PPVH and portal hypertension for 19 cases where long term follow up was available, 13 remained asymptomatic for a period ranging from 5 months to 9 years (median 2.9 years) after diagnosis. In the same study a number of dogs were euthanized before final diagnosis was reached because of a presumed poor prognosis (Bunch et al., 2001). In the present case clinical signs related to PPVH were adequately controled following medical management for 2 years.

CONCLUDING REMARKS

PPVH with portal hypertension, although an uncommon vascular anomaly in the dog, must be considered in young dogs presenting with ascites. Symptomatic treatment is adequate for sufficient control of the symptoms in a long term basis. Due to the many similarities of PPVH with other life threatening liver diseases, liver histopathology is essential before establishing a prognosis. Owners, therefore, should be discouraged to choose euthanasia after reaching a diagnosis since PPVH carries a favorable prognosis (Bunch et al., 2001).

CONFLICT OF INTEREST STATEMENT

None of the authors of this article has a financial or personal relationship with other people or organizations that could inappropriately influence or bias the content of this paper.

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