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Diamond–Blackfan Anemia Associated With β-Thalassemia Trait

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A 14-month-old boy was referred to our hospital for evaluation of severe anemia. In the bone marrow aspiration smear, normal cellularity with severe erythroblastopenia (3%) was observed. The hemoglobin electrophoresis of the patient and his father were compatible with the β-thalassemia trait. Because macrocytosis of Diamond–Blackfan anemia (DBA) is masked by microcytosis of β-thalassemia trait, the diagnosis of DBA co-existing with β-thalassemia trait might be challenging. We report herein a case of DBA co-existing with β-thalassemia trait in a Turkish boy. Am. J. Hematol. 81:214–215, 2006. © 2006 Wiley-Liss, Inc.

Diamond–Blackfan anemia (DBA) is a rare, congenital hypoplastic anemia, often diagnosed early in infancy. The disease is characterized by a moderate to severe normochromic, usually macrocytic anemia [1–3].

β-Thalassemia is not rare in Turkey. The overall frequency of β-thalassemia in Turkey is 2%, and there are some significant regional differences [4]. The co-existence of β-thalassemia with other congenital disorders would not be surprising in Turkish population. Patients with β-thalassemia trait have reduced MCV and increased HbA_2, whereas patients with DBA typically have a high MCV [1,4,5].

Because macrocytosis of DBA is masked by microcytosis of β-thalassemia trait, the diagnosis of DBA co-existing with β-thalassemia trait might be challenging. Some characteristic hematological parameters and the expression of the disease have been altered. Herein we report a case of DBA co-existing with β-thalassemia trait in a Turkish boy.

A 14-month-old boy was referred to our hospital for evaluation of severe anemia. His past history revealed that the first presentation of severe anemia had occurred when he was 6 months old, and he received transfused packed red blood cells in a local hospital (Hb: 3.8 g/dL). He is a product of a consanguineous marriage and has three healthy siblings. He had an uncomplicated birth and no delay in his mental–motor development. There was no family history of either hematological or other disorders.

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The physical examination revealed growth retardation, paleness, and bilateral undescended testes. His body weight was 13 kg (3–10 percentile); height, 92 cm (3 percentile); and head circumference, 46 cm (25–50 percentile).

The hematological parameters of the patient and his father are shown in Table I. When he arrived at our hospital, his MCV value was 80 fL. In follow-up laboratory studies, his MCV value was ranged between 57 and 82 fL. However, all of the MCV values were lower than estimated. In the bone marrow aspiration smear, normal cellularity with severe erythroblastopenia (3%) was observed. Serum iron was 106 μg/dL; serum iron binding capacity, 252 μg/dL; transferrin saturation, 42%; and ferritin, 239 ng/mL. The hemoglobin electrophoresis of the patient was compatible with the β-thalassemia trait (HbF 0.5%, HbA_2 4.8%). DNA analysis of the patient and the father showed β-thalassemia IVS I-110 (G→A) mutation. The erythrocyte adenosine deaminase (ADA) level was moderately raised. As a result

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TABLE I. Some of the Hematological Parameters of the Patient and Father

	Hb (g/dL)	RBC (10^{12}/L)	MCV (fL)	RDW (%)	WBC (10^9/L)	Platelet (10^9/L)	Reticulocyte (%)	HbA_2 (%)	HbF (%)	β-Thalassemia mutation
Patient	3.4	2.3	80	16	9.8	625	0.2	4.8	0.5	IVS I-110 (G→A)
Father	14	6.2	68	14	10	338	1	5	0.5	IVS I-110 (G→A)

of these laboratory investigations, the diagnosis of DBA co-existing with β-thalassemia trait was established and the patient was treated with prednisolone. He is 14 years old now. At his last follow-up (in July 2004), he was well with a Hb of 11.2 g/dL, Htc of 34%, and MCV of 76 fL.

Patients with macrocytic anemia typically have macrocytosis, but with co-existing disorders that produce microcytosis such as iron deficiency, thalassemia, or anemia of chronic diseases over MCV to a normal or low value [6–8]. Alter reported that macrocytic anemia may not be macrocytic in the face of microcytosis caused by genetic or acquired hematological diseases [9]. DBA may be overlooked when the MCV value is in the normal range in such patients. Reticulocyte count and bone marrow examination are important in the differential diagnosis of DBA. Our patient had β-thalassemia trait masking the macrocytic anemia of DBA. Hb electrophoresis of the patient and parents resolved the picture, and the diagnosis of DBA co-existing with β-thalassemia trait was established. This observation indicated that in DBA with an unexpected MCV value, co-existence of another hematological disorder should be suspected.

In populations with a high incidence of β-thalassemia, such as Turkey, the combination of β-thalassemia and congenital hematological diseases may occur. In Turkey, where the incidence of Fanconi anemia (FA) seems high, the co-existence of β-thalassemia trait and FA in a patient has not been surprising [7]. Imerslund–Gräsbeck syndrome (specific vitamin B_{12} malabsorption) co-existing with β-thalassemia trait has also been reported from Turkey [8].

Finally, this case suggests the general concept that macrocytic anemia may not be macrocytic when macrocytosis is masked by the microcytic effect of the any cause of the microcytic anemia. This case also indicates the importance of detailed hematological evaluation of the patient and parents. Such a detailed study will help to detect the presence of another genetically transmitted hematological abnormality.

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