Clinical and clinicopathologic abnormalities in young dogs with acquired and congenital portosystemic shunts: 93 cases (2003–2008)

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**Objective**—To determine whether clinical and clinicopathologic data could assist differentiation of congenital portosystemic shunts (CPSSs) from acquired portosystemic shunts (APSSs) in young dogs.

**Design**—Retrospective case series.

**Animals**—Dogs < 30 months of age with CPSSs (n = 62) or APSSs (31).

**Procedures**—Medical records from 3 referral centers identified 31 dogs with APSSs and 62 dogs with CPSSs diagnosed from July 2003 to July 2008. Signalment, clinical signs, physical examination, and clinicopathological data were recorded, and statistical analyses were performed to determine differences between groups.

**Results**—Univariable analysis showed APSS patients were older, heavier, and in poorer body condition, compared with CPSS patients. In CPSS patients, diarrhea was less prevalent, and neurologic signs were more prevalent. Ascites was more prevalent in APSS (Fishers exact test; OR, 50.2; 95% confidence interval [CI], 6.2 to 409.7), with no significant difference in albumin concentration between groups. The logistic regression model used to assess clinicopathological parameters showed lower Hct (OR, 1.42 X 10^-6; 95% CI, 1.42 X 10^-6 to 4.0 X 10^-5), higher mean corpuscular volume (OR, 1.27; 95% CI, 1.08 to 1.50), and higher alanine aminotransferase concentrations (OR, 1.005; 95% CI, 1.001 to 1.009) were more likely in APSS patients.

**Conclusions and Clinical Relevance**—Several clinicopathologic differences between dogs with congenital and acquired shunts were identified; however, assessed alone, these would be unlikely to enable differentiation between the 2 conditions. Awareness of the rarity of ascites in CPSS cases should prompt recognition of a likely diagnosis of APSS, allowing the veterinarian to target further diagnostics and counsel the owner appropriately. (J Am Vet Med Assoc 2012;241:760–765)

Portosystemic shunting in dogs occurs from either congenital portosystemic communication or acquired shunting vessels that develop in response to sustained prehepatic or intrahepatic portal hypertension.1 Portosystemic shunting results in hyperammonemia and elevated circulating bile acids concentrations and may lead to a wide variety of clinical signs. Acquired PSSs in dogs constitute up to 20% of all PSSs in dogs2 and are enlargements of rudimentary embryonic connections between the portal and caval circulations that have developed in response to sustained prehepatic or intrahepatic portal hypertension.3 The most commonly reported etiologies in dogs include portal vein hypoplasia, acquired hepatopathies, and hepatic arteriovenous malformations.4-6 Dogs with CPSSs and concurrent APSS have previously been reported.7,8

In most dogs, congenital CPSSs are diagnosed at < 1 year of age.9-11 Comparatively few cases of dogs with APSSs are reported, and a number of etiologies exist, including acquired conditions considered to be more common in older patients.5,8,12-15 Often, therefore, younger dogs may be assumed to have congenital rather than acquired PSSs, but in previous case series,8 a considerable number of dogs with APSS were initially examined as young animals. Differentiation of APSSs and CPSSs is important because treatment options and prognoses differ.

**Abbreviations**

| ALT | Alanine aminotransferase |
| APSS | Acquired portosystemic shunt |
| CI | Confidence interval |
| CPSS | Congenital portosystemic shunt |
| PSS | Portosystemic shunt |
Diagnostic imaging techniques used for the identification and classification of PSSs include ultrasonography, contrast CT and MRI, scintigraphy, and portovenography. Ultrasonography is considered by many to be the modality of choice for confirmation of PSSs; it is noninvasive and offers reasonable sensitivity, specificity, and accuracy. Diagnostic performance is optimized by the use of spectral Doppler and color-flow mapping techniques and sufficient operator experience. Adjunctive ultrasonographic diagnostic techniques include transpleenic injection of agitated saline and heparinized blood, which may aid identification and characterization of portosystemic shunting conditions. In first-opinion practice, operator inexperience and the use of less sophisticated equipment hinder the identification and classification of PSSs. Knowledge of other clinical features of PSSs (eg, bilateral renomegaly, presence of microhepatomegaly, and urate urolithiasis) can be used to increase suspicion for the diagnosis; however, specific observations that may assist differentiation of CPSSs from APSSs are unknown. Metabolic profiling to detect changes in populations of low-molecular weight metabolites has been shown to enable differentiation of dogs with CPSSs from those with acquired hepatopathies; however, expense and availability render this a research tool at this time. It would be beneficial to be able to use clinical information readily available to veterinarians in first-opinion practice to differentiate such cases. Therefore, the objective of the study reported here was to establish whether signalment, physical examination findings, clinical signs, and clinico-pathologic findings could assist veterinarians without access to advanced diagnostic imaging modalities in differentiating CPSSs from APSSs in young dogs with suspected PSSs.

Materials and Methods

Data were retrieved from the case records of 3 United Kingdom small animal referral centers from a 5-year period (July 2003 to July 2008) via computer search facilities in each center to identify dogs < 30 months of age with a diagnosis of PSS. Inclusion criteria for patients included an age at diagnosis of < 30 months, complete signalment and data regarding owner-reported clinical signs, and physical examination findings. Diagnosis of APSS and CPSS was made by use of 1 or more of the following methods as previously described: abdominal ultrasonography, portovenography, or identification of shunting vessels during celiotomy or postmortem examination. Procedural reports from ultrasonographic examinations, portovenograms, celiotomies, and postmortem examinations were reviewed prior to case inclusion to ensure the shunting vessels had been directly observed during the procedure reported. The etiologies associated with APSS were recorded in cases where the authors considered that the investigations performed allowed their determination.

For each APSS case, 2 CPSS comparison cases were selected from the same referral center during the same period of study that used the same age criterion. For each referral center, a list was generated of all patients with a diagnosis of CPSS during the study, and these patients were randomly selected by use of an Internet-based random number generator.

A complete medical record was required for inclusion in the study, which included patient signalment, physical examination findings including body condition score, and owner-reported clinical signs. The results of hematology, serum biochemistry and fasting, and postprandial bile acids test results were recorded when present but were not prerequisites for study inclusion. Hematology parameters recorded were RBC count, Hct, mean corpuscular volume, mean corpuscular hemoglobin concentration, and platelet count. Biochemistry parameters recorded were urea, creatinine, cholesterol, total bilirubin, glucose, total protein, and albumin concentrations and alkaline phosphatase and ALT activities. Urinalysis results were not included because of limited availability, varying recorded data points, and nonstandardized urine collection techniques.

Statistical analysis was performed taking significance as probability (P value) ≤ 0.05, for 2-sided analyses. Mann-Whitney tests were used to assess signalment data (age, sex, and body weight). χ² and Fisher exact analyses were used to examine the presence or absence of owner-reported clinical signs, physical examination findings, and the prevalence of small- and large-breed dogs within APSS and CPSS groups. Small- and large-breed dogs were defined as those reported to be < 20 kg and ≥ 20 kg, respectively, on the online breed standard database of the Kennel Club of the United Kingdom. A Fisher exact analysis was also used to compare the use of portovenography at each referral center. Descriptive statistics were applied to bile acids concentrations following assessment of normality with an Anderson-Darling test. Multivariable backwards stepwise logistic regression was performed to investigate differences between hematologic and biochemical variables. The 3 centers were included as covariables within the model. The hematologic parameters used in the multivariable backwards stepwise logistic regression were Hct, mean corpuscular volume, and mean corpuscular hemoglobin concentration. The biochemical parameters used in the logistic regression were urea, cholesterol, total protein, and albumin concentrations, alkaline phosphatase, ALT activities, and fasting and postprandial bile acids concentrations.

Results

Thirty-one young dogs < 30 months old with APSS fitted the inclusion criteria: 16 from the University of Liverpool Small Animal Teaching Hospital, 10 from Davies Veterinary Specialists, and 5 from University of Cambridge Veterinary School. During the study period, the APSS patients represented 13%, 13%, and 14% (mean, 13%) of all dogs < 30 months of age diagnosed with PSSs seen at each center. No patients with concurrent APSS and CPSS were identified.

Of the 62 CPSS patients selected for comparison, 36 were extrahepatic and 26 were intrahepatic. For dogs with APSS, diagnostic tests included ultrasonography (30/31), portovenography (13/31), and postmortem examination (1/31), whereas diagnostic investigations used in CPSS cases were ultrasonography (32/62) and portovenography (23/62). All dogs had at least 1 diagnostic procedure performed, but the attending clinician made the decisions on which tests to perform.
in each respective patient. Portovenography was performed significantly (P = 0.008) more frequently at 1 center than the other 2 centers.

Radiographs were performed in 7 APSS patients without palpable ascites. In 2 of 7 cases, poor body condition impaired radiographic contrast such that liver and kidney size could not be determined. In the remaining 5 dogs, microhepatica was present in 3 and bilateral renomegaly was present in 2 dogs. Both abnormalities were present in 1 of 5 dogs, and 1 patient had neither. One of the patients with bilateral renomegaly had a diagnosis of an acquired hepatopathy; in the remaining patients with microhepatica or bilateral renomegaly, portal vein hypoplasia was subsequently diagnosed following further investigations.

Following review of the APSS cases, we considered that the etiologies underlying the APSS had been determined in 24 of 31 dogs. Twenty-three of these patients had had hepatic biopsies as part of the diagnostic work-up. Thirteen of 24 were considered to have portal vein hypoplasia, 10 had a diagnosis of an acquired hepatopathy, and 1 patient had a portal vein thrombus; there were no cases of hepatic arteriovenous malformation. Dogs with APSS (median, 12 months; interquartile range, 9 to 18 months) were older than dogs with CPSS in this selected population of dogs < 30 months of age (median, 7 months; interquartile range, 4 to 12 months; P < 0.001). The breeds represented in the APSS group included small- and large-breed dogs: Cavalier King Charles Spaniel (n = 4), Yorkshire Terrier (2), German Shepherd Dog (2), Labrador Retriever (2), Rottweiler (2), and single patients from a number of other breeds. The breeds represented in the extrahepatic CPSS group included Jack Russell Terrier (n = 6), Bichon Frise (3), Yorkshire Terrier (3), and West Highland White Terrier (2). Breeds represented in the intrahepatic CPSS group included Labrador Retriever (n = 5) and Great Dane (2), with single cases of other breeds within each group. There was no significant (P = 0.1) difference in the distribution of large dogs and small dogs between the APSS and CPSS groups when Kennel Club breed standards were used to define size. Dogs with APSS (median body weight, 18.6 kg; interquartile range, 8.3 to 24.8 kg) had a higher body weight than dogs with CPSS (median body weight, 5.9 kg; interquartile range, 3.7 to 13.9 kg; P < 0.001) but were also more likely to have poor body condition (P = 0.01). Poor body condition was defined as < 4 of 9.31

Diarrhea was more common in dogs with APSS (29/31 APSS dogs and 20/62 CPSS dogs; P = 0.004), and owner-reported neurologic signs (including seizure activity, central blindness, behavioral changes, and obtundation) were more common in dogs with CPSS (16/31 APSS dogs and 46/62 CPSS dogs; P = 0.04). Palpable ascites was identified on physical examination and confirmed by ultrasonography or postmortem examination; it was more common in dogs with APSS (Fisher exact test; P < 0.001; OR, 50.2; 95% CI, 6.2 to 409.7), being noted in 14 of 31 and 1 of 62 dogs with APSS and CPSS, respectively. The dog with CPSS that had ascites had marked hypoalbuminemia (13 g/L), a regenerative anemia, and melena presumed to be secondary to gastrointestinal ulceration. The diagnosis of CPSS in this patient was made during ultrasonography and confirmed during celiotomy at the time of surgical attenuation of the shunt; no concurrent APSSs were detected. Abdominocenteses were performed in all ascitic patients and were consistent with transudates in all patients.

The logistic regression model used to examine hematologic and biochemical parameters identified several significant (P < 0.0001) variables that were associated with shunt group (APSSs vs CPSSs). Hematologic profiles were available for 83 of 93 dogs (31/31 with APSSs and 52/62 with CPSSs) and biochemical profiles were available for 89 of 93 dogs (31/31 with APSSs and 38/62 with CPSSs). Hematocrit was below the laboratory reference interval in 13 of 31 APSS dogs and 21 of 52 CPSS dogs, with reduced mean corpuscular volume in 7 of 31 APSS cases and 25 of 52 CPSS cases, and reduced mean corpuscular hemoglobin concentration present in 2 of 31 APSS dogs and 14 of 52 CPSS dogs. Hematocrit was lower in the APSS group (P = 0.0002; OR, 1.42 × 10⁻⁴⁻¹; 95% CI, 1.42 × 10⁻⁴⁻¹ to 0.000004), and mean corpuscular volume was lower in the CPSS group (P = 0.004; OR, 1.27; 95% CI, 1.08 to 1.50). The ALT activity was elevated above the laboratory reference interval in 24 of 31 APSS cases and 31 of 38 CPSS cases. The ALT activity was higher in dogs with APSSs (P = 0.03; OR, 1.005; 95% CI, 1.001 to 1.009). Albumin concentration was below the laboratory reference interval in 9 of 31 APSS dogs and 9 of 58 CPSS dogs. Albumin concentration was not significantly different between APSS and CPSS groups (P = 0.52; OR, 0.92; 95% CI, 0.7 to 1.2). Bile acids concentration results were available in the majority of patients and were elevated above the laboratory reference interval in all instances (fasting bile acid concentration available in 30/31 APSS dogs and 56/62 CPSS dogs; postprandial bile acid concentration available in 29/31 APSS dogs and 49/62 CPSS dogs). In the APSS group, bile acid concentration median and interquartile range values were 87 µmol/L (35 to 195 µmol/L) for fasting samples and 183 µmol/L (121 to 285 µmol/L) for postprandial samples (reference interval, 0 to 15 µmol/L). In the CPSS group, median bile acid concentrations and interquartile ranges were 68 µmol/L (35 to 126 µmol/L) in fasting samples and 138 µmol/L (108 to 321 µmol/L) in postprandial samples. Neither bile acid concentrations nor the degree of change between fasting and postprandial concentrations were significantly different between the groups (fasting bile acids concentration, P = 0.33; postprandial bile acids, P = 0.89; difference between fasting and postprandial bile acids concentrations, P = 0.09).

**Discussion**

In the present study, several clinicopathologic differences between dogs with CPSSs and APSSs were identified in an attempt to aid differentiation of these patients in the absence of advanced diagnostic imaging. However, assessed alone, these differences would be unlikely to enable distinction between the 2 conditions. Nonetheless, ascites was a strong predictor of a diagnosis of APSSs; therefore, any young dog with elevated bile acid concentrations and ascites should lead to a higher suspicion of APSS than CPSS.

In our clinical experience, young dogs with suspicion of portosystemic shunting are often assumed to
have CPSS, whereas greater consideration of APSS is given in older patients. The aim of the study in determining the prevalence of APSSs in young dogs and directly comparing disease features between young dogs with APSSs and CPSSs was to assist differentiation in first-opinion practice where access to advanced diagnostic imaging may be limited, and to promote consideration of a diagnosis of APSS in young dogs as well as in older patients.

Young dogs with CPSSs were compared with young dogs with APSSs. Age and breed matching were not performed as signalment data between the populations was disparate on initial examination, and thus it was suspected that the data may prove useful when attempting to identify differentiating factors for APSSs and CPSSs. The CPSS group included dogs with both intrahepatic and extrahepatic PSSs. Although differences in signalment and clinical features of extrahepatic and intrahepatic CPSSs are known, the aim of the CPSS comparison group was to be representative of young dogs with PSSs seen in first-opinion practice. The range of both small- and large-breed dogs within the APSS group would make both extrahepatic and intrahepatic CPSSs key differential diagnoses for patients within this group. The proportions of extrahepatic and intrahepatic CPSSs within the selected CPSS comparison group were not different from the total CPSS population seen at the University of Liverpool Small Animal Teaching Hospital (data not shown).

The objective of the present study was to compare young dogs with APSSs and CPSSs; however, even in this preselected population, there was a significant difference between the groups with the APSS group being older than CPSS group. The youngest case of APSS was 2 months of age, and 40 of 62 (65%) of the CPSS dogs of the present study were older than this. A 2-month-old dog with APSS has been reported, suggesting that very young age should not be the sole criterion used to exclude a diagnosis of APSS. The population selection in the present study (≤30 months of age) precludes broader comment on the comparative ages of patients with APSSs and CPSSs at the time of initial examination.

A wide variety of breeds were noted in the APSS group in this study, including several dogs of breeds predisposed to CPSSs (ie, Yorkshire Terrier and Labrador Retriever). It has been suggested that features supportive of portosystemic shunting in a breed not typically affected by CPSSs should prompt the veterinarian to consider APSSs, and our study would support this with the inclusion of breeds such as English Springer Spaniel, American Bulldog, Russian Terrier, and Belgian Shepherd Dog in the APSS group.

Dogs with APSSs were significantly heavier than those examined for CPSSs in the present study. This finding is likely the result of a combination of factors, including differences in age and breed, and may also relate to the increased prevalence of ascites in the APSS group. Although statistical analysis did not show a difference between the proportion of small- and large-breed dogs in the APSS and CPSS groups, this may be because of the small number of dogs. Poor body condition was significantly more frequent in patients with APSSs. Weight loss and poor condition score have previously been frequently reported in dogs with APSSs. Therefore, poor body condition should increase the suspicion for a diagnosis of APSS in young dogs with PSSs. Dogs with APSSs were also significantly more likely to be examined with ascites, diarrhea, or both, compared with those with CPSSs in this study. The high OR of ascites in the APSS group is not surprising, since portal hypertension is key to the development of both APSSs and abdominal effusion. The lack of significant difference in albumin concentrations between the 2 groups in the present study supports the supposition that portal hypertension, rather than reduced oncotic pressure, was the cause of the ascites in dogs with APSSs. Interestingly, however, ascites was noted in 1 patient with CPSS with concurrent marked hypoalbuminemia (13 g/L) presumed secondary to gastrointestinal ulceration and hemorrhage. Although such a finding is uncommon, it does contradict previous suggestions that dogs with CPSSs cannot have hypoalbuminemia of a magnitude severe enough to cause an abdominal effusion to develop.

Patients with CPSSs were significantly more likely to exhibit signs of hepatic encephalopathy in this study. However, this finding should be interpreted with caution, because it can be challenging to make a definitive diagnosis of hepatic encephalopathy. In this respect, some neurologic signs such as central blindness and seizures are considered to be strong indicators of hepatic encephalopathy, whereas others (ie, signs of depression) are more nonspecific.

Many of the clinical pathology findings commonly reported in dogs with CPSSs have also been noted in dogs with APSSs, including low urea concentration, hypercholesterolemia, hypoalbuminemia, erythrocyte microcytosis, and hypochromasia. Abnormalities in urinalysis may occur in dogs with portosystemic shunting (low specific gravity, presence of ammonium biurate crystals, or positive bacterial cultures); however, it is not known whether these occur with differing frequencies in APSS and CPSS patients. Unfortunately, limited data availability and nonstandardized approaches between the 3 study centers in the present study prevented analysis of urinalysis data as a differentiating factor, but this may be an interesting area of future study.

Hunt commented that dogs with APSSs were not distinguishable from those with CPSSs on the basis of clinical signs or biochemistry results, but data were not presented. The results from our study show that ALT activity, mean corpuscular volume, and Hct were significantly different, but there was considerable overlap and the ORs were very small; thus it is unlikely that these factors, when assessed in isolation, would allow differentiation of CPSSs from APSSs in an individual patient.

The significant difference between RBC mean corpuscular volume in patients with CPSSs versus those with APSSs may relate to the differences in the hypothesized iron metabolism derangements in PSS patients. Microcytosis has been reported in patients with both CPSSs and APSSs. The significantly higher ALT activities in APSS cases are perhaps not surprising because acquired hepatopathies can initiate the development of APSSs. However, it is interesting to note that 31 of 58 dogs with CPSSs also had elevated ALT activities. Although the reason for this
is unknown, hypoxic damage resulting from poor hepatic perfusion would be a possible cause. Alternative reasons may include the presence of concurrent hepatopathies or the effects of antiseizure medications given to control the effects of hepatic encephalopathy; however, to our knowledge, no CPSS patients were receiving anti-seizure medication in this study. Further studies could include assessment of other liver enzymes activities (aspartate transaminase and gamma glutamyl transpeptidase) as differentiating factors, but unfortunately, these data were not available in this study.

Plain abdominal radiography is readily accessible in first-opinion small animal practice and can show characteristic microhepatica and bilateral renomegaly in some CPSS patients. D’Anjou et al. showed a 100% positive predictive value for CPSS in a case series of dogs when microhepatica, bilateral renomegaly, and urolithiasis were all present. Although the prevalence of each of these features in patients with APSSs is less well described, they have all also been demonstrated in patients with APSSs. Abdominal radiography was available for very few dogs with APSSs because of the prevalence of ascites in this group in our study; therefore, comparisons between the APSS and CPSS groups were not possible. Future studies to determine whether microhepatica and bilateral renomegaly are helpful for differentiating between APSSs and CPSSs would be interesting but would require ultrasound because of the prevalence of ascites in APSS cases. Ultrasonographic assessment of organ size requires a standardized series of measurements and therefore cannot be performed retrospectively unless all imaging studies had these measures recorded for all animals.

Limitations of the present study include the fact that, given the low prevalence of APSSs, case numbers were small; a multicenter study was performed for this very reason. The retrospective, observational nature of the study also carries limitations, including incomplete availability of data and variability in record keeping. Every retrospective observational case series is vulnerable to these factors, and thus, thorough accrual of pertinent clinical information was anticipated. Nonetheless, these findings should be interpreted with caution and, ideally, should be confirmed with prospective studies (i.e., assessing the ability of the various clinicopathologic findings to predict the diagnosis in a new case series).

The diagnoses of APSSs and CPSSs were made via combinations of ultrasonography, portovenography, and direct observation at surgery or postmortem examination. The sensitivity and specificity of ultrasonography are both excellent for the diagnosis of CPSSs but are less well described for APSSs. However, precise features including dilatation of the left gonadal vein have been reported to be highly specific and sensitive indicators of APSSs. Although it remains possible that some dogs within this population were diagnosed incorrectly on the basis of ultrasonography alone, experienced operators performed the diagnostic procedures. Portovenography was available in all centers and was used in 26 of 93 PSS patients, thus allowing for confirmation of diagnoses in instances where ultrasonographic examination was not definitive.

Portovenography, although invasive, is regarded as a robust method to determine shunt location and morphology. The use of portovenography was more common at 1 center than the other 2, likely reflecting differing clinician preferences among institutions. Therefore, it is perhaps less likely that portovenography was only performed in dogs where ultrasonography had not been diagnostic. Distinguishing cases where portovenography was essential in facilitating the diagnosis of APSS or CPSS versus those where it was an adjunct was not possible retrospectively; thus, it was not possible to discern the sensitivity and specificity of ultrasonography for differentiating APSSs and CPSSs.

Determination of APSS etiology was reported in a limited number of dogs in this study. The examination of a population of young dogs may have altered the distribution of APSS etiologies when compared with all dogs with APSSs; it could be hypothesized that congenital causations may play a larger role in a group of younger animals. The proportions of congenital and acquired causes could alter the initial clinical features of the group because the primary disease process underlying the development of APSSs may contribute directly to the initial features of the disease. However, the dogs of the present report were accrued from 3 referral centers with nonoverlapping catchment areas to maximize the accuracy of the representation of a wider population. Thus, it is assumed that they would be comparable with those in the wider population of young dogs with APSSs. Future prospective studies of large numbers of young dogs with APSSs including hepatic biopsies would allow greater understanding of the most prevalent causations.

References


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