Intraerythrocytic Crystalloid Bodies in Cats

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Rectangular-shaped crystalloid bodies (C.B.) were demonstrated within the erythrocytes of intact and splenectomized cats and after incubation in hypertonic NaCl. The morphologic appearance of the C.B. is strikingly similar to that of crystals present in the erythrocytes of individuals with hemoglobin C.

Several hemoglobinopathies of man are known to produce striking morphologic changes in erythrocytes. In vivo sickling, occurring under low oxygen tension, is well documented in hemoglobin S (Hb S) disease. Osmotic dehydration produced by incubation in hypertonic salt solutions fosters sickling in these cells. This phenomenon is explained on the basis of a single amino acid substitution, valine for glutamic acid, at the beta-six position of the hemoglobin molecule.

Erythrocytes from most species of deer will also sickle but, in contrast with the behavior of Hb S in man, deer erythrocytes sickle in vitro upon incubation under high oxygen tension and elevated pH. This potential to form sickle cells has no apparent pathologic consequences in deer. Amino acid analyses of the various chains of the deer hemoglobin molecules do not permit an explanation of the sickling phenomenon on the basis of a single amino acid substitution as in Hb S disease of man.

Disordered molecular configuration of the hemoglobin molecule has also been documented in individuals with hemoglobin C (Hb C) disease. In this disorder lysine is substituted for glutamic acid at the same locus in the B chain as in Hb S. Occasional rectangular crystals can be found in blood smears from patients with Hb C disorders. Incubation of erythrocytes from these patients in hypertonic salt solution fosters crystal formation, perhaps by a combination of osmotic dehydration and "salting out" of a relatively insoluble protein.

Crystalloid inclusions resembling those seen in Hb C disease have not previously been described in an animal model. In the present study, square- and rectangular-shaped crystalloid bodies (C.B.) have now been observed within the circulating erythrocytes of cats.
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CASE REPORT

The first such observation occurred in a family of inbred Siamese cats. One queen from this family had five litters, all of which consisted of male kittens. The kittens were weak, failed to thrive, and died before 10 wk of age. Anemia could only be demonstrated in the terminal stages and may have been related to debility. The blood smear from one kitten demonstrated large C.B. within approximately 10% of the erythrocytes. The C.B. appeared to be rigid, straight-sided hemoglobin condensations that in many cases distended the erythrocyte membrane (Fig. 1A and B). The membrane remained intact, and free C.B. were rarely seen. In formalin-fixed tissue sections from this kitten, C.B. were present in blood vessels in all organs (Fig. 1C).

SPECIAL STUDIES

A litter mate with no C.B. in stained blood smears was splenectomized to determine if this would enhance C.B. formation. Within 5 hr, C.B. could be repeatedly demonstrated in the peripheral blood of this animal (Figs. 1D and E). Similar observations have been made in patients with Hb C, where splenectomy has resulted in the development of rodlike inclusions in greater numbers than in nonsplenectomized C-Hb patients.

A group of six male and six female random-bred kittens, 7 wk of age, was splenectomized. Blood smears made at 5 hr postsurgery contained C.B. in all animals. The red cells demonstrated severe anisopoikilocytosis postsplenectomy, but, except for a transitory leukocytosis, the hemogram remained within normal limits. All the kittens remained healthy, and C.B. were still present at 1 yr of age. Two other unrelated, intact kittens were made anemic by repeated bleeding, and C.B. were not observed in the peripheral blood. Incubation in 3% NaCl of washed erythrocytes from 20 nonsplenectomized, random-bred cats also resulted in the production of small numbers of the C.B. (Fig. 1F).

Hemoglobin electrophoresis on starch gel and cellulose acetate revealed no significant differences in patterns between control kittens and those with C.B. Two hemoglobin types, previously designated as a major component, Hb A, and a minor component, Hb B, were present in similar proportions in each animal both pre- and postsplenectomy.

DISCUSSION

The resemblance of cat C.B. to the inclusions found in red cells of patients with hemoglobin C disorders is striking. The studies reported here suggest that crystalloid formation is an intrinsic property of cat hemoglobin and that splenectomy serves to uncover this characteristic in these animals, as it does in man.5

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