

A Case of Erythrophagocytosis in a T-cell Lymphoblastic Lymphoma

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Abstract—A case of non-Hodgkin lymphoma with erythrophagocytosis by the tumor cells is reported. The patient was an eight-year-old Korean boy who had multiple enlarged lymph nodes. Characteristically marked erythrophagocytosis by the tumor cells was seen in the lymph node and bone marrow biopsy. Immunohistochemical study showed that those cells were T-cell in origin.

Key Words: *Erythrophagocytosis, T-cell lymphoblastic lymphoma*

INTRODUCTION

Non-Hodgkin lymphoma(NHLs) are a group of heterogeneous malignant neoplasms of lymphoreticular cell origin with distinct histopathological and biological properties. NHLs in children are quite different from the lymphomas commonly seen in adult patients. Almost all childhood NHLs demonstrate a diffuse pattern, and diffuse lymphoblastic lymphoma, which is one of the most common histological types in NHLs (Murphy *et al.*, 1989), is predominantly a T-cell neoplasm (Link 1985).

Hemophagocytosis in leukemia, lymphoma or other solid tumors has been reported frequently, but in most cases, erythrophagocytosis is associated with the proliferation of histiocytes simulating malignant histiocytosis. Hemophagocytosis by tumor cells is a rare phenomenon especially in lymphomas (Kuratsune *et al.*, 1988). Some cases have been reported in adult T_γ lymphoma (Kadin *et al.*, 1981) or in Sezary syndrome (Schechter *et al.*, 1982).

In this paper we describe the case of a unique

T-cell lymphoblastic lymphoma associated with hemophagocytic syndrome. Histopathologic findings of the lymph node and bone marrow showed erythrophagocytosis by the tumor cells. To our knowledge, such an erythrophagocytosis by the tumor cells has not yet been reported in Korea.

CASE REPORT

An eight-year-old boy was admitted to another hospital in December 1986 because of swelling of the left side of the neck. Malignant lymphoma was diagnosed by lymph node biopsy, and the whole body CT revealed multiple enlarged lymph nodes in both sides of the neck, superior mediastinum and paraaortic area. He did not receive any specific therapy.

The patient was brought to Seoul National University Children's Hospital in March 1987. On examination a 9 × 4 cm-sized mass was palpable on the left side of the neck. He also had multiple small supraclavicular, axillary and inguinal lymph nodes. CBC included Hb of 11.4g/dl, WBC count of 5,000/mm³ (blast 3%, stab 4%, seg 67%, lympho 17%, mono 3%, baso 2%, immature cell 4%), and platelet count of 175,000/mm³. Lactic dehydrogenase was 193U/L, IgG, A, M, D were 802, 171, 339, 3.1mg/dl respec-

tively, and IgE was 44U/ml. A biopsy specimen from the left neck mass was interpreted as malignant lymphoma, a diffuse lymphoblastic type. Bone marrow finding showed infiltration of the immature lymphoid cells with erythrophagocytosis. He received induction chemotherapy with AD-COMP (L-asparaginase, Daunomycin, Cyclophosphamide, Vincristine, Methotrexate and Prednisolone), and remission was achieved. After maintenance chemotherapy until August 1988, immature lymphocytes which showed erythrophagocytosis were found in the follow-up bone marrow study in September 1989. He received induction chemotherapy again with CCG (Childrens Cancer Study Group)-106 B regimen. No residual neoplastic cells were found in the bone marrow after four weeks of induction chemotherapy. He is now under maintenance chemotherapy.

Summary of pathologic and immunohistochemical findings: In the bone marrow, immature cells including blast forms were totaled up to 37% of all nucleated marrow cells. Erythrophagocytosis by these immature lymphoid cells was frequently found (Fig. 1 and 2). Tumor cells were negative on PAS staining and partially positive on acid phosphatase staining. In the specimen from the left cervical lymph node, tumor cells with medium-sized nuclei showing fine homogeneously dispersed chromatin pattern in the cytoplasm were infiltrated interstitially, and erythrophagocytosis was frequently seen. Immunohistochemical studies with Leu-1, 2, 3, and Pan-B reagents showed helper (T_H) phenotype of Leu-1⁺(CD 5⁺), Leu-3⁺(CD 4⁺), Leu-2⁻(CD 8⁻).

DISCUSSION

Non-Hodgkin lymphomas comprise several distinct clinical and pathological entities which are, in most cases, immunologically distinct as well. A modification of the Rappaport Classification Scheme and the recently-reported Working Formulation for Clinical Usage can be applied to pediatric NHL, and it correlates quite well with biological and immunological phenotyping (Berard *et al.*, 1978). In childhood, follicular lymphomas are rare, and virtually all NHLs are of the diffuse type (Murphy *et al.*, 1989). Childhood NHLs can be divided into three major subgroups which seem to correlate immunological subtype

and biologic behavior: (1) diffuse undifferentiated lymphomas are virtually all B-cell derived, (2) lymphoblastic lymphomas are primarily of T-cell origin, and (3) large-cell lymphomas are variable (Berard *et al.*, 1978). The clinical feature of the lymphoblastic lymphoma is concerned with the cell of origin, which in most cases, is a cell at some stage on the differentiation pathway of the T lymphocytes. An anterior mediastinal mass is common, as is the involvement of the peripheral lymph nodes. The cervical, supraclavicular and axillary nodes are most often involved (Murphy *et al.*, 1989). Dissemination to the bone marrow and peripheral blood is common upon relapse in all patients (Amylon *et al.*, 1986).

The relationship between acute lymphoblastic leukemia and non-Hodgkin lymphoma needs further investigation, especially in the distinction between the T-cell ALL and the T-cell lymphoblastic lymphoma (Takasaki *et al.*, 1987). Early studies demonstrated that T-ALL is derived from T cells at the earliest stage of immunologic differentiation, whereas malignant cells of T-NHL arise from more mature T cells. The differences in clinical behavior between T-ALL and T-NHL relate to the differences in the extent of the tumor present at diagnosis rather than to a fundamental biologic difference (Bernard *et al.*, 1981).

Erythrophagocytosis is an uncommon, poorly understood feature of various tumors, including leukemias, lymphomas and solid tumors. In the hemophagocytic syndrome associated with malignant lymphoma that simulates malignant histiocytosis (Jaffe *et al.*, 1983), there is a marked proliferation and activation of histiocytes, but the proliferating histiocytes are benign and bland-looking, unlike in malignant histiocytosis (Warnke *et al.*, 1975). It has been proposed that systemic activation of histiocytes and hemophagocytosis may be related to the release of lymphokines by the T-lymphoma cells (Jaffe *et al.*, 1983; Chi-sing *et al.*, 1986). Kadin *et al.* (1981) reported on erythrophagocytic T_H lymphoma in two adult patients. In this case, neoplastic T_H cells exhibited erythrophagocytosis and a tissue distribution characteristic of cells of mononuclear phagocytic systems. They suggested that erythrophagocytosis seemed to be mediated by the Fc receptor, since phagocytosis by the tumor cells occurred *in vitro* only with IgG-co-

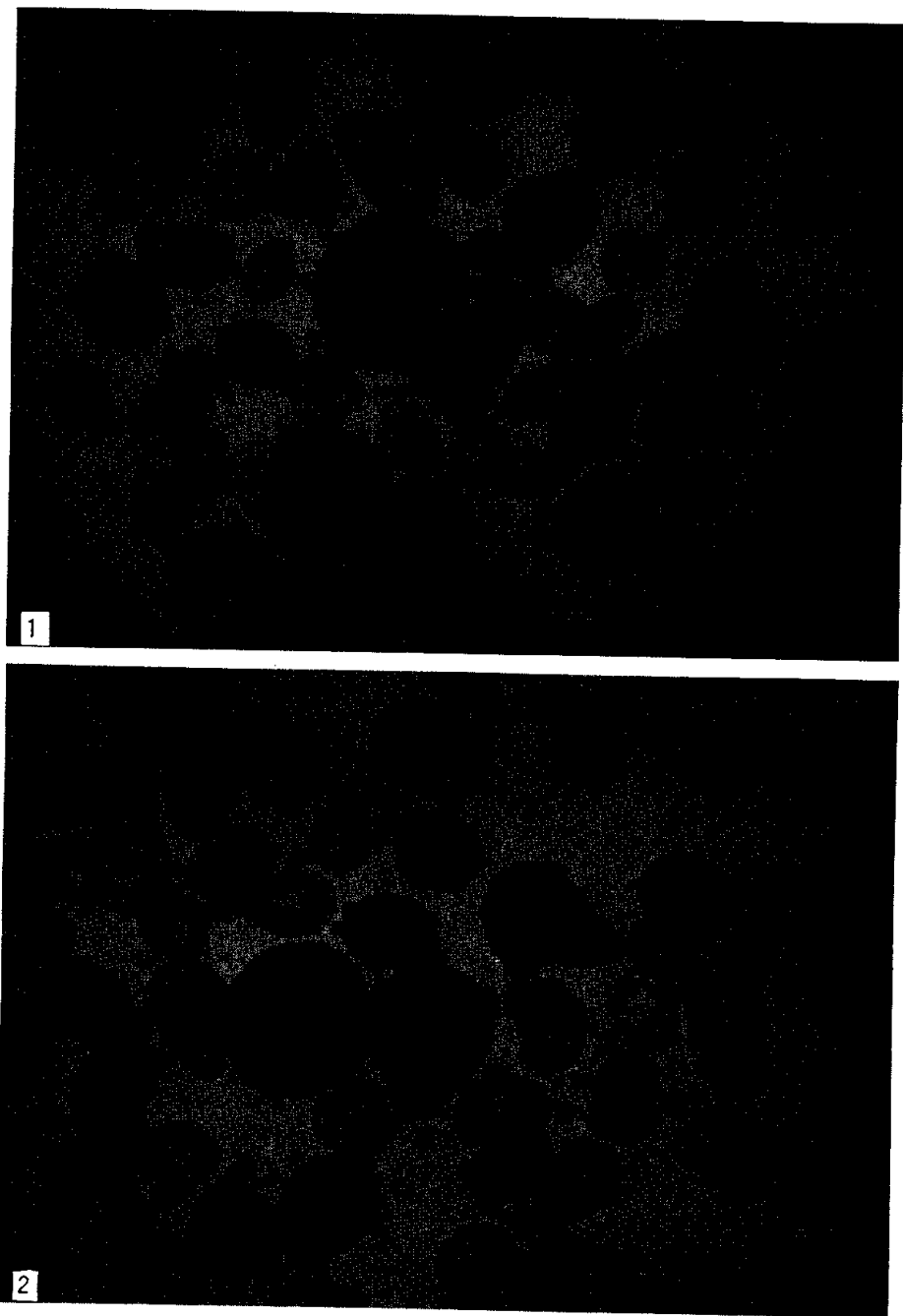


Fig. 1 and 2. Bone marrow aspiration specimen showing erythrophagocytosis by the tumor cells (arrow) (Wright stain, $\times 1000$)

ated erythrocytes.

In our case, the patient presented multiple lymphadenopathy. The immature cells including blast forms totaled more than 25% in the bone

marrow, which can be considered to be compatible with the criteria of acute lymphoblastic leukemia. Immunohistochemical studies showed that most tumor cells are positive for T₄ (helper)

marker. Erythrophagocytosis by the immature lymphoid cells is frequently found in the bone marrow and lymph node biopsy specimen unlike in the case of Kadin *et al.* The significance of erythrophagocytosis by tumor cells is uncertain and needs further investigation.

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= 국문초록 =

T-세포 림프아구성 림프종세포에 의한 적혈구탐식증 1례

서울대학교 의과대학 소아과학교실 및 병리학교실*

김기중 · 전인상 · 김철우* · 안효섭

종양세포의 적혈구탐식은 백혈병, 림프종 및 기타 고형종양등에서 매우 드물게 관찰되는 현상이다. 저자들은 표지검사상 T_h형을 보이는 8세된 림프종 남아의 림프절 및 골수표본에서, 종양세포가 적혈구탐식을 보이는 증례를 경험하였기에 문헌고찰과 함께 보고하는 바이다.