THE COINCIDENCE OF MEDITERRANEAN ANEMIA AND PERNICIOUS ANEMIA IN A YOUNG SICILIAN

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PERNICIOUS anemia is ordinarily a disease of the middle years and old age. In individuals under 30 years of age, it is uncommon but not remarkable.[1] Mediterranean anemia particularly in its mild forms (target-oval-cell trait or thalassemia minor) is fairly common, occurring in about 6 to 8 per cent of all Italians studied.[2] The simultaneous occurrence of both pernicious anemia and Mediterranean anemia in one person has not previously been described. We report this association in one case, in which opportunity for careful studies of the blood and bone-marrow was afforded.

Case History

The patient, an enlisted man on duty at a fire station was born at Houston, Texas, July 19, 1920 of Sicilian parents. Family history was negative for blood diseases. The patient's mother died in childbirth while he was a boy. His father, one brother and one sister were known to have diabetes mellitus. One brother was killed in action in World War II. Four other siblings are living and well. The patient had the usual childhood diseases, and except for minor illness, had been well before the onset of his anemia.

The patient enlisted in the Army Air Forces in September 1946. In December 1946 he developed a severe and intractable diarrhea after eating the fruit of a cactus plant. This persisted with six to twelve watery stools per day for a month. Toward the end of this bout he felt weak, easily fatigued and breathless on moderate exertion. When he fainted on two occasions he went to his dispensary. On January 30, 1947 he was hospitalized at the Station Hospital, Forth Worth Army Air Field.

Physical examination on admission to that hospital showed a patient with a pallid skin, a yellowish tinge and pale mucous membranes. The tongue was very smooth. No other abnormalities were elicited. Blood pressure 110/70.

Laboratory work was reported as follows: RBC 3.0 million, hemoglobin 10.5 Gm., color index 1.2. The blood smear demonstrated macrocytes and "tailed" erythrocytes. The leukocyte count was 5700. Except for a shift to the right in neutrophils, the differential count was normal. Gastric analysis showed no free hydrochloric acid. The feces were negative for blood and parasites. Urinalysis and serologic test for syphilis were negative. Therapy with liver extract was begun on February 14. Reticulocyte count on February 21 was 3.5 per cent. Polychromasia was noted. On March 3 the blood picture was as follows: RBC 4.0 million; hemoglobin 14 Gm. There were many macrocytes and "tailed" erythrocytes. Some erythrocytes had basophilic stippling. The blood platelets were 498,000; the WBC 8,800. Liver extract was discontinued on March 5.

The patient was transferred to Brooke General Hospital on March 22. Physical examination on admission was unchanged from that reported earlier. The patient seemed pallid and listless. He was slender, with dark complexion, hazel eyes and a sprinkling of gray hairs. There was no evidence of metallic line in his gums. There was no remarkable lymphadenopathy; the liver and spleen were not palpable. Neurologic examination was negative. The blood counts were essentially unchanged from that of March 3. The patient was group ON, Rh negative. There were no sickle cells. Hypotonic fragility was slightly decreased: 0.40–0.32. The blood serum was negative for cold agglutinins. Feces were repeatedly negative for blood, parasites and excessive fat. Gastric analysis with histamine was repeatedly negative for free hydrochloric acid. Urinary urobilinogen was 3.25 mg. per 24 hours. Indirect van den Bergh was 1.0 mg.

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gastric mucosa is reported to be found in about 40 per cent of patients with pernicious anemia. Some of those who show atrophy will improve with liver therapy.[5]

It was noted further that in June our patient had been three months without treatment, yet had a normal erythrocyte count. Many cases of pernicious anemia will relapse in this time but some have gone as long as two years without treatment before they relapsed.[6]

There was absence of neurologic changes: vibratory and position sense were intact; there was no paresthesia. Pernicious anemia need not be accompanied by such changes. One of four clinical types of the disease, as classified by Dameshek, is a "purely hematologic type, characterized by severe macrocytic anemia and by little if any neurologic involvement."[7]

The target cells found in the peripheral blood could only be explained by supposing there were two diseases. Adding this unlikelihood to the others discussed above we thought it best to make no definite diagnosis.

When the patient returned in relapse, the clinical picture of pernicious anemia was inescapable. There was a macrocytic anemia which responded with reticulocytosis and an increased total red cell count. The bone marrow demonstrated megaloblasts and hypersegmented polymorphonuclear neutrophils. There was absolute achlorhydria after histamine. There was evidence of increased hemoglobin dissolution manifested by a mild acholuric jaundice and increased urinary urobilinogen excretion in the absence of liver disease. There was inflammation and atrophy of the tongue. Lacking only was evidence of central nervous system involvement.

Mediterranean anemia. When the "mask" of pernicious anemia with its large and distorted red cells was removed, the target-oval-cell trait became very evident. Mediterranean anemia occurs in degrees of severity varying from the fatal disease which is Cooley's anemia to the target-oval-cell trait, so benign that it cannot be called a disease.[8] The anemia is hereditary, following a mendelian pattern. Its severe form occurs in children whose parents both have a milder form of the disease. The mechanics of transmission have recently been well discussed by Daland and Strauss.[9]

It is of interest that with the simultaneous occurrence of these two diseases, the picture of pernicious anemia dominated. In patients observed with pernicious anemia occurring simultaneously with chronic blood loss the picture was hypochromic.

Our patient returned to Brooke General Hospital for a follow-up examination in February 1948. His blood picture was as follows: RBC 5.88 million, hemoglobin 16.5 Gm., hematocrit 47 VPC, MCH 28, MCV 80, MCHC 35. Cells on stained spreads were slightly hypochromic. The patient was examined at this time by Dr. William Dameshek of Boston who pointed out that hypochromic "polycythemia" is characteristic of mild Mediterranean anemia. Dr. Dameshek suggested, however, that this diagnosis be confirmed by examination of other members of the patient's family. This was done.

For most of the material we are indebted to the Medical Service of the Veterans Administration in Houston, Texas which made blood counts and sent blood smears to us for examination.

The patient's wife, age 21. Group O Rh positive. Irish extraction. She was negative for the target-oval-cell trait.

S.B. (father of patient), age 63. Diabetic. Group A, Rh negative. RBC 4.35 million, hemoglobin 13 Gm. Target-oval-cell trait positive.

M.B.N. (sister of patient) age 38. RBC 4.53 million, hemoglobin 12.5 Gm. Target-oval-cell trait negative.

J.L.B. (brother of patient), age 33. Diabetic. Group A, Rh positive. RBC 4.39 million, hemoglobin 13.5 Gm. Target-oval-cell trait positive.

J.B. (brother of patient), age 28. RBC 5.37 million, hemoglobin 15 Gm. Target-oval-cell trait positive.

F.B. (brother of patient), age 24. Group A, Rh positive. RBC 4.74 million, hemoglobin 14 Gm. Target-oval-cell trait negative.

M.B.C. (sister of patient), age 20. Severe diabetic. Group O, Rh positive. RBC 4.67 million, hemoglobin 14 Gm. Target-oval-cell trait negative.

P.B. (daughter of patient) age 3. Group O, Rh positive. Target-oval-cell trait positive.

One maternal uncle and his daughter were negative for target-oval-cell trait.

When last examined in March 1948 the patient was in good health. His red cell count was 6.0 million; his blood showed a high proportion of oval cells but only an occasional target cell was observed. When re-examined in November 1948, the patient's physical condition and blood counts were unchanged. He has continued to receive liver injections two to four times monthly.

Summary

1. Coincidental Mediterranean anemia and pernicious anemia were found in a 26 year old soldier of Sicilian parentage.

2. The diagnosis of pernicious anemia was made on the finding of achlorhydria after histamine, glossitis, megaloblastic bone marrow and macrocytic anemia which responded to liver extract on two occasions.

3. The diagnosis of mild Mediterranean anemia was made by finding the target-oval-cell trait in the patient and in five members of his family.

4. It is of interest that target cells were not found in the peripheral blood until treatment with liver was begun. While pernicious anemia dominated, the character of the peripheral blood picture was macrocytic. Liver therapy corrected this, whereupon "hypochromic polycythemia" characteristic of mild Mediterranean anemia was found.

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