Haematology and Blood Transfusion Vol. 28
Modern Trends in Human Leukemia V
Edited by Neth, Gallo, Greaves, Moore, Winkler

NK and K Cells in Malignant Lymph Nodes

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A. Introduction

Natural killer (NK) cells and effector cells of the antibody-dependent cellular cytotoxicity (K cells) show a striking organ distribution. Above all they occur in blood, bone marrow, and spleen. Cells of other lymphoreticular organs display a very low, if any, spontaneous killer cell activity (Table 1). Normal lymph node cells are nearly inactive [1, 2, 8, 14]. There are no data, however, on to what extent lymph node cells from lymphoma patients have killer cell activity. It is conceivable that the expansion of malignant transformed lymph node cells gives rise to functionally different cells. Tests with blood or bone marrow cells from patients suffering from acute lymphoblastic or acute nonlymphoblastic leukemia suggest the existence of malignant blasts with NK- or K-cell activity [3, 6, 7].

B. Patients and Methods

Basic data of four nontreated patients suffering from a non-Hodgkin lymphoma (NHL) or a lymphoma-like disease are shown in Table 2. Mononuclear leukocytes from axillary or inguinal lymph nodes (LK), peripheral blood (PBL), or bone marrow (KM) were prepared by Ficoll-visotrast centrifugation, and killer cell activities were estimated by the ^{51}chromium-release technique. Ten-thousand target cells in 100 µl were incubated with an excess of 50 times and 10 times the effector cells at 37 °C for 4 h. Targets were cells of the K-562 cell line for NK cell and mouse leukemia cells coated with rabbit antibodies for K-cell estimation.

Table 1. Distribution of NK and K cells in different lymphatic organs

Organ	n[a]	NK	n	K
Blood	118	38 (0 – 78)[b]	165	43 (0.5 – 81)
Bone marrow	11	35 (8 – 69)	14	43 (14 – 61)
Spleen	7	24 (9 – 92)	9	33 (12 – 72)
Lymph node	18	4 (0 – 13)	15	2 (0 – 4)
Tonsil	18	4 (0.5 – 11)	18	4 (1 – 8)
Thymus	10	1 (0 – 4)	10	1 (0 – 2)

Origin of organs: Blood (healthy donors), bone marrow (healthy donors or patients with cholecystitis), spleen (Hodgkin patients), lymph nodes (patients with intestinal solid tumors), tonsils (persons with tonsillitis), thymus (young children). Data refer to mononuclear leukocytes prepared by Ficoll-Visotrast centrifugation

[a] Number of donors tested

[b] Mean percentage of specific ^{51}Cr-release (range) at a ratio of effector: target cells of 50 : 1

Table 2. Basic data of the lymphoma patients

Patients	Age	Sex	Diagnosis	Clinical stage	Blood leukocytes/ mm^3
H.G.	64	m	Sezary syndrome	(III A)	4,550
K.B.	45	m	Angioimmunoblastic lymphadenopathy	III B	15,400
J.H.	52	f	Centrocytic-centroblastic lymphoma	III A	4,750
I.G.	46	f	Centrocytic-centroblastic lymphoma	IV A	5,250

C. Results and Discussion

Figures 1–5 illustrate the spontaneous killer cell activity of lymph node cells isolated from patients suffering from NHL. Figure 1 shows that the lymph node cells of a patient with Sezary syndrome were only K-cell active, but not NK-cell active. This finding is surprising insofar as there has been no example for K-cell active lymph node cells. The attempt to stimulate normal lymph node cells immunologically, e.g., by a lymphocyte-mixed culture, leads only to an increase in NK-cell similar activity, but not in K-cell activity [7].

In view of the anomalous behavior of the lymph node cells it may be assumed that the lymphoma cells themselves are functioning as K cells.

The Sezary syndrome is the leukemic variant of a cutaneous T-cell lymphoma [15]. The case described here resembles or

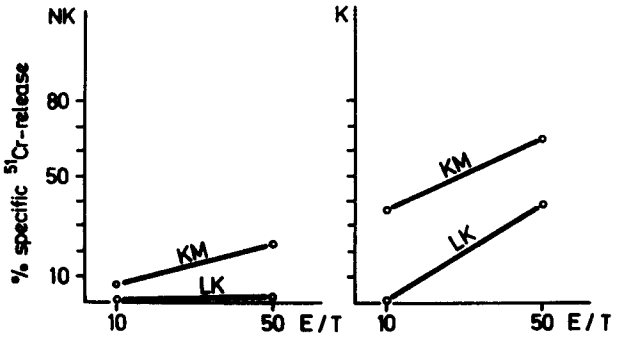

Fig. 1. NK- or K-cell activity of lymph node and bone marrow cells from a patient suffering from a Sezary syndrome

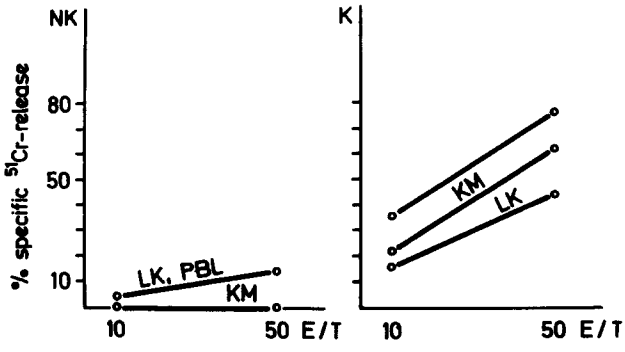

Fig. 3. The same patient as in Fig. 2; lymph nodes started rapidly regressing 2 weeks after discontinuing polychemotherapy

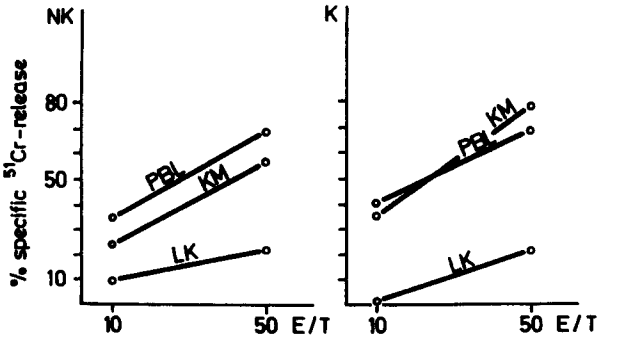

Fig. 2. NK- or K-cell activity of lymph node, peripheral blood, and bone marrow cells from a patient with an angioimmunoblastic lymphadenopathy

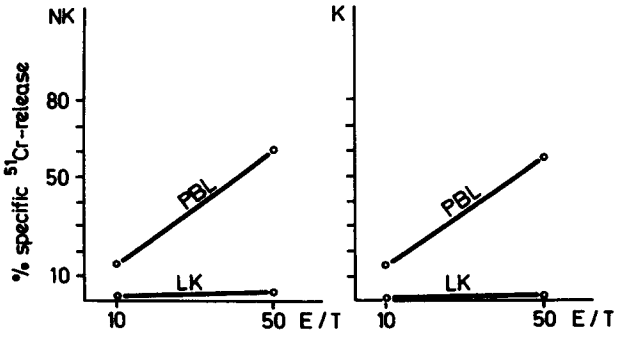

Fig. 4. NK- or K-cell activity of lymph node and peripheral blood cells from a patient suffering from a centrocytic-centroblastic lymphoma (Brill-Symmers)

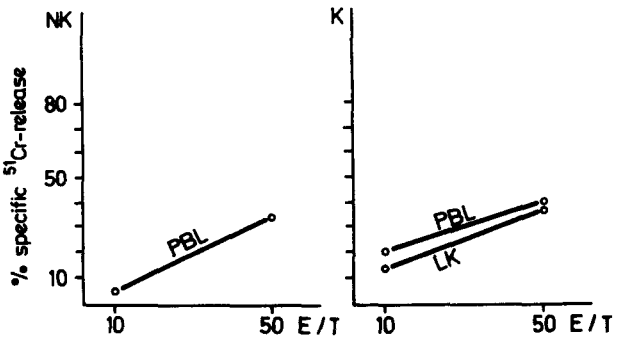

Fig. 5. NK- or K-cell activity of lymph node and peripheral blood cells from another patient with a centrocytic-centroblastic lymphoma

corresponds to those cases of a chronic lymphatic leukemia of the T-cell type in which T-lymphocytes from the blood have an immunosuppressive action, have Fc receptors for IgG and are either only K-cell active [9, 12] or both NK- and K-cell active [13]. Figure 2 shows the activity of lymph node cells of a patient with an angioimmunoblastic lymphadenopathy (AIL). The AIL or "lymphogranulomatosis X" is a lymphoma-like systemic disease, and may have rather different courses. Both spontaneous remissions and progression into a malignant lymphoma are possible [4, 5, 10, 11]. Because of the low NK- and K-cell activity of the lymph node, cells it was not possible to decide whether the spontaneous killer cells had arisen in the lymph node or had entered the lymph node through the blood stream. The patient had been treated with polychemotherapy. The lymph nodes swelled during treatment, but started to return rapidly to normal 2 weeks after discontinuing therapy. At this time, another lymph node was removed and studied. Figure 3 shows that the lymph node cells were K-cell active, but hardly NK-cell active. It is unclear whether there exists a relationship between the remission of the lymph nodes and the killer cell activity. The strongly reduced NK-cell activity of the blood and bone marrow cells seems to reflect the influence of chemotherapy. The activity of NK-cells is more strongly inhibited by chemotherapy than that of K cells [7].

The determination of functional and antigenic properties aims at finding a still more subtle classification of lymphomas and leukemias in order to obtain more prognostically relevant data. Estimation of the spontaneous killer cell activities may be a step in this direction.

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