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VACUOLATED WHITE BLOOD CELLS IN THALASSEMIA MAJOR*

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We report a case of thalassemia major in which severe cytoplasmic vacuolization was seen in white blood cells as well as in their precursors. Cytochemical examination of the vacuoles revealed Sudan Black staining. Consequently, we believe that our patient had Jordans' anomaly coexisting with thalassemia major. *Key words: vacuolated white blood cells, thalassemia major.*

Vacuolization of polymorphonuclear leukocytes (PNLs) has been described in various conditions, but is not known to be associated with thalassemia major. Here we report the occurrence of vacuolization of PNLs in a case of thalassemia major.

Case Report

A ten-year-old boy, the product of a marriage between cousins, was diagnosed with thalassemia major at the age of three years. In September 1990, when the patient was nine years old, he was referred to our institution because of an increased transfusion requirement and an extremely enlarged spleen. On admission, he looked pale with a typical thalassemic face. He was 24 kgs in weight and 120 cms in height with no signs of infection (hematological findings are shown in Table I). The differential leukocyte count revealed 72% PNLs, 5% eosinophils and 23% lymphocytes. Three to twelve round, regular, cytoplasmic vacuoles were noted in 70% of the PNLs on peripheral blood smear, a feature which had persisted since he was first diagnosed. Bone marrow aspiration smear revealed similar vacuoles in most myeloid precursors (Fig. 1). Vacuoles were stained only with Sudan Black (SB) but not with Periodic Acid Schiff (PAS) (Fig. 2). Among all of the patient's family members, scant vacuoles in a few leukocytes were detected only on his mother's peripheral blood smear.

Except for a slight increase in transaminases (SGOT 60 IU, SGPT 66 IU), all blood biochemical determinations were found to be normal, with a vitamin B_{12} level of 539 pg/ml and folic acid of 9.8 ng/ml.

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Table I: Some Hematologic Data of the Patient and His Parents (on Admission)

	Hb g/dl	WBC /mm^3	MCV fl	RBC 10^{12}/L	HbF %	HbA_2 %	Spleen in cm	Liver in cm
Patient	6.4	6500	63	2.4	17.4	7.8	10	6
Mother	10.2	8000	74	5.6	2.0	5.1	–	–
Father	10.5	9200	76	5.9	2.4	5.3	–	–

Hb : Hemoglobin.
WBC : White blood cell count.
MCV : Mean corpuscular volume.
RBC : Red blood cell count.
HbF : Hemoglobin F.
HbA_2 : Hemoglobin A_2

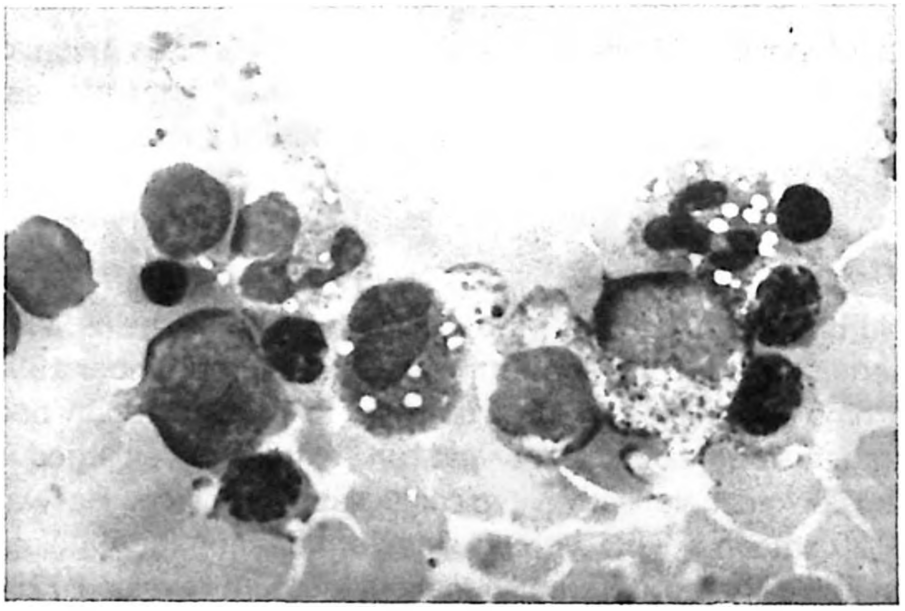

Fig. 1: Patient's bone marrow smear stained with Wright's stain.

Since vacuolization of white blood cells has been described in riboflavin and pyridoxine deficiencies, a therapeutic course of riboflavin (15 mg/day) and pyridoxine (25 mg/day) was given for fifteen days. Vacuolization in PNLs persisted following splenectomy.

Currently, the patient receives red blood cell transfusions monthly along with daily folic acid and penicillin prophylaxis.

Discussion

Vacuolization of blood cells may be found in various conditions, such as chloramphenicol administration[1], phenylketonuria[2], riboflavin[3] or copper

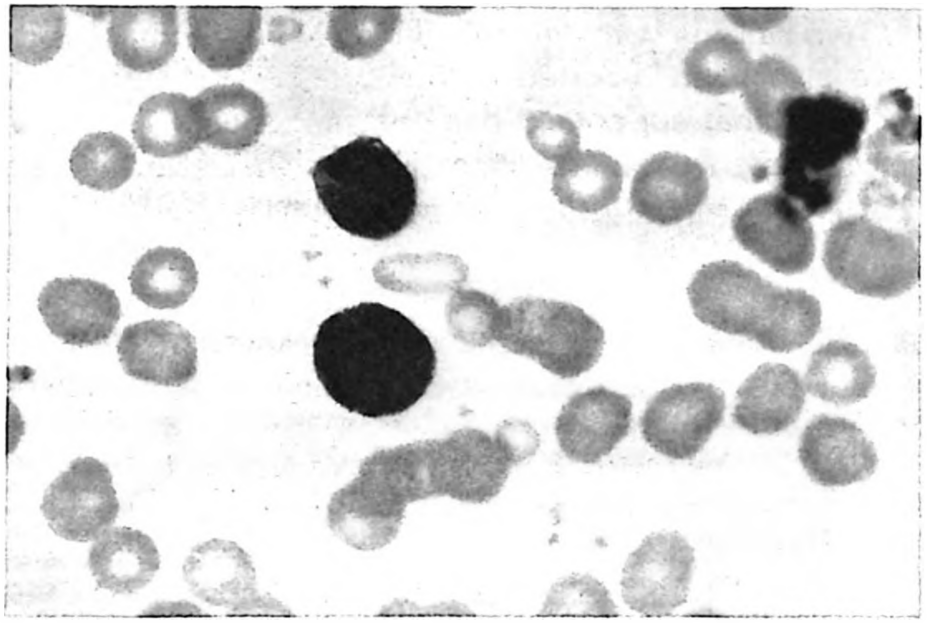

Fig. 2: Peripheral blood smear stained with Sudan Black. Note stained vacuoles in white blood cells.

deficiency[4], pyrazinamide toxicity[5], alcohol consumption[6], severe megaloblastic anemia[7] and infections[8].

In the present case, there was no history of chloramphenicol or pyrazinamide administration; the patient's alcohol usage, vitamin B_{12} and folic acid levels were normal, and no megaloblastic changes were observed on bone marrow aspiration smear. Since we were not able to determine riboflavin and pyridoxine levels he was given a therapeutic trial of these vitamins with no response. Actually, vacuolization in the above-mentioned conditions has generally been described as occurring in the erythroid cell line, whereas it was strikingly in the myeloid cell line in our case.

Vacuolization of lymphocytes has been described in association with lipid metabolism diseases[9], but in our patient's case the cholesterol and lipid levels were normal. Vacuolization in the myeloid cell line has been defined in Shwachman-Diamond syndrome[10], Pearson's bone marrow and pancreatic insufficiency syndrome[11,12]. Our patient, however, had no evidence of malabsorption or leukopenia, as is described in those syndromes. He also suffered from no severe or frequent infections, despite being diagnosed with thalassemia major. Therefore, an immunodeficiency or functional abnormality in his vacuolated leukocytes was not suspected.

In 1953, Jordans described a syndrome with the presence of fat-containing vacuoles in the white blood cells of two brothers with progressive muscular dystrophy[13]. Shortly thereafter, a similar anomaly of white blood cells coexisting with ichthyosis was reported in several families with autosomal recessive

inheritance[14]. Two siblings with Jordans' anomaly but no muscular dystrophy or ichthyosis have also been reported in Turkey[15].
We strongly believe that our patient has Jordans' anomaly and that his case is unique in the coexistence of this anomaly with thalassemia major.

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