Langerhans Cell Histiocytosis with Transformation to Acute Leukemia Showing 45,X, t(8; 21), 5q-, -Y Karyotype

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A 31-year-old man was admitted to hospital with onset of difficulty in walking and urinary incontinence, leading to the diagnosis of Langerhans cell histiocytosis (LCH) which was replacing a thoracic vertebra. Four months after the completion of radiation therapy, he was referred to our department with persistent fever and severe pyogenic ulceration mainly affecting the right hip. A diagnosis of acute non-lymphoblastic leukemia (ANLL) was made. Cytogenetic studies showed 45,X, t(8;21), 5q-, -Y. We report this case because, development of acute leukemia after LCH is rare and the literature searched for any cytogenetic study in these kind of cases yielded no data.

Keywords: Langerhans cell histiocytosis; Acute leukemia; Karyotype

INTRODUCTION

Langerhans cell histiocytosis (LCH) is characterized by mononuclear phagocytic cell proliferation and evidence of granulomas in liver, spleen, lymph nodes, central nervous system and bone marrow. The etiology of LCH remains unknown. The granulomas consist of histiocytosis predominantly; mature eosinophils, lymphocytes and rarely neutrophils and plasma cells. The majority of cases are infants and young adults [1,2]. It has a wide clinical spectrum, from single bone involvement to multisystemic disease with organ failure [3]. The development of LCH and malignant neoplasms especially leukemias and lymphomas in the same individual appears to be frequent [4–6]. Here we describe the case of acute non-lymphoblastic leukemia (ANLL) in a patient with LCH showing 45,X, t(8;21), 5q-, -Y abnormality and the literature searched for any cytogenetic study of these cases yielded no data.

CASE REPORT

A 31-year-old man was admitted to the hospital with complaints of inability to walk and urinary incontinence. His neurologic examination showed spastic paraparesis, hypoesthesia under 7th thoracic vertebrae, bilateral clonus and Babinsky sign on the right side. Magnetic resonance imaging scan of the thoracic spine showed and extradural mass 44 × 7 × 15 mm in dimension located between upper level of 7th thoracic vertebra body and lower level of the 8th thoracic vertebra body, displacing the cord anteriorly. The patient underwent subtotal tumor excision and a diagnosis of LCH was made. Subsequently he received 150 cGy a day radiation therapy over a week. Four months after radiation, the patient was brought to our department with a history of paralysis, right-hip pyogenic ulceration and fever. His physical examination showed a temperature of 38.6°C, signs of pallor, bilateral pulmonary crackles, hepatomegaly, hypoesthesia under the level of T7 and pyogenic hip lesion (4 × 3 cm in diameter).

Laboratory results showed white blood cells 1.9 × 10⁹/l, hemoglobin 6.76 g/dl, platelets 14 × 10⁹/l. The examination of peripheral blood smear involved granular blast cells with low nucleocytoplasmic ratio as well as Auer bodies in some. Normoblasts were rarely seen. Serum chemistry was as follows: blood urea nitrogen (BUN) 42 mg/dl (normal range 5–20 mg/dl), creatinine 1.7 mg/dl (normal range 0.5–1.1 mg/dl), uric acid 10.3 mg/dl (normal range 2.3–7.0 mg/dl), sodium 124 mEq/l (normal range 135–150 mEq/l), potassium 2.8 mEq/l (normal range 3.5–5 mEq/l), total protein 5.0 g/dl (normal range 6–8.5 g/dl), albumin 1.9 g/dl (normal range 3.5–5 g/dl), lactate dehydrogenase (LDH) 784 U/l (normal range 98–270 U/l), total bilirubin 4.8 mg/dl (normal range 0–0.9 mg/dl), direct bilirubin 4.1 mg/dl (normal range 0–0.3 mg/dl).

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FIGURE 1 Blasts with a low nucleocytoplasmic ratio, intracytoplasmic granules and Auer bodies in the bone marrow aspiration (Wright × 2000).

A bone marrow aspirate contained 80% blasts with a low nucleocytoplasmic ratio, intracytoplasmic granules and vacuoles, rare Auer bodies, and cytoplasmic blebs (Fig. 1). The leukemic cells were myeloperoxidase (MP) and Sudan black stain (SBB) positive, alpha naphyl acetate acid esterase (ANAE) negative, periodic acid Schiff (PAS) negative. Immunophenotypic studies demonstrated CD19, CD33, CD13, anti-HLADR on the leukemic cells. Histopathologic examination of the bone marrow biopsy revealed both hypercellular and normocellular areas between the bone trabeculae. Immature myeloid cells were increased especially near the trabecular bone. Most of the sinusoids were disrupted or obliterated by blasts, promyelocytes, erythroid precursors, histiocytes and plasma cells. One or four nucleoli and scant pale cytoplasm were present in the blasts. Erythroid precursors were reduced in number and dyserythropoiesis was evident. There were phagocytic histiocytes some with lobulated vascular nuclei (Figs. 2 and 3). Lysosome-like structures were observed in a few histiocytes. Megakaryocytes were decreased in number in these areas; however abnormalities in localization and nuclear lobation increased near the hypercellular zones. Some of them had a large ovoid mononuclear nucleus or had 2 and 3 small separate nuclei with irregular contour. Reticulin staining revealed mild to moderate reticulin fibrosis. Cyto genetic studies of the bone marrow showed 45,X, t(8;21), 5q−, −Y (Fig. 4). The diagnosis of ANLL-M2 was made.

The patient was started on cefapiramine + sulbactam, amikacin and metronidazole therapy for febrile neutropenia. He failed to respond within 48h requiring vancomycin. On day 6 of hospitalization, the patient developed massive hemoptysis. Radiograms showed reticulonodular infiltrations in the lungs and the patient was found to be hypoxic (arterial blood determination showed PO₂: 48 mmHg). He continued to develop acute respiratory failure requiring mechanical ventilation. Twelve hours after extubation, he died.

DISCUSSION

The association of LCH with a malignant neoplasm, especially hematologic malignancies is not that rare. Egeler et al. reported a series of 91 patients with LCH; 39 of these had malignant lymphoma, 22 acute leukemia, 12 lung carcinoma and 18 other solid tumors in combination with LCH [4]. The latency of malignant neoplasm after the diagnosis of LCH is suggestive of impaired immunity or therapy-related process [7].

In the literature the time between diagnosis of LCH and subsequent leukemia was found to be a median of 4 years [5]; but in our patient LCH preceded the diagnosis of acute leukemia within a year of initial neurological symptoms and within 4 months of histopathological diagnosis. LCH transforming to ANLL appears more frequently than acute lymphoblastic leukemia (ALL) and it is likely that the occurrence of subtype acute monoblastic leukemia (M₅) is even greater [4]. In our patient the subtype of acute myeloblastic leukemia was M₂−FAB.

In LCH (t(7; 12) (q11; p13) may appear [8]. To the best of our knowledge there is no case in the literature with a cyto genetic study in the LCH-leukemia cases seen so far. In our patient cyto genetic studies showed 45,X, t(8; 21), 5q−, −Y and while t(8; 21) suggested a good probability for survival the 5q− is a marker of unfavorable prognosis. The cyto genetic abnormalities seen in our case suggest that an

FIGURE 2 Immature myeloid cells, blasts, erythroid precursors, plasma cells and phagocytic histiocytes are seen in the hypercellular area. Myeloid cells and plasma cells are engulfed by some histiocytes (Hematoxylin-eosin × 400).

FIGURE 3 (A) A group of histiocytes are seen in the bone marrow biopsy (Trichrome-Masson × 800). (B) Two histiocytes which having lobulated vesicular nuclei (Trichrome-Masson).
existing cytogenetic abnormality may perhaps lead to LCH.

In conclusion, because of its unfavorable course, bone marrow transplantation is probably to be an appropriate treatment after the initial diagnosis of LCH. Close follow-up of these patients is always needed because of the associated increased incidence of malignant neoplasms; mostly acute leukemia.

References


