Fatty Liver Syndrome In Puppies

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Introduction

Fatty liver or hepatic steatosis in puppies is a morphological entity often observed in the post-mortem room at the Department of Veterinary Pathology, University of Utrecht. Nevertheless, occurrence of fatty livers in puppies has not been mentioned specifically in literature. Hepatic steatosis is a well-known entity in other animals and is associated with anoxic, toxic, metabolic, or nutritional causes.[1-3] To investigate pathogenesis and specificity, a retrospective study of clinical history, clinical signs, and postmortem findings was performed in puppies with fatty livers.

Materials and Methods

During the years 1984 to 1987, 364 puppies between 3 and 16 weeks of age were necropsied; 28 were toy breeds. In this period, 43 puppies with hepatic steatosis were seen. In most cases liver, kidneys, heart, intestine, and brain were fixed in 10% buffered forinalin. After embedding in paraffin, 5 mμ-thick sections were made and stained routinely with hematoxylin and eosin and van Gieson's stain. In some cases frozen sections from the liver were stained for neutral fat with oil-red-0; also some were fixed in osmium tetroxide for two to four hours before embedding in paraffin.

In 28 cases routine aerobic and anaerobic bacteriological examination was performed. In five, biochemical examination on fat content of the liver also was done according to the method described by Kates.[4]

Results

Clinical History

Age of the animals varied from 4 to 16 weeks; median age was 9.0 weeks [Table]. Most remarkable in the clinical history was the presence of anorexia which often occurred directly or after purchase by a new owner (15 cases), vaccination (eight), weaning (four), tattooing (three), or surgery (one). In three, puppies showed anorexia following severe excitation during playing with the owner of other dogs. In the four cases of anorexia after weaning, concerning fox terriers all from the same breeder, they were fed with leavings of a home for aged people. When the breeder

Breeder changed the food to commercial puppy food, there were no problems in the ensuing litters. In nine cases clinical history did not mention a specific event before onset of anorexia. In some of these cases anamnesis was incomplete.

TABLE

Breed	Number	Range Of Age (wks)	Average Age (wks)
Bouvier	1	9	9
Chihuahua	8	4-14	8.5
Fox terrier	5	6-7	6.5
Labrador	1	9	9
Pekingese	1	8	8
West Highland terrier	1	9	9
York terrier	24	7-16	10
Mixed breed (small)	2	7	7

Apart from anorexia, main clinical signs were neurological (29 cases), vomiting (24), and diarrhea 20). Vomiting and diarrhea often preceded neurological signs. In the cases with diarrhea, feces often were described as dark green with mucus, resembling bile. Neurological signs varied between individual dogs and consisted of muscular weakness, ataxia, apathy, convulsions, opisthotonus, and coma.

In the toy breeds (n=41) death usually occurred within one to six days after onset of clinical signs. Three died at 9, 12, and 14 days following initial response to medical treatment. The two puppies of larger breeds died seven days after onset of clinical signs.

Blood glucose concentrations were determined in four (three Yorkshire terriers and one fox terrier). Severe hypoglycemia was present.

Pathology

Macroscopy. Nutritional state of the dogs varied. In 28 cases it was normal to good, in 15 moderate to poor. Two (bouvier and Pekingese) were anemic. In each puppy, the liver was moderately enlarged and pale yellow [Figure 1]. In some cases, liver tissure floated in formalin, indicating its high fat content. Other parenchymatous organs including heart and kidneys also appeared "fatty" with a pale-yellow color. Other observations included gastric erosions (n=1), absence of ingesta within stomach and intestine (n=32), gas-filled intestinal loops (n=1, thymic atrophy (n=18), and hydrocephalus (n=3).

Microscopy. All livers showed diffuse microvesicular vacuolation {Figures 2, 3}. In two cases mixed macro- and microvesicular steatosis was observed. Except for two which also showed nonsepecific reactive hepatitis, no other abnormalities were seen.

From 29 animals with neurological signs 22 showed neuron necrosis in the cerebral cortex [Figure 4]. Extent and morphology of the lesions varied from solitary acidophilic necrotic neurons to severe laminar neuron necrosis of cortex cerebri with edema and astrocytic swelling and secondary lesions as vascular proliferation, swelling of endothelium, cuffing, gliosis, and slight to moderate mononuclear meningitis. In five with neurological signs no lesions were found in the brain. In the two remaining cases the brains were not available for microscopical examination. From the 14 without neurological signs the brains were available for microscopical examination in eight cases. Four of these also showed moderate to severe cerebrocortical neuron necrosis.

Bacteriological Examination

Bacteriological examination including liver, spleen, kidney, and intestines was performed in 28 cases. In 25 cases bacteriological findings were negative. *Escherichia coli* sepsis was found in an eight-week-old Yorkshire terrier. From the small intestine of another Yorkshire terrier mainly hemolytic *Streptococci* and only some *Enterobacteriaceae* were isolated, suggesting dysbacteriosis possibly secondary to antibiotic treatment. In the

bouvier *Clostridium perftingens* enteritis was diagnosed.

Biochemical Examination

Fat content in the liver of five puppies ranged from 32% to 54% of dry weight. Fat content of a control liver from a normal Yorkshire terrier puppy was only 2 % of dry weight. Accumulated lipid was predominantly triacylglycerols.

Discussion

In the authors' findings fatty liver occurs in puppies between 4 and 16 weeks of age. Most belong to toy breeds; only two were larger breeds. The animals have a common clinical history of anorexia, also evidenced at post mortem by presence of an empty gastrointestinal tract. This strongly suggests a relation between anorexia and fatty livers in puppies.

According to clinical histories anorexia seems to be provoked by a constraining event such as purchase, tattooing, weaning, or extreme excitement. Although anorexia and depression are not unexpected after routine "puppyhood" events, especially in toy breeds, these events seemt to evoke clinical disease and even death. In the cases of the fox terriers quality of food could have been of importance, because improvement of the ensuing litters was seen after changing the food. In dogs with parvovirus enteritis and *Clostridium* enteritis, these infections couuld have led to anorexia. Also toxins and anemia due to intestinal blood loss could have promoted fatty infiltration of the liver in these cases.

In ponies, cows, and cats hepatic steatosis or fatty liver syndrome is a well-known entity. The disease morphologically is characterized by marked steatosis of the liver; other parenchymatous organs such as heart and kidneys may be involved. In these animals, fasting may provoke steatosis. [1-3, 5] Fasting results in lipolysis of adipose fat which cannot be processed adequately by the liver.[1-3, 5]

Cause of abnormal fat accumulation in the liver is not well understood. Several pathogenetic mechanisms such as increased hepatic lipogenesis, enhanced mobilization of free fatty acids from adipose tissue, decreased hepatic oxidation of fatty acids, impairment of hepatic triacylglycerol secretary mechanism, or a combination of these factors are suggested.[5]

In cases presented here neurological signs were the most frequently observed abnormality, followed by vomiting and diarrhea. Fasting hypoglycemia also produces similar neurological signs, especially in toy breeds.[6-8] Larger breed puppies and adults seem to be comparably resistant to fasting hypoglycemia.[9] Toy-breed puppies may be predisposed to fasting hypoglycemia due to their limited supply of body energy reserves, immature mechanisms for gluconeogenesis and glycogenolysis, and higher metabolic demands.[10] Hypoglycemia is a well-known cause of necrosis of neurons, especially in the cerebral cortex.[11] The frequent finding of cerebrocortical neuron necrosis in the authors' puppies and presence of severe hypoglycemia in all four puppies investigated for blood glucose levels suggest hypoglycemia as the main cause for neurological signs in the authors' puppies. In three puppies hydrocephalus may have contributed directly or indirectly to the neurological signs.

As both hepatic steatosis and hypoglycemia may be provoked by anorexia and fasting, fatty livers in puppies probably are the pathomorphological expression of the clinical syndrome of fasting hypoglycemia. In literature a connection between hepatic steatosis and hypoblycemia in toy breeds is not mentioned. In contrast, starvation with hypoglycemia in neonatal animals results in dark small livers (own observations), possibly because neonates have less fat deptos.

The frequent finding of fatty livers in puppies of toy breeds at postmortem examination indicates that this syndrom is an important problem in these animals. Further investigations to demonstrate the triad fasting, hypoglycemia, and fatty liver and the pathogenetic mechanisms involved are in progress.

References

1. Kelly WR. The liver and bilary system. In: Jubb KVF, Kennedy PC, Palmer N, eds. Pathology of domestic animals. Vol. 2. Orlando: Academic Press, 1985:251-4.

2. Barsanti JA, Jones BD, Spano IS, Taylor HW. Prolonged anorexia associated with hepatic lipidosis in three cats. Feline Pract 1977;52-7.

3. Thomburg LP, Simpson S. Digilo K. Fatty liver syndrome in cats. J Am Anim Hosp Assoc 1982;18:397-400.

4. Kates M. Technics of lipidology. New York: Am Elsevier Publishing Co, 1972:349.

5. Reid JM. An ultrastructural and morphometric study of the liver of the lactating cow in starvation ketosis. Exp & Mol Path 1973;18:316-30.

6. Leifir CE. Hypoglycaemia. In: Kirk RW, ed. Current veterinary therapy IX, small animal practice. Philadelphia: WB Saunders, 1986:982-5.

7. Strombeck DR, Rogers Q, Freedland R, McEwan LC. Fasting hypoglycaemia in a pup. J Am Vet Med Assoc 1978;1'73:299-300.

8. Vroom MW, Stappendel RI. Transient juvenile hypoglycaemia in a Yorkshire terrier and in a Chihuahua. Vet Quarterly 1987;9:172-6.

9. Bruijne JJ, Altzuler N, Hampshire J, Visser TJ, Hackeng WHL. Fat mobilization and plasm hormone levels in fasting dogs. Metabolism 1981,30:190-4.

10. Johnson RK, Atkins CE. Non-neoplastic causes of canine hypoglycaemia. In: Kirk RW, ed. Current veterinary therapy VII small aninal practice. Philadelphia: WB Saunders, 1980:1023-7.

11. Sullivan ND. The nervous system. In: Jubb KVF, Kennedy PC, Palmer N. Pathology of the domestic animals. Vol 1. Orlando: Academic Press, 1985:250-1.