Neutropenia in Cats with the Chediak-Higashi Syndrome

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ABSTRACT

Thirteen cats with Chediak-Higashi syndrome and 22 control cats from the same colony, were evaluated for neutropenia. The absolute neutrophil counts of the Chediak-Higashi syndrome cats were significantly less ($P<0.05$) than those of the control cats. It is concluded that Chediak-Higashi syndrome cats, like Chediak-Higashi syndrome humans, have a neutropenia associated with the other manifestations of the syndrome. Lysozyme activity which was undetectable in the serum of both Chediak-Higashi syndrome and control cats was not of use for determining if the neutropenia was the result of neutrophil destruction.

Key words: Chediak-Higashi syndrome, neutropenia, cats, animal model, lysozyme.

RÉSUMÉ

Cette expérience consistait à évaluer la neutropénie chez 35 chats d'une même colonie, dont 13 manifestaient le syndrome Chediak-Higashi, tandis que les 22 autres représentaient autant de témoins. La neutrophilie absolue des premiers se révéla significativement inférieure ($P<0,05$) à celle des seconds. Les auteurs conclurent par conséquent que les chats, tout comme les humains, atteints du syndrome précité, affichent une neutropénie qui en accompagne les autres manifestations. L'activité du lysozyme, non décelable dans le sérum des chats atteints du syndrome précité ou témoins, se révéla d'aucune utilité pour déterminer si la neutropénie résultait d'une destruction des neutrophiles.

Mots clés: syndrome Chediak-Higashi, neutropénie, chats, modèle animal, lysozyme.

The Chediak-Higashi syndrome (CHS) is an autosomal recessive disorder characterized by enlarged cytoplasmic granules in many types of cells, incomplete oculocutaneous albinism, a platelet storage pool deficiency, deficits of leukocyte function and a decreased resistance to infectious disease (1,2,3). Subsequent to the reports of CHS in humans, similar inherited conditions were described in mink, cattle, mice, a killer whale, and cats (4,5). The cats with CHS have been the most recently recognized of the animal models with CHS and the feline condition appears to be homologous with human CHS (6,7).

Neutropenia is often present in humans with CHS (1,3). Neutropenia has not been observed in animals with CHS. Mice with CHS (beige mice) have been examined hematologically and have been shown to have normal numbers of circulating neutrophils (8). Mink and cattle with CHS have apparently not been evaluated to determine if they, like humans with CHS, experience neutropenia. Cats with CHS have not been examined. In this report we present our observations indicating that CHS cats do develop neutropenia.

The cats used in this study were from a colony maintained at Washington State University. The CHS cats were descendants of the originally reported CHS cats and were determined to have CHS by the presence of characteristically enlarged melanin granules in hair and enlarged cytoplasmic granules in neutrophils (4,6). The control cats were housed in the same rooms as the CHS and although they were phenotypically normal, were genotypically heterozygous for CHS. The rooms were on a 12 hour light:dark cycle with light from 6 a.m. to 6 p.m. Thirteen CHS cats (nine males and four females) ranging in age from 1.4 to 5.1 years (mean age 3.05 years), and 22 control cats (6 males and 16 females) ranging in age from 0.75 to 6.5 years (mean age 2.85 years), were used for the main portion of this study. The cats were healthy and free of feline leukemia virus infection.

Blood was obtained from the cats by venipuncture from either a jugular or cephalic vein between 7:30 and 9:30 a.m. Approximately 2 mL of blood was collected in a 5 mL plastic syringe and transferred immediately to an EDTA tube. Blood was obtained from the 13 CHS cats four times at 14 day intervals. The 22 control cats were bled twice at seven day intervals.

Blood was also obtained from one CHS male cat (6.3 years of age), which was observed to have a profound neutropenia, 23 times at approximately seven day intervals for six months. The data from this cat were not included with those of the other CHS cats.

On each blood sample, a white blood cell (WBC) count and differential count were performed. Absolute neutrophil counts were calculated for

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each sample from each cat. A one tail Student's *t* test was used to evaluate the significance of differences in the absolute neutrophil counts between CHS and control cats.

In preliminary studies to determine if the neutropenia in the CHS cats resulted in elevations of serum lysozyme, as in humans with CHS (1), blood was collected from the jugular veins of five CHS and five control cats. Serum was removed and assayed for lysozyme activity by a previously described modification (9) of the lysoplate method of Osserman and Lawlor (10).

The mean absolute neutrophil count (±SEM) of the CHS cats was 8.609 ± 0.985 × 10^9/L, and of the control cats was 12.113 ± 1.363 = 10^9/L. The mean absolute neutrophil count of the CHS cats was significantly less ($P<0.05$) than that of the control cats (Fig. 1).

The 6.3 year old male CHS cat with the profound neutropenia had an absolute neutrophil count that ranged from 0 to 8.066 × 10^9/L with a mean of 2.735 ± 0.501 over six months.

Neither the CHS nor the control cats had detectable levels of lysozyme activity in their serum. This observation is in accord with the report by Rausch and Moore (11) that neutrophils of cats do not contain lysozyme. Consequently, even if there is an increased destruction of neutrophils in cats with CHS, it would not be detectable by assay of serum lysozyme activity.

Although the presence of neutropenia in humans with CHS is well-established, the cause of the neutropenia is less clear. An increased intramedullary neutrophil destruction has been proposed as the cause of the neutropenia in one study (1). Another possibility relates to natural killer cells. Humans with CHS are deficient in natural killer cell activity (12) and natural killer cells have been shown to function in regulating hematopoiesis (13).

The data from this study indicate that cats with CHS, like humans with CHS, have a neutropenia in association with the other manifestations of the syndrome. Consequently CHS cats may provide a valid animal model to study the mechanisms of neutropenia associated with CHS.

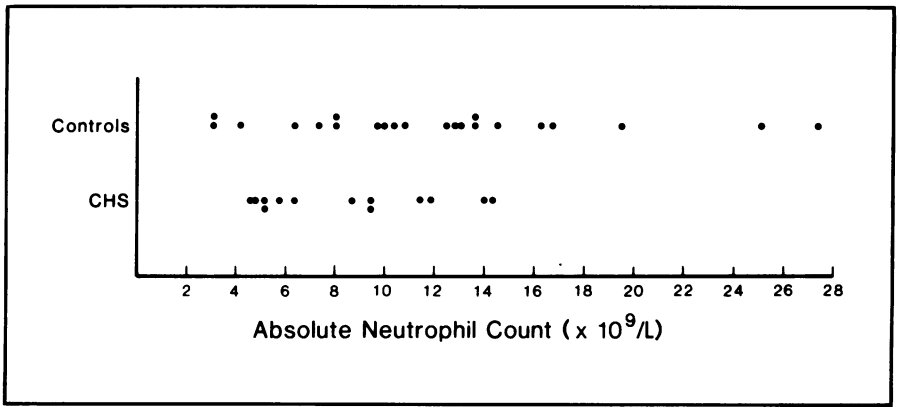

Fig. 1. The mean neutrophil count of the CHS and control cats in this study. Each of the points for CHS cats represents the mean of four counts and each of the points for control cats the mean of two counts.

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