TABLE 1. Blood Cell Parameters, Hemoglobin Electorphoresis, and Thalassemia Gene Types of Patient and His Parents

	Blood Cell Parameter						Hemoglobin Electrophoresis			Thalassemia Gene Type	
	Hb (g/L)	RBC (10^9/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	RET (%)	HbA_2 (%)	HbF (%)	Hb H	α	β
Patient	23	1.33	58	17.4	298	6.3	2.2	0.6	+	—	—
Father	155	4.87	90	31.8	353	1.1	2.8	0.2	—	—	—
Mother	131	4.29	85	30.5	360	0.6	2.5	0.5	—	—	—

Hb H indicates hemoglobin H; MCHC, mean corpuscular hemoglobin concentration; RBC, red blood cells; RET, reticulocytes.

Here, we report a boy diagnosed with acquired Hb H disease and Down syndrome. In October 2009 a 10-year-old boy with severe anemia was first diagnosed with thalassemia. Clinical examination also revealed that he had profound mental and severe growth retardation, hypotonia, joint laxity, pale and soft skin, hepatosplenomegaly, skeletal changes associated with osteoporosis, severe anemia, prominent facial features including a flat facial profile; thin, straight hair; protruding tongue and small nose. Therefore, he was also diagnosed as having Down syndrome. His somatic chromosomes were prepared from peripheral blood lymphocytes by a standard procedure. Using the trypsine-giemsa banding (GTG), his karyotype was found to be 47, XY, +21. Blood cell parameters are shown in Table 1. Analysis of his hemoglobins using high-performance liquid chromatography showed the presence of a manifest Hb H strand, which was confirmed by Tris-ethylene diaminetetra acetic acid-borate electrophoresis and agarose isoelectrofocusing. However, molecular analysis by GAP-polymerase chain reaction and reverse dot blot test did not show any mutation in his α and β genes, and neither in the blood cell parameters and globin gene structures of his parents (Table 1). Therefore, this patient was finally diagnosed as acquiring Hb H disease secondary to Down syndrome.

Acquired Hb H disease occurs most commonly in patients with myelodysplastic syndrome (MDS).[5] In 2002, a 10-year-old girl with congenital Fanconi anemia had been reported to develop acquired Hb H disease secondary to MDS.[6] MDS and acute myeloid leukemia are common in Down syndrome.[7] It is hypothesized that this patient acquired Hb H disease after developing MDS.

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Langerhans Cell Histiocytosis in a Child With Non-Hodgkin Lymphoma

To the Editor:

Langerhans cell histiocytosis (LCH) is a rare disorder, characterized by proliferation of the Langerhans cells. The disease predisposes patients to a wide spectrum of clinical manifestations with high rate of morbidity and mortality, especially in children.[1–3] LCH may precede, coincide with, or develop after treatment of some malignancies such as leukemia and lymphoma [Hodgkin disease and non-Hodgkin lymphoma (NHL)].[4–6] Although the majority of cases develop malignancies after LCH therapy, some patients present cancers before the diagnosis of LCH. Herein, we describe a girl with diagnosis of NHL, who developed LCH after a 7-year period.

The patient is a 15-year-old Iranian girl who had been referred to our center at the age of 6 years with right-knee pain and fever, right inguinal lymphadenopathies, and left eye proptosis. Abdominal ultra sonography revealed hypoechoic areas in both kidneys, which indicated renal infiltrations. Orbital magnetic resonance imaging revealed round hypointense foci in retroorbital space, whereas some lytic lesions in the lumbar vertebrae, head of femur, and iliac bone were found in bone surveys. Although bone marrow aspiration and biopsy were normal, biopsy of the inguinal lymph node revealed immunoblastic lymphoma (large cell lymphoma); in immunohistochemistry (IHC) studies, leukocyte common antigen (LCA), Desmin, and Vimentin were negative. The diagnosis of NHL (stage IV) was made for the patient. Treatment based on COAP (Cyclophosphamide, Vincristine, Doxorubicin, Prednisone), Methotrexate, L-Asparaginase protocol was started. She responded well to this treatment.

She was well until the age of 13 years, when she was complicated with a frontal mass. Bone survey revealed multiple cortical lytic lesions in the superior metaphysis of the left tibia, left fibula, femur and frontal bone, and reduction of the height of the T12 vertebrae, which was confirmed by whole body bone scan. Biopsy of the frontal bone revealed irregular grooved nuclei and eosinophilic infiltration compatible for diagnosis of histiocytosis, which was confirmed by IHC study. Treatment with Vinblastine and prednisolone was started. After induction-phase therapy and reevaluation, maintenance therapy with cyclosporine, 6-mercaptopurine, and Methotrexate has been administered. After 2 years of successful maintenance therapy, the treatment was discontinued. She is under regular follow-up now without any further complication.

TABLE 1. Selected Reports of Secondary Histiocytosis Associated With Malignant Lymphoma

Authors	Type of Study	Description	Reference
Egeler et al	Review of literature, including the report from the University of Minnesota	11 patients with secondary LCH associated with malignant lymphoma (2 NHL)	5
Egeler et al	The LCH-malignancy study group of the Histiocyte Society	54 patients with secondary LCH and history of malignancies	6
Celkan et al	Multicenter study in Turkey	4 patients with secondary HLH associated with malignant lymphoma (2 NHL)	7
Kjeldsberg et al	Case series from USA	6 patients with LCH associated with malignant lymphoma (3 NHL)	8
Burns et al	Case series from USA	6 patients with LCH associated with malignant lymphoma (1 NHL)	9
Veerakul et al	Case series from Thailand	15 patients with HLH associated with NHL	10

HLH indicates hemophagocytic lymphohistiocytosis; LCH, Langerhans cell histiocytosis; NHL, non-Hodgkin lymphoma.

Association between malignancies and LCH seems to be more frequent than earlier thought.[5] However, there are only few reported cases that malignant neoplasm preceded the LCH (Table 1).[4,6,7] Although acute leukemia was introduced as the most common malignancy associated with LCH, Hodgkin disease and NHL could also precede secondary LCH (Table 1).[8–10] In our case, LCH was diagnosed 7 years after the treatment of malignant disorder. In more than half of reported LCH-lymphoma cases, LCH was diagnosed within 2 years after development of malignancies, which could suggest the LCH as a reaction to the lymphoma. However, in the majority of LCH-lymphoma cases, the LCH was closely involved pathologically with the primary malignant neoplasm and the diagnoses usually were made concurrently.[5]

Although development of malignancies in patients with LCH was well-documented after treatment, presence of LCH after malignancies could suggest regular follow-up of patients, whereas timely diagnosis and appropriate treatment can prevent furthermore complications.

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