Copper toxicosis in Bedlington Terriers in the United Kingdom

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ABSTRACT

This paper summarizes the clinical and laboratory data on two adult Bedlington Terriers with liver disease associated with copper toxicosis. The younger dog, at 3 years, had elevated serum levels of alanine aminotransferase and alkaline phosphatase with active parenchymal cell degeneration and hepatitis. The second dog developed chronic hepatic failure at 5 years with advanced cirrhosis. Both dogs had stainable copper granules in the liver and chemical analysis of their livers revealed elevated copper contents (1,027 and 10,728 μg/g dry weight; normal less than 300 μg/g). These are the first published cases of this inherited abnormality of copper metabolism in this breed in this country.

INTRODUCTION

An unusual progressive and fatal liver disease affecting the Bedlington Terrier was first recognized in the USA (Hardy, Stevens & Stowe, 1975). The disease is characterized by toxic accumulation of copper in the liver, leading eventually to hepatitis and, ultimately, to cirrhosis (Twedt, Sternlieb & Gilbertson, 1979). This copper toxicosis results from a metabolic abnormality that is inherited in an autosomal recessive manner (Johnson et al., 1980; Owen & McCall, 1983). This paper records the first two published cases of this copper toxicosis occurring in the Bedlington Terrier in the United Kingdom.

CASE REPORTS

Case 1

A 3-year-old female Bedlington Terrier was presented with anorexia, profound weight loss (from 11.81 to 6.36 kg), vomiting and depression. Significantly
abnormal blood biochemical values were: elevated alanine aminotransferase (ALT) (313 iu/l) and serum alkaline phosphatase (SAP) (446 iu/l) normal values 10–27 and 10–45 iu/l—Rushton, 1981). Red and white blood cell counts, blood urea and bilirubin were within the normal range. Although total serum protein level was within the normal range (68 g/l) the albumen (27 g/l) was slightly below the lower limit of normality, and the globulin level (41 g/l) was slightly higher than the upper limit of normality (Rushton, 1981). Exploratory laparotomy was carried out revealing a liver that was described as swollen and yellow. A wedge of liver was obtained at laparotomy for chemical and histological examinations. The bitch was treated with d-penicillamine and methionine but no real clinical improvement was seen and euthanasia was carried out two months after liver biopsy. During the post-operative period, clinical chemistry monitoring revealed persistently elevated levels of ALT and SAP. The tendency for a slightly lowered albumen/globulin ratio persisted during this period.

**Case 2**

A 5-year-old male Bedlington Terrier was presented with the owner’s complaint of anorexia, vomiting and polydipsia. Physical examination revealed a dog with normal temperature, jaundice and buccal hyperaemia. Urinalysis revealed haematuria and proteinuria. Over the succeeding four weeks the jaundice became more profound and the dog’s physical condition deteriorated. Following an episode of haematemesis the dog was killed humanely.

**PATHOLOGY**

**Case 1**

The wedge biopsy consisted of firm, granular tan-brown liver. Histological examination revealed foci of parenchymal cell necrosis with a scattered inflammatory response of neutrophilic leucocytes and mononuclear cells. Early piecemeal necrosis adjacent to portal areas was accompanied by an inflammatory response of neutrophilic leucocytes, macrophages, lymphocytes and plasma cells. Fine fibrous septa extended from the portal areas into the lobules. Hepatocyte cytoplasm was vacuolated and contained conspicuous yellow-brown granules. A second sample of liver obtained post mortem showed similar degenerative and inflammatory changes with portal-central bridging. In both samples the parenchymal cell granules were positive for copper by the rubeanic acid staining method. Copper content of a post mortem liver sample (determined by atomic absorption spectrophotometry) was 1,027 µg/g (dry matter basis).

**Case 2**

Post mortem examination revealed profound jaundice without evidence of either haemolysis or extrahepatic obstruction. The liver was uniformly shrunken and tan with a finely nodular capsular surface. A wedge of liver (Fig. 1) was submitted for histological examination and copper analysis.
Histological examination revealed variable size nodules of parenchymal cells with focal degeneration and neutrophilic leucocyte accumulations. Nodules were separated by bands of fibrous connective tissue with portal-central bridging and there was conspicuous dilatation of capsular lymphatics. Intrcanalicular bile plugs were conspicuous. Parenchymal cell cytoplasm contained large numbers of faintly yellow granules that stained positively for copper by the rubeanic acid sequence. These copper granules were most conspicuous in the periphery of the nodules. Ferric iron was plentiful in the cytoplasm of Kupffer cells, parenchymal cells and in portal macrophages and connective tissue. The histological features are illustrated in Figs 2–4. Copper content of this liver was 10.728 μg/g (dry matter basis).

DISCUSSION

Both dogs had clinical, biochemical and morphological evidence of liver disease. The last was characterized by degenerative changes of parenchymal cells, and was associated with an inflammatory response and fibrosis. In the second dog the
Fig. 2. Irregular nodules of parenchymal cells separated by bands of fibrous connective tissue. Gordon and Sweets' Reticulin stain x 48.

Fig. 3. Heavy coarse granularity of parenchymal cell cytoplasm caused by copper accumulation. The less heavy granular appearance in the more centrally situated cells is due to haemosiderin accumulation. Rubeanic acid-Perls' Prussian Blue x 120.
hepatic lesion had progressed to frank micronodular cirrhosis (Anthony et al., 1977), possibly reflecting the longer duration of the abnormality. In both dogs there was a heavy accumulation of copper in the liver: the values of 1,027 and 10,728 µg/g are well outside the upper limit of normality (300 µg/g) for the dog (S. Haywood, unpublished observations; Keen, Lönneldal & Fisher, 1981). The morphological and analytical data are similar to those in previously published accounts of copper toxicosis in the Bedlington Terrier, confirming the existence of this genetically determined abnormality in this country.

The nature of the basic biochemical abnormality in this disease is at present unclear but it is known that copper accumulates to excess within hepatic parenchymal cell lysosomes; the concentration of copper increases with time and this is followed by progression from focal and chronic hepatitis to cirrhosis (Ludwig et al., 1980; Sternlieb, 1982). Early recognition of affected dogs is important: since the disease is inherited as an autosomal recessive (Johnson et al., 1980) the dam and sire of any affected dog must be considered to be carriers of the genetic trait (Owen & McCall, 1983).

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REFERENCES


