Studies of Abnormal Leukocyte Bodies in the Mink

By ROBERT W. LEADER, GEORGE A. PADGETT AND JOHN R. GorHAM

In 1961, NEUTROPHILS with unusual cytoplasmic structures were observed in peripheral blood smears of mink homozygous recessive for the Aleutian gene aa. Subsequent observations also revealed abnormal eosinophils, monocytes and lymphocytes. These abnormal cells have a striking resemblance to those observed in the Chediak-Higashi syndrome (C-H S) of man. These intracellular bodies are hereafter referred to as Aleutian mink bodies (AMB).

METHODS

Peripheral blood smears were made from 195 normal mink of various genotypes. The smears were fixed for 6 minutes in absolute methyl alcohol unless a special stain was contemplated. The stains and technics were: Giemsa, Wollbach’s modification; peroxidase, modified method of Sato and Sekiya; Feulgen reaction, modified method of Feulgen and Rossenback; Schiff’s reagent, prepared by the method of de Tomasi; oil red O, method of Lillie; acidine orange; Prussian Blue; methyl green-pyronin; and periodic acid Schiff.

Schilling differential counts using the Giemsa stain were performed on 56 of the mink, 28 with abnormal cells and 28 without abnormal cells. One hundred cells were enumerated on each smear. Bone marrow smears were made from mink with and without the abnormal cells.

The mink were equally divided by sex and by genotype aa (Aleutian), Aa or AA (Non-Aleutian). Mink from our stock herd and from several commercial ranches in Eastern and Western Washington were used. None of the animals had known experience with virulent or vaccine strains of distemper virus. All mink were negative when tested by iodine agglutination test for Aleutian disease and were apparently normal by clinical observation.

RESULTS

Abnormal cells were observed in 78 of the mink. Abnormal eosinophils, lymphocytes and monocytes were found in all smears in which bodies were seen in neutrophils. Smears of the remaining 117 were free of AMB.

Distribution by genotype was:

<table>
<thead>
<tr>
<th>Type</th>
<th>AMB Present</th>
<th>AMB Absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aleutian: aa</td>
<td>78</td>
<td>0</td>
</tr>
<tr>
<td>Non-Aleutian: Aa or AA</td>
<td>0</td>
<td>117</td>
</tr>
</tbody>
</table>

See table 1 for results of Schilling differential counts.

Neutrophils

The number of abnormal neutrophils varied with each animal. The average
Table 1.—Mean Schilling Differential Counts Comparing Smears from 28 Mink with Normal Blood to 28 with Blood Containing AMB

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Abnormal</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Segmented neutrophils</td>
<td></td>
<td></td>
</tr>
<tr>
<td>With bodies</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>With one body</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>With two bodies</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>With three bodies</td>
<td>0.6</td>
<td>0</td>
</tr>
<tr>
<td>With four bodies</td>
<td>0.2</td>
<td>0</td>
</tr>
<tr>
<td>With five or more bodies</td>
<td>0.2</td>
<td>0</td>
</tr>
<tr>
<td>Bands</td>
<td>1.5</td>
<td>1</td>
</tr>
<tr>
<td>With bodies</td>
<td>0.2</td>
<td>0</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>28</td>
<td>28</td>
</tr>
<tr>
<td>With bodies</td>
<td>0.5</td>
<td>0</td>
</tr>
<tr>
<td>Monocytes</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>With bodies</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Abnormal eosinophils</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

for one series of counts was 4 abnormal cells to 51 normal cells. Each pathologic cell contained one or more large granules (fig. 1). The granules were peroxidase positive, methyl green-pyronin negative, periodic acid Schiff negative, Feulgen negative, acridine orange negative, Prussian blue negative and oil red O negative. This staining pattern was consistent with the staining of

Fig. 1.—Neutrophil showing abnormal cytoplasmic granules. Peripheral blood. X1600.
normal neutrophil granules and with the staining of the neutrophilic granules in the C-H S.2,3

Eosinophils

The staining reactions of the granules of normal and abnormal eosinophils were identical. A normal cell is shown in figure 2. The nuclei usually contained one, two or three lobes. In the abnormal cells there was marked variation in the granules. Some cells contained five or six very large granules while in other cells there were many of varying size (fig. 3). In every case where blood cell abnormalities were found, all of the eosinophils were affected.

Lymphocytes and monocytes

The inclusions in these cells varied in size and usually only one was seen in each cell, although occasionally two were found (figs. 4 and 5). The staining reactions were negative with stains listed above for neutrophils.

In bone marrow, AMB were present in young and mature neutrophils (fig. 6), eosinophils (fig. 7), and lymphocytes (fig. 8). The staining characteristics of the bone marrow cells were similar to mature cells in the peripheral blood.

Discussion

When abnormal structures (AMB) were first observed in peripheral blood smears, it was thought that they probably represented one manifestation of Aleutian disease of mink. Subsequent studies, however, indicate that they are...
Fig. 3.—Abnormal eosinophil. Peripheral blood. X1600.

Fig. 4.—Lymphocyte with cytoplasmic body. Peripheral blood. X1600.
Fig. 5.—Monocyte with cytoplasmic bodies. Peripheral blood. X1600.

Fig. 6.—Myeloid series showing abnormal granules. Bone marrow. X1600.
Fig. 7.—Abnormal eosinophil. Bone marrow. X1600.

Fig. 8.—Lymphocyte-containing body. Bone marrow. X1600.
ABNORMAL LEUKOCYTE BODIES IN MINK

a genetic characteristic inherited as a Mendelian recessive trait traveling on or with the aa gene. There does not appear to be any sex linkage.

The striking resemblance of AMB to the intracellular bodies seen in the Chediak-Higashi syndrome of children leads to speculation as to whether they may share other similarities.

Since the occurrence of the mutation in Oregon in 1941, Aleutian mink (aa) have been observed to possess less vigor and greater disease susceptibility than heterozygous (Aa) or homozygous dominant (AA) mink. Their death losses are far greater during the first year of life. They are more susceptible to abscesses. Several studies have indicated a significantly greater predilection to Aleutian disease.

Aleutian mink, however, have been shown to form neutralizing antibody directed against distemper virus. Healthy mink of this genotype also respond to botulism toxoids as evidenced by protection when subjected to intraperitoneal injection of toxin. Thus, there may be some defect in the protective mechanisms of these individuals which is related to leukocyte activity rather than antibody response.

Preliminary studies using skin window preparations by one of us (G.A.P.) indicate that a lesser degree of positive chemotaxis is exhibited by the leukocytes of Aleutian mink.

Saraiva et al. found that patients with C-H S formed normal antibodies to typhoid vaccine, and Page et al. confirmed this using typhoid, diphtheria and mumps vaccine. However, there is indication of marked susceptibility to bacterial infections, suggesting possible deficiency of some mechanism other than antibody formation.

If this parallel between mink with AMB and children with C-H S can be confirmed, the mink may serve as a “ready made” experimental animal to help elucidate Chediak-Higashi syndrome.

SUMMARY

The occurrence of abnormal bodies in the cytoplasm of neutrophils, eosinophils, monocytes and lymphocytes of Aleutian (aa) mink is reported. Similarities of these bodies to the leukocyte abnormalities of Chediak-Higashi syndrome of children are pointed out.

SUMMARIO IN INTERLINGUA

Es reportate le occurrentia de anormal corpores in le cytoplasma de neutrophilos, eosinophilos, monocytes, e lymphocytes de aleutian visones aa. Es signalate similitudes inter iste corpores e le anormalitates leucocytic in juveniles con le syndrome de Chediak-Higashi.

REFERENCES


2. Saraiva, L. G., Azevedo, M., Correa, J.
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