

## Case Report

# Successful treatment of a case of acute myeloid leukemia following Langerhans cell histiocytosis in an adolescent: a case report and review of the literature

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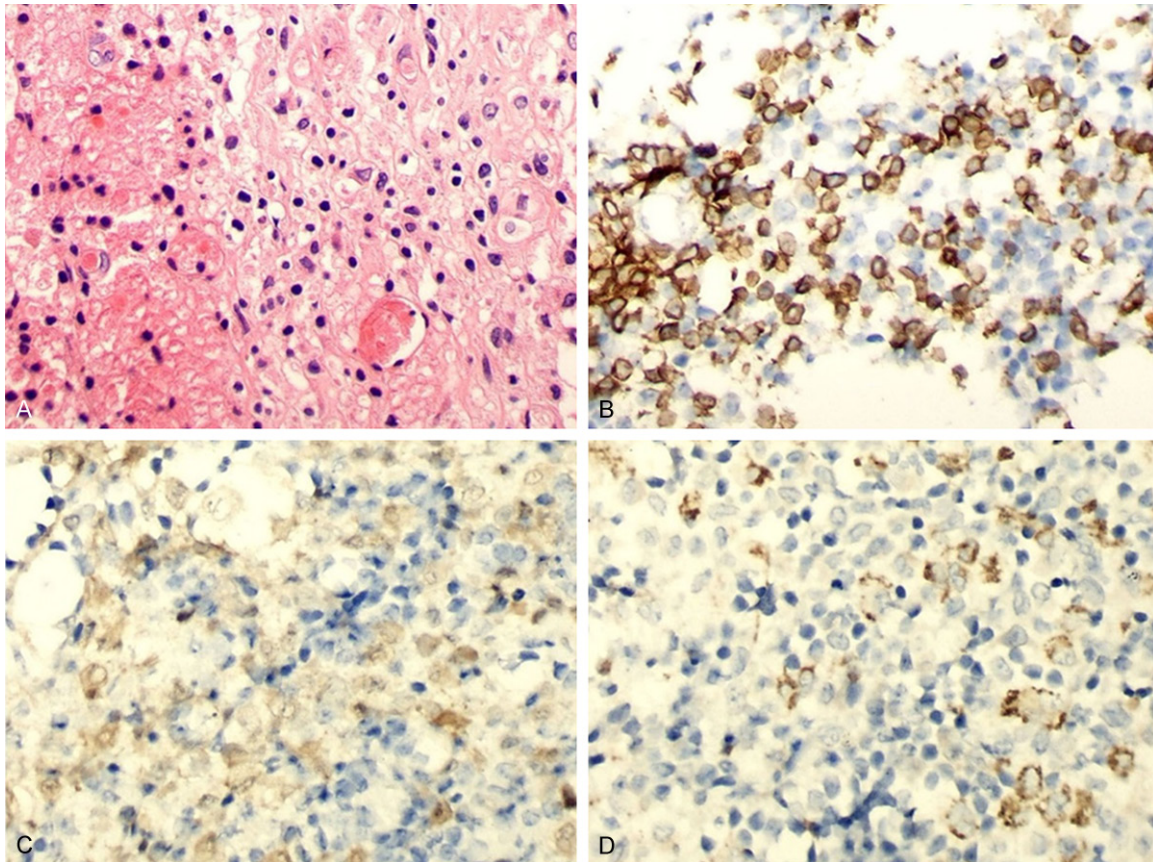
**Abstract:** Langerhans cell histiocytosis (LCH) is a rare histiocytic disorder of unknown etiopathogenesis. Its clinical presentation is variable and ranges from isolated skin or bone disease to a life-threatening multisystem condition. LCH can occur at any age but is more frequent in the pediatric population. The diagnosis depends on clinical, histopathological and radiographic examination and should be confirmed by immunohistochemical study with CD1a, S100 protein and langerin, three markers used widely for identifying Langerhans cells. Herein, we report an adolescent with acute myeloid leukemia (AML-M2) who was treated just with surgical management alone for LCH. As far as we know, this is the first case that the LCH patient without chemotherapy evolved into AML and was successfully cured. Cooperative studies of large numbers of LCH patients are needed to evaluate a possible association between LCH and acute leukemia, and to identify common risk factors or predisposing agents if such be present. The previously reported cases of LCH concomitant with other hematological disorders are also summarized and described compared with the present case.

**Keywords:** Acute myeloid leukemia, Langerhans cell histiocytosis, adolescent

## Case report

A 14-year-old girl presented to our orthopedic clinic with a left thigh pain for 3 months on 13 Dec, 2011. She did not have any fever or hypothermia, anorexia or disturbed sleep. A blood count showed WBC  $6.6 \times 10^9/L$ , leucocytes,  $1.9 \times 10^9/L$ , hemoglobin, 124 g/d and platelets,  $128 \times 10^9/L$ . Bone MRI showed the upper section of the left femur osteomyelitis. Histiocyte-like cell infiltration was seen in the bone biopsy of the lesion. CD3, CD20, CD15, CD30, CD5, CD138, Lambda, Kappa, Bcl-2, ALK, CD23, CD10, Bcl-6, keratin, EMA, HMB-45, and Cyl D1 were negative. However, these histiocytes were positive for CD1a, S-100 protein and CD68 (Figure 1A-D) According to Lavin-Osband grading and clinical type, the girl was divided to Class I and surgical resection was administrated only. The pain was disappeared after the operation and thereafter the girl was going into the orthopedic out-patient clinic for following-up. When she came to orthopedic clinic due to

dizzy on 12 Mar, 2013, the blood routine examination was done and the result showed significantly abnormal in blasts cells. She was transferred to the hematology department immediately. Bone marrow aspiration reveals: Primitive myeloid cell abnormalities increased, occupies 45% of nucleated cells. AML1-ETO and FLT3-ITD are negative. Immunophenotyping shows: myeloblasts accounted for 35.96% of non-erythroid. A cytogenetic analysis of the leukaemic cells showed 46, XX. A diagnosis of acute myeloid leukemia (AML)-M2 was made. The patient responded well to chemotherapy. A standard HAA (homoharringtonine 2 mg/m<sup>2</sup> per day on days 1-7, cytarabine 100 mg/m<sup>2</sup> per day on days 1-7, and aclarubicin 20 mg/day on days 1-7) was given and the girl achieved a complete remission (CR) after one cycle. After additional several consolidation chemotherapy including 3 cycles of HAA and 1 cycle of IA (cytarabine 100 mg/m<sup>2</sup> per day on days 1-7, and idarubicin 12 mg/m<sup>2</sup> per day on days 1-3), the patient received an allogeneic hematopoietic stem cell



**Figure 1.** A: A diffuse infiltration of the bone biopsy of the lesion with Histiocyte-like cell (Original magnification, ×200); B: CD1a Positive (Original magnification, ×100); C: S-100 positive (Original magnification, ×100); D: CD68 positive (Original magnification, ×100).

transplant. Her sister gave her bone marrow and fortunately they matched very well. The patient received a conditioning protocol composed of busulphan and cyclophosphamide. She was given fluconazole, acyclovir and bac-trim as infection prophylaxis and methotrexate and cyclosporine as graft versus host disease (GVHD) prophylaxis. Fortunately up to 13 Sep, 2014, the girl is in the state of persistent CR 20 months after the first diagnosis of the AML.

### Discussion

Langerhans cell histiocytosis (LCH) is a class of histiocytic cell neoplasm with a clonal neoplastic proliferation of Langerhans-type cells that express CD1a, langerin, and S100 protein and show evidence of Birbeck granules by ultra-structural examination. Concurrent LCH and malignancy have been reported occasionally. LCH occurred before or after malignancies including acute myeloid leukemia, acute lymphoblastic leukemia, and several solid tumors

such as malignant lymphoma, retinoblastoma, lung carcinoma, ependymoma, hepatocellular carcinoma, skin tumor, etc. LCH in association with leukemia occurs mainly in two clinical patterns: LCH preceded by acute lymphoblastic leukemia (pathogenesis undefined) and LCH treated by etoposide/vinblastine followed by therapy-related AML [1, 2]. Concomitant LCH and AML have very rarely been reported [3, 4]. Two explanations for this extraordinary phenomenon have been proposed: LCH and AML deriving from the same neoplastic precursors or LCH being reactive to the AML [1-4]. Haupt R et al [5] reported that high doses of VP-16 appear to increase the risk of s-ANLL in LCH patients. The following cases reported which suggested that high doses of etoposide in subjects of Latino origin may lead to aberrations on chromosomes 15 and 17 [5]. Chang NY et al [6] described the first case of Hand-Schuller-Christian disease (LCS) in a chronic myelogenous leukemia (CML) patient undergoing ima-

tinib mesylate therapy. Yohe SL et al [7] reported four patients presented with acute leukemia of ambiguous or myeloid lineage in association with LCH and provided evidence suggesting a common origin of the two neoplasms. Bohn O et al [8] reported an adult patient with simultaneous LCH and AML with t(9;11). ALL their findings support the concept that coexistent Langerhans cell histiocytosis and acute leukemia is clonally related in some cases. Furthermore, these cases of acute myeloid or acute leukemia of ambiguous lineage with LCH share some unique features suggesting a common underlying neoplastic hematopoietic stem cell. We report a rare case of solitary LCH involving the femur of an adolescent who was diagnosed AML 15 months after the onset of LCH without any chemotherapy for LCH. Our case illustrates that the onset of acute myeloid leukemia in the patient of LCH is not only associated with chemotherapy, certain underlying mechanism may exist. Cooperative studies of large numbers of LCH patients are needed to evaluate a possible association between LCH and acute leukemia, and to identify common risk factors or predisposing agents if it such be present. Here, our case shows that the standard HAA [9] based chemotherapy joint allogeneic hematopoietic stem cell transplantation may be a good choice for these patients.

## Disclosure of conflict of interest

None.

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