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COPPER TOXICOSIS IN BEDLINGTON TERRIERS

By

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ERIKSSON, J.: *Copper toxicosis in Bedlington Terriers.* Acta vet. scand. 1983, *24*, 148—152. — Copper toxicosis of Bedlington Terriers (Chronic progressive hepatitis) is a genetically transmitted disease. The typical feature of this disease is accumulation of copper in the liver tissue. The changes vary from mild hepatitis to chronic progressive hepatitis and cirrhosis.

The material of this study consists of 2 cases of copper toxicosis examined at the Department of Pathology in Helsinki in the years 1980—82. Moreover a re-examination of tissue samples was made of all Bedlington Terriers examined during the years 1969—1982 at the same department. Six of the 14 examined dogs showed a positive reaction for copper in their liver tissues. The possible relationship of the examined dogs is not yet known.

copper toxicosis; chronic progressive hepatitis; Wilson's disease.

Copper toxicosis (Chronic Progressive Hepatitis) is a genetically transmitted disease in Bedlington Terriers. Its inheritance was found to follow an autosomal recessive pattern of inheritance (*Johnson et al.* 1980). The abnormalities in the dog's liver in connection with this disease have been divided into 4 grades: 1) pigment granules without any further hepatic tissue changes, 2) mild hepatitis, 3) periportal hepatitis, resembling chronic active hepatitis and 4) finally cirrhosis. In the present study, the clinical features and post mortem examination results of all examined (14) Bedlington Terriers are described.

MATERIALS AND METHODS

Two female Bedlington Terriers, 1 and 4 years old respectively, were clinically examined at the Small Animal Clinic of the College of Veterinary Medicine at Helsinki. The clinical

symptoms were vomitus, weakness and diarrhea. They had highly elevated ASAT enzyme values in their blood (ASAT 450 and 500 U/l 37°C).

After euthanasia the dogs were necropsied and tissue samples were taken from the livers, kidneys and myocardium. The samples were fixed in 10 % neutral formalin and processed in the usual manner in paraffin. Sections were stained with hematoxylin eosin and with a specific stain for copper (*Uzman* 1956).

A re-examination of all the Bedlington Terriers examined during the years 1969—1982 was also made. The paraffin embedded tissue samples of their livers, kidney and myocardium were stained with hematoxylin eosin and with Uzman's method for copper. The blood values for the re-examined dogs were taken from the records of the Central Laboratory of the College of Veterinary Medicine at Helsinki.

RESULTS

Macroscopic findings

Both dogs that were necropsied showed a moderate nutritional condition and were massively icteric. The livers were small, with the extensive nodularity typical of post necrotic cirrhosis. The yellowish nodules had a bronze hue and they varied from 1 millimeter to several centimeters (3 cm) in size. The mesenteric lymph nodules were moderately enlarged. The younger of the 2 dogs had a slightly enlarged spleen.

Microscopic findings

Microscopic examination revealed active hepatitis in both dogs (Fig. 1). Microfoci of acute necrosis of hepatocytes were randomly distributed in the hepatic lobules. Degenerative changes in the hepatocytes such as swelling and vacuolisation were also noticed. Adjacent to the sites of necrosis, bile stasis was seen. Kuppfer cells were prominent. Fibrosis was prominent and extended from the portal areas into the center of the lobules.

Uzman's staining showed numerous black granules located in the hepatocytes (Figs. 2 and 3). In the one dog's kidney there was copper in the tubules. The granules were very small in size and often appeared in clumps of dozens of granules. Copper accumulation was centrolobularly distributed, while the portal tract was almost copper free.

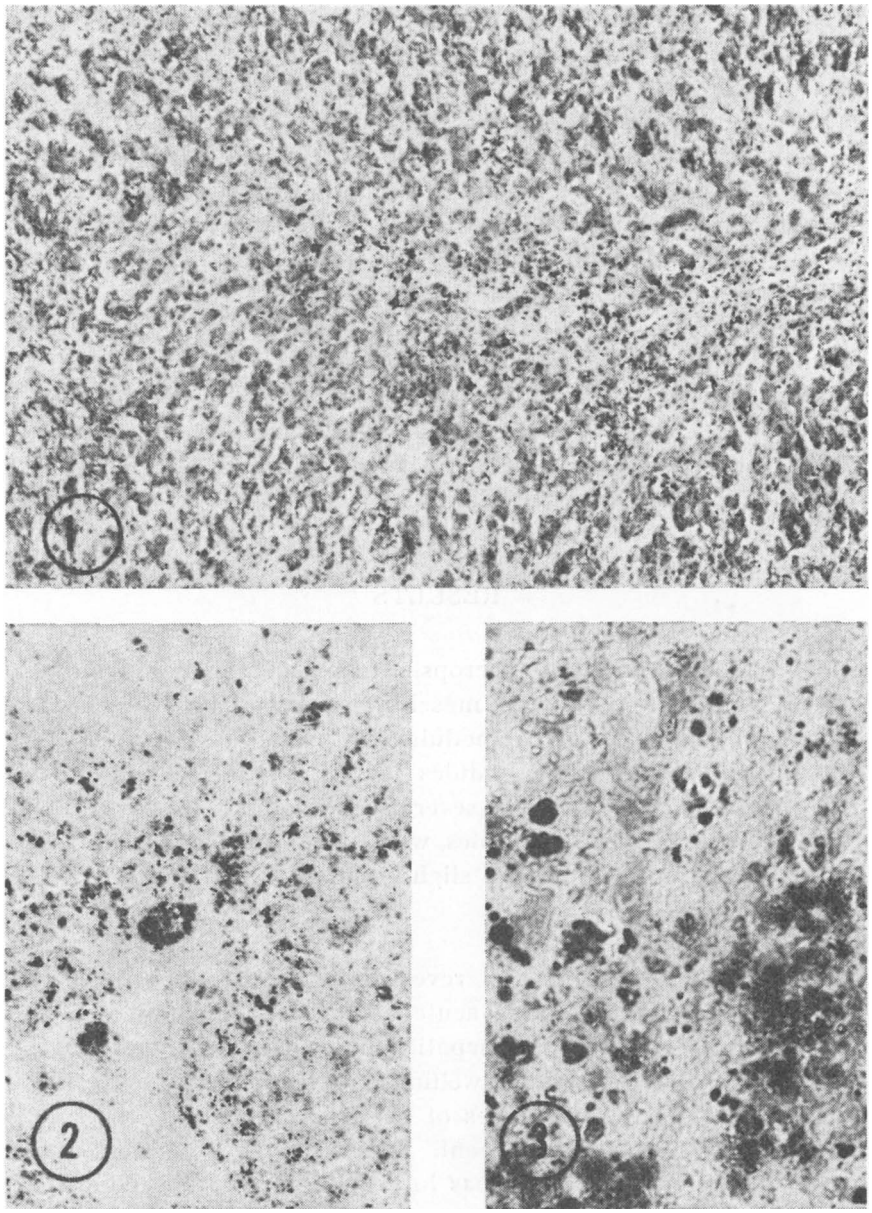

Figure 1. Photomicrograph of liver from a 1 year old Bedlington Terrier. There is a striking accumulation of copper-containing granules in most hepatocytes. HE × 42.

Figure 2. A clear copper accumulation, stained with a specific (Uzman's method) method for copper. × 42.

Figure 3. Shows the central area of Fig. 2. at a higher magnification. Uzman's method × 170.

Table 1. Results of examination of 14 Bedlington Terriers during the years 1968—1982.

Dog No.	Age	Sex	Blood values (ASAT, Urea)	Post mortem diagnosis	Microscopical copper findings[1]
1	7 years	♂		fat liver: adipositas, nephritis acuta;	—
2	8 months	♂		glom. nephritis osteodystrofia parath. hypertrophia;	—
3	5 months	♂	ASAT 175 U/l	glom. nephritis, uremia;	—
4	5 years	♂		uremia, nephritis;	++
5	10.5 years	♀		endocardosis, endometritis;	++
6	11 years	♂		hemangiosarcoma;	++
7	10 years	♂		glom. nephritis;	—
8	10 years	♀		chron. nephritis;	—
9	4 years	♀		nephritis;	—
10	11 years	♂		hemangiosarcoma;	—
11	1 year	♀	ASAT 450 U/l urea 78 mol/l	chr. hepatitis;	++
12	6 years	♀		hepatitis;	tissue sample not obtained
13	4.5 years	♀	ASAT 500 U/l	hepatitis;	+++
14	7 years	♂	ASAT 130 U/l	chron. hepatitis;	+++

[1] The amount of copper in liver tissue is registered from — to +++.

The results for these 2 dogs and the re-examined dogs are summarised in Table 1. A positive copper reaction was found in the liver tissue of 6 out of 14 animals. Copper appears in both young and old dogs. This disease is not sex-linked.

DISCUSSION

In the 2 cases of chronic progressive hepatitis described in this paper, the hepatocytes contain a large number of copper granules. Copper accumulation in liver tissue is typical and patognomic of Bedlington Terriers liver disease (*David et al.* 1979). A comparison has been made between this disease and a similar inherited copper storage disease of man, Wilson's disease. Similarly to copper toxicosis in dog, Wilson's disease appears to be an autosomally inherited disease (*Owen & Ludvig* 1982). Without treatment, Wilson's disease leads in spite of hepatic

cirrhosis to degeneration of the brain, especially the lenticular nucleus and cornea.

The re-examination of the old material revealed that Bedlington Terrier copper toxicosis is quite widespread in Finland. Six out of the 14 dogs examined had various amounts of copper in their liver tissues.

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SAMMANDRAG

Koppar toxikos hos Bedlington Terriers.

Koppar toxikos är en ärftlig sjukdom hos Bedlington Terriers och typiskt för den är en accumulering av koppar i levern. Koppar lagras i hepatocyterna med leverskador varierande från lindriga degenerative ändringar till cirros som följd. I detta arbete undersöktes njure, lever och hjärtmuskulatur av 14 hundar med en speciell koppar färgning. Sex av de 14 undersökta hundarna hade olika mängder av koppar i levern. Då sjukdomen är ärftlig, skall den beaktas i hundaveln även i Finland.

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