Chronic Granulomatous Disease and McLeod Syndrome in a Black Child

Senih M. Fikrig, MD, Juana C. D. Phillipp, MD, Elizabeth M. Smithwick, MD, Ragnhild Øyen, and William L. Marsh, FIMLS, MI Biology

From the State University of New York Downstate Medical Center, Brooklyn, the Memorial Sloan-Kettering Cancer Center, New York, and the Lindsley F. Kimball Research Institute, The New York Blood Center, New York

ABSTRACT. A 3-year-old black male child with X-linked chronic granulomatous disease and red cells of the rare McLeod phenotype is presented. The red cells showed acanthocytosis and did not react with anti-KL. Similarly the leukocytes were nonreactive with anti-Kx. The Xk and Xg linkage could not be investigated since all members of his family were Xg (a*). Pediatrics 66:403-404, 1980; chronic granulomatous disease, McLeod syndrome, Kx antigen, acanthocytosis.

Chronic granulomatous disease (CGD) of childhood arises through a defect in bactericidal activity of neutrophil leukocytes and monocytes. In most instances affected children are male, and inheritance is through an X-borne gene transmitted by the carrier mother. Some boys with X-linked CGD have red cells of the rare McLeod phenotype in which common antigens of the Kell blood group system are present in a markedly depressed form.

McLeod red cells lack an antigenic marker called Kx, which is believed to label a precursor utilized in the Kell biosynthetic pathway; absence of Kx appears to be responsible for the depressed Kell system antigenicity. More than 20 examples of the McLeod phenotype are known, all of whom are male children, and the condition has an X-linked mode of inheritance. McLeod red cells have striking acanthocytic changes in morphology and male children with McLeod red cells have a hemolytic condition, which is usually well compensated. This interrelated serologic, hematologic, and clinical condition is called McLeod syndrome.

Normal neutrophil leukocytes and monocytes have Kx antigen but it is absent from leukocytes of boys with X-linked CGD. The X-linked locus responsible for Kx synthesis is called Xk. One common (X2k) and three rare (X3k, X4k, X5k) alleles are each responsible for a different permutation of Kx antigenicity between red cells and leukocytes. Hemizygous inheritance of X2k allows no production of Kx by red cells or leukocytes and these boys have McLeod syndrome and CGD (type 2 CGD). Thus far this rare phenotype has been recognized only in white boys.

We have studied a 3-year-old black male child with CGD and red cells of the McLeod phenotype with associated hematologic anomalies. The findings are the subject of this report.

CASE REPORT

R.L. is a 3-year-old black male child who soon after birth had a bladder neck obstruction associated with bilateral hydrenephrosis. Following surgery osteomyelitis developed in the right calcaneous bone and Serratia marcescens was grown from cultures of excisional biopsy. The diagnosis of CGD was made following abnormal quantitative nitroblue tetrazolium and leukocyte bactericidal tests. He was treated successfully with gentamycin and carbenicillin. After a relatively quiet period, at the age of 2 years he had an extracardiac continuous murmur and an extended lung shadow over the left lung field. An arterial catheterization revealed an anterior vascular mass in the left lung field fed by collaterals from the left subclavian artery, with mammillary and thoracic vessels going into the two distal arteries. He also developed a soft growth over the seventh rib. X-rays of the chest and gallium scan demonstrated osteomyelitis of the 6th, 7th, and 8th left ribs and density on the upper lung field. Cultures from the affected areas grew Aspergillus fumigatus and the patient was treated successfully with amphotericin B and rifampin. The patient has been given...
blood transfusions on two occasions without clinical complications.

RESULTS

Hematologic Results

The hemoglobin level of the patient averages about 7.0 mg/100 ml, with mean corpuscular hemoglobin of 22.3 and mean corpuscular volume of 61 cuμ. Reticulocytes were between 1.8% and 2.7% and tests for sickle cells were negative; however, his red cells showed marked morphologic changes, with anisocytosis and acanthocytosis being the most prominent features. The quantitative nitroblue tetrazolium test showed a value of 0.015 Δ optical density(OD)/30 min/2.5 × 10⁶ WBC cells. (Normal values in our laboratory were 0.135 to 0.295.)

Serologic Results

The patient’s red cells reacted weakly with antibodies to common antigens of the Kell system and were nonreactive with anti-KL. Other blood groups were pedestrian. His separated leukocytes did not react with anti-Kx with the antibody procedure previously described. Tests for blood group antibodies made three months after the blood transfusions, which were with blood of common Kell type, showed no Kell-related or other alloantibodies.

Family Studies

Neutrophil leukocytes from the patient’s mother and maternal grandmother gave intermediate levels of activity in tests with nitroblue tetrazolium (0.043 and 0.062, respectively). Serologic studies on blood from the patient’s mother showed red cell mosaicism, in which the majority of cells were of common Kell phenotype and a minority were nonreactive with anti-KL and were, therefore, of McLeod type. The mosaicism was also recognizable hematologically by the presence of small number of acanthocytes.

DISCUSSION

X-linked chronic granulomatous disease and the McLeod syndrome, either separately or together, have been reported thus far only in white male children. The present patient is black and has clinical and hematologic findings typical of CGD. His leukocytes lack the Kx antigen and the results of Kell blood group studies on his red cells are characteristic of the McLeod phenotype. His red cells also show the acanthocytic morphologic changes that are associated with this blood type. The X-born (Xk) locus that is responsible for CGD and the McLeod syndrome is inactivated by the Lyon effect. The resulting mosaicism, as present in the mother of this black boy, is seen as a mixture of normal red cells of common Kell type and McLeod acanthocytes, and by an intermediate level of activity in leukocyte nitroblue tetrazolium studies.

Recent data indicate with good probability that the Xk and Xg blood group loci are linked. However, all members of this black family are Xg(a') and therefore noninformative. Whether the variant Xk allele present in this family is a true black characteristic, or whether it results from introduction of a white Xk gene somewhere into their ancestry cannot be established.

ACKNOWLEDGMENT

This work was supported in part by grant HL09011 from the National Heart and Lung Institute, by a grant from the House of Bernstein Foundation, and by grants CA-08748 and CA-19627 from the National Institutes of Health.

REFERENCES

Chronic Granulomatous Disease and McLeod Syndrome in a Black Child
Senih M. Fikrig, Juana C. D. Phillipp, Elizabeth M. Smithwick, Ragnhild Øyen and
William L. Marsh

Pediatrics 1980;66:403

Updated Information & Services
including high resolution figures, can be found at:
/content/66/3/403

Permissions & Licensing
Information about reproducing this article in parts (figures, tables)
or in its entirety can be found online at:
/site/misc/Permissions.xhtml

Reprints
Information about ordering reprints can be found online:
/site/misc/reprints.xhtml
Chronic Granulomatous Disease and McLeod Syndrome in a Black Child
Senih M. Fikrig, Juana C. D. Phillipp, Elizabeth M. Smithwick, Ragnhild Øyen and William L. Marsh
Pediatrics 1980;66;403

The online version of this article, along with updated information and services, is located on the World Wide Web at:
/content/66/3/403