Spontaneous Hepatic Rupture Secondary to Amyloidosis in a Chinese Shar Pei

A Chinese shar pei (CSP) was presented for spontaneous rupture of the liver due to severe, hepatic amyloid protein A (AA) amyloidosis. The dog had a history of febrile episodes and was related by pedigree to CSPs with familial renal amyloidosis.

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Case Report

A three-year-old, castrated male Chinese shar pei (CSP) was presented for acute collapse after a one-day history of lethargy, tachypnea, dyspnea, and vomiting. The dog was recumbent, minimally responsive, and tachypneic. Mucous membranes were pale, and capillary refill time could not be determined. On physical examination there were tachycardia (160 beats/min) and tachypnea (40 breaths/min), and femoral pulses were weak but synchronous. Pertinent medical history included several brief episodes of fever of unknown origin (103.8° to 104.8° F). These episodes were accompanied by leukocytosis, lethargy, anorexia, trembling, and pain on manipulation of the abdomen or hind limbs. The first episode occurred at 10 weeks of age, nine days after the dog received its first vaccination for canine distemper, hepatitis, parainfluenza, leptospirosis, and parvo virus (DAPLP). The second and third episodes began at 14 weeks of age and occurred three and 13 days (respectively) after the second DAPLP vaccination. The fourth episode occurred at 18 months of age, one month after annual boosters for DAPLP and rabies virus.

Blood was drawn, and shock therapy was instituted with intravenous lactated Ringer's solution, dexamethasone sodium phosphate (5 mg/kg body weight), and cephalothin[a] (22 mg/kg body weight). Emergency laboratory test results included hematocrit of 20%, total protein of 6.0 g/dl, glucose of 169 mg/dl, and blood urea nitrogen in the 15 to 26 mg/dl range. An electrocardiogram showed sinus tachycardia. Thoracic radiographs were unremarkable, but abdominal radiographs revealed hepatomegaly and splenomegaly with a possible splenic mass. A sanguineous fluid without evidence of exfoliant neoplastic cells was obtained via abdominocentesis. Repeated attempts at abdominocentesis failed to obtain more than 20 ml of blood for autotransfusion. An abdominal wrap was applied, and several hours after presentation the dog was alert and responsive, and the hematocrit had stabilized at 18%.

On the next day, the dog again was lethargic with a low hematocrit (16%) with a stable total protein concentration (6.0 g/dl), leukocytosis (32,780 cells/µl), and mature neutrophilia (29,502 cells/µl). A whole blood transfusion was administered prior to surgery. The dog was anesthetized with isoflurane,[b] and a midline exploratory celiotomy was performed.

The liver was pale and friable. Only the extreme edges of the hepatic lobes had a normal appearance. Numerous hematoma-like masses were scattered throughout the liver, ranging in size from 2 mm to 4 cm. A capsular tear was noted on the visceral aspect of

the right medial liver lobe. Hepatic biopsy was performed. The owners elected euthanasia rather than recovery from anesthesia.

On histopathological examination, there were large foci of hemorrhage within the hepatic parenchyma. There were multiple foci of centrilobular coagulation necrosis in adjacent areas of hepatic parenchyma. The spaces of Disse contained acellular, eosinophilic material which was aggregated heavily around vessels, including the central veins. This material stained positively with Congo red stain and exhibited bright, apple-green birefringence when viewed via polarized light. A diagnosis of hepatic hemorrhage and centrilobular coagulation necrosis due to diffuse hepatic amyloidosis was made. The Congo red-stained sample was treated with potassium permanganate and diluted sulfuric acid and reevaluated microscopically. No Congo red staining was retained, and there was an absence of apple-green birefringence under polarized light. This finding is consistent with the presence of secondary (reactive) amyloid protein A (AA) amyloidosis.[1,2]

Discussion

According to a computer search of the literature, this appears to be the first reported case of spontaneous hepatic rupture and hemorrhage due to extensive hepatic amyloidosis in the dog. A review of the human literature revealed eight reported cases of spontaneous rupture, severe intrahepatic hemorrhage, or both, due to hepatic amyloidosis; all but one human case were fatal.[3-9] Two of the human cases also involved spontaneous splenic rupture[6,8] which has been reported as a singular finding as well.[5,10] Most of these cases were associated with primary systemic amyloidosis (light chain amyloid [AL] type). A history of acute collapse due to hepatic hemorrhage and nonAA amyloidosis has been reported recently in Siamese, Oriental, and domestic shorthair cats.[11,12]

Hemorrhagic episodes are relatively common in human patients with amyloidosis. In one report, 41 out of 100 patients with amyloidosis experienced single or multiple hemorrhagic episodes. Three of these were severe enough to cause death due to retroperitoneal hemorrhage (n=1) and severe upper gastrointestinal tract bleeding (n=2).[13] These bleeding episodes may be associated with abnormalities in coagulation parameters, clotting factor deficiencies, or increased vascular fragility.[3,5,6,13-16] Spontaneous cerebral hemorrhage was reported in six of nine dogs with amyloid angiopathy.[17] If amyloidosis is suspected, the clinician should anticipate the possibility of hemorrhage even when normal coagulation tests are obtained.

Recently, DiBartola *et al.* reported 14 related Chinese shar peis with renal amyloidosis.[18] All dogs presented with chronic renal failure, and many had nephrotic syndrome. The dog reported here was related to at least six of the dogs in the pedigrees investigated by DiBartola. Although none of these six dogs were diagnosed with amyloidosis, the paternal great-grandsire of this dog was the central male prominent in DiBartola's pedigree shown in Figure 1 of that article.[18]

The type of amyloid in this case, with its lack of Congo red-stain retention after potassium permanganate treatment, also was consistent with that reported by DiBartola. This finding suggests the presence of reactive or AA amyloidosis. Further research is required to determine whether the AA amyloidosis was a result of the numerous, chronic, inflammatory conditions common to the dog in this case and CSPs in general, or if this represents a specific immunologic defect. Rivas *et al.* demonstrated increased levels of interleukin-6 in CSPs with histories of febrile episodes ("Shar Pei Fever") even during afebrile, quiescent periods.[19] It also should be determined whether serum amyloid A (SAA) protein levels (the presumed precursor to AA amyloidosis) are characteristically higher in affected animals or carrier animals, or both. In human medicine it has been shown that people with reactive systemic amyloidosis may have SAA levels up to 24 times higher than controls.[20] However, SAA levels were not found to be predictive for amyloidosis associated with Abyssinian cats.[21] Ultimately, a genetic marker is needed to identify at risk, affected, or carrier animals.

The prior history in this case carries important parallels to those cases reported by DiBartola. Half of DiBartola's cases had histories of intermittent febrile episodes with or without concomitant swelling of the tibiotarsal joints.[18] These signs commonly are called "Shar Pei Fever" or "Swollen Hock Syndrome" by Chinese shar pei breeders. These episodes may become important markers for clinicians to investigate the possibility of amyloidosis or to counsel their clients regarding the potential genetic implications. Further study is needed to uncover the prevalence and mode of inheritance of this disorder in the Chi-

nese shar pei breed, although an autosomal recessive mode has been suggested.[19,22]

Conclusion

The case reported here is unique in that this animal presented as an acute abdominal emergency without any prior or current history referable to renal signs or involvement, unlike the cases reported by DiBartola.[18] This case is one of three cases seen by or known to this author where hepatic rather than renal signs predominated the clinical presentation of familial amyloidosis in the Chinese shar pei. The differential diagnosis of hepatic or renal amyloidosis and the possibility of acute hemorrhage should be considered in this breed.

[a] Keflin, Eli Lilly, Indianapolis, IN

[b] AErrane, Anaquest, Madison, WI

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