Gaucher's Cells in Thalassemia

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Gaucher or Gaucher-like cells are described in the spleen and bone marrow of patient with thalassemia major, by light and electron microscopy. The ultrastructure shows intracytoplasmic tubules and phagocytosis of mature and immature erythrocytes. The spleen has an increase in monohexosyl ceramide. These findings support the concept that the intracytoplasmic tubular material of the Gaucher's cells is of extracellular origin. Erythrophagocytosis common in Gaucher's disease, chronic myelogenous leukemia, and thalassemia suggest that impaired catabolism of erythrocytes may give rise to the increased glucocerebroside.

The intracytoplasmic glucocerebroside accumulation gives the Gaucher's cell its characteristic microscopic appearance. In Gaucher's disease, it is as a result of a glucocerebrosidase deficiency and in chronic myelogenous leukemia it is presumed to be due to excessive granulocytic turnover.

Fig. 1.—Aspirated bone marrow. Gaucher cell is shown adjacent to a megakaryocyte. × 1000.
We are reporting the presence of Gaucher or Gaucher-like cells in thalassemia, as demonstrated by light and electron microscopy. Evidence is presented supporting a relationship between Gaucher's cells and the phagocytosis and breakdown of erythrocytes.

CASE REPORT

A 15-yr-old, white female was admitted to Mercy Hospital for splenectomy and anemia. A diagnosis of Cooley's anemia was made at the age of 4½ years; at that time she had moderate hepatosplenomegaly. The patient had never had a blood transfusion prior to the hospital admission. She complained of frontal headaches, palpitations, tiredness, and shortness of breath. On physical examination she was small in size. There was pallor, scleral icterus, bossing of the parietal bones and prominence of the zygoma. The liver and spleen were enlarged; the liver was 4 cm and the spleen 8 cm below the costal margin. There was cardiac enlargement with a grade 4/6 systolic murmur, and a hepatojugular reflux.
The lungs were clear to percussion and auscultation; there was no ankle edema present.

Both parents are of Italian extraction and show evidence of thalassemia minor, with target cells, basophilic stippling, and no anemia.

Her hemoglobin on admission was 6.5 g/100 ml. The peripheral blood smear showed hypochromia, target cells, anisocytosis, poikilocytosis, basophilic stippling, and normoblasts. She had a fetal hemoglobin of 75%, increased A2 hemoglobin (8%), decreased fragility to saline, a bilirubin of 4.0 mg, mainly indirect, and normal BUN, calcium, total protein, alkaline phosphatase, and SGOT. X rays of the skull showed osteoporosis and characteristic "hair on end" appearance. The aspirated bone marrow, smears and sections, were very cellular, with many red cell precursors, hemosiderosis, and PAS-positive foam cells (Figs. 1 and 2). She was given two units of packed red cells and the spleen was removed. Sections of the spleen showed hemosiderosis and PAS-positive foam cells (Fig. 3). These cells were also present in the accessory spleen and a lymph node. The liver biopsy showed hemosiderosis and no foam cells.

Electron microscopy showed the characteristic structure of Gaucher's cells, with many
moderate-sized tubules in the cytoplasm (Fig. 5). The smooth endoplasmic reticulum was dilated and the mitochondria were at times swollen with fading cristae (Figs. 4 and 5). Some of these cells also showed phagocytosis of normoblasts and mature erythrocytes (Fig. 4).

The spleen had a slight increase in glucocerebroside, 0.08 µmole monohexosyl ceramide per gram of wet tissue. A control, surgically removed spleen, of an anemic hyperbilirubinemic similar-aged female with hereditary spherocytosis and no Gaucher cells in the spleen or bone marrow, had 0.06 µmole monohexosyl ceramide per gram of wet tissue.

The patient made an uneventful recovery; she was discharged and returned to school. Her hemoglobin gradually dropped, and she required blood transfusions 13 mo after the splenectomy.

**MATERIALS AND METHODS**

Part of the bone marrow and tissue samples from the spleen were fixed in 6.25 phosphate-buffered glutaraldehyde (pH 7.6), postfixed in osmium tetroxide (pH 7.4) washed with phosphate buffer dehydrated in acetone and embedded in epoxy resin (Durcupan, Fluka AG). The sections were cut with a Porter Blum microtome and transferred on formvar (polyvinyl formal plastic) coated copper grids, stained with uranyl acetate and lead citrate, and examined with a Hitachi electron microscope.

The bone marrow and tissue were also fixed in formalin and stained with hematoxylin and eosin and PAS. The bone marrow smears were stained with Giemsa, tetrachrome, and PAS.

The fresh-frozen spleen samples were sent to Dr. D. S. Fredrickson and Dr. H. R. Sloan at the National Heart and Lung Institute for lipid analysis. They were extracted with chloroform methanol and a silicic acid column. Cholesterol and esters were eluted with chloroform, and then with ethyl acetate. Acetone then completely removed all the mono-, di-, and trihexosyl ceramides from the column. Following alkaline methanolysis, the
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glycolipids were separated by Silica gel G thin-layer chromatography and quantitated by gas chromatography.7

DISCUSSION

Foam cells have been described by light microscopy but not by electron microscopy in the spleen and bone marrow in Cooley's anemia.8 PAS-positive material is present in the red cell9 of thalassemia as early as the erythroblast10 and is regarded by Astaldi9 as a mucopolysaccharide resulting from an inherent red cell defect in carbohydrate metabolism. It was further postulated that the histiocytes had a similar defect.11

The patient in this report has classical beta thalassemia major. The foam cells in the bone marrow prior to blood transfusion indicates that they were not of donor-cell origin. There was phagocytosis of erythrocytes, reticulocytes, normoblasts, and characteristic tubular ultrastructure of Gaucher's cells. The increase in glucocerebrosides is significant in that there were only small scattered collections of these cells. The glucocerebroside increase in Gaucher's disease is dependent on the degree of infiltration with Gaucher's cells. These findings support the concept that the "Gaucher" cells that we are describing in thalassemia are identical to the previously described foam cells, and that they result from the breakdown of erythrocytes. The intracytoplasmic tubular material may represent incomplete catabolism of red cells, possibly their glycolipid-rich membranes.12

Engulfed erythrocytes are present in the Gaucher cells of Gaucher's disease13-16 chronic myelogenous leukemia,14 and, in this report, thalassemia. The intracytoplasmic red cell fragments, ferritin-like particles,14 and the iron in Gaucher's disease15 support the concept that the source of the cerebroside may be the phagocytized erythrocyte.

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