Chinese Journal of Cancer Research 9(2):138 — 141, 1997

STUDIES OF THE CHARACTERISTIC FEATURES OF KI-1 POSITIVE NON-HODGKIN'S LYMPHOMA

Xiao Weiguo 肖卫国 Yang Ruixue 杨瑞雪 Hou Ping 候平 He Anguang 何安光
Shionoya Shigeru 盐谷 茂

Department of Hematology, The First Clinical Hospital, China Medical University, Shenyang, 110001

The clinical histopathological and immunophenotypic features in 5 patients with Ki-1 positive non-Hodgkin's lymphoma (NHL) were studied. When first seen, 4 patients presented enlargement of superficial lymph nodes, with skin lesions in 2 patients. Two patients in stage IV with fever, hepato-splenomegaly and bone marrow invasion, died. Histologically, the tumor cells showed diffused or patchy hyperplasia. The cells were relatively large in size, rich in basophilic or slightly eosinophilic cytoplasm with irregular-shaped nuclei, prominent nucleoli, and distinct anaplasia and pleomorphism. Some of the cells looked very much like the Reed-Sternberg cells. Multinucleated giant cells were seen. Immunophenotypically, all the cells were CD30 (Ki-1) and CD25 (IL-2 receptor) positive but CD15 (Leu M1) negative. Thus, the 5 patients with Ki-1 positive NHL were all of T cell type.

Key words: Lymphoma, non-Hodgkin's, Hodgkin's disease antigens, CD30 Immunophenotyping

Ki-1 antigen (CD30) was 105000/120000 glycoprotein distinguished by monoclonal antibody Ki-1 which was made from Hodgkin's disease (HD) cells strain L-428,[1] expressed on HD cells and Reed-Sternberg (R-S) cells at first thought. It was found by Stein and others in 1985, who named Ki-1 strong positive NHL as Ki-1 lymphoma, that Ki-1 antigen was also expressed on some NHL.[2] The researches on this special type of lymphoma have already appeared abroad. We have collected five cases of Ki-1 positive NHL and now discuss their clinical histopathological and immunophenotypic features.

Accepted Jan 28, 1997

MATERIALS AND METHODS

The author gathered five cases of Ki-1 positive NHL of in-patient and out-patient when engaging in advanced studies from 1992 to 1993 at Japan Kitasato University. Among them, two cases were patchy positive, others were diffused strongly positive. Their specimens of paraffin and fresh freezing were made separately.

Histopathological examination: The paraffin-embedded specimens were cut into 4 μm thin sections then stained with hematoxylin and eosin.

Immunophenotypic examination: The fresh frozen specimens processed to obtain 4 μm-thick sections, then fixed with cold acetone about two minutes after airdrying. The negative control was done by means of not adding first or second antibody. The monoclonal antibodies and their specificity were seen in Table 1.

Table 1. Monoclonal antibodies

MoAb	Source	Specificity
MT1	Fist Bioche, Corp.	Pan-T cell
CD3	Becton Dickinson	Pan-T cell
CD4	Becton Dickinson	Helper/inducer T cell
CD8	Becton Dickinson	Suppressor/cytotoxic T cell
Ia	Becton Dickinson	B cell, monocyte, macrophage, activated T cell
CD15	Becton Dickinson	Monocyte, granulocyte
CD25	DAKO	IL-2 receptor, activated T cell
CD30	DAKO	Hodgkin & R-S cell
CD19	Coulter	Pan-B cell
CD20	Coulter	Pan-B cell

RESULTS

1. Clinical features: Among five cases of Ki-1 positive NHL, the youngest was 15 years old, the oldest was 78. all of them were men. Four patients presented enlargement of superficial lymph nodes, with fever in 3 cases, skin eruption in 2 cases, hepato- splenomegaly in 3 cases, bone marrow invasion in 2 cases. Two patients were in clinical stage Ia, one in stage IIIb, and two in stage IVb.

2. Histological features: Among the five cases, two persons originated from cervical lymph nodes, one from inguinal lymph nodes, one from pharynx and one from tonsil. Histologically, their lymphatic structures were destroyed. The tumor cells showed diffused or patchy hyperplasia, mainly infiltrated into the T zone and subcapsular sinus. The cells were relatively large in size, rich in basophilic or slightly eosinophilic cytoplasm with irregular-shaped nuclei, prominent nucleoli and distinct anaplasia and pleomorphism. Some of the cells looked very much like the R-S cells, but their nucleoli were smaller than those of R-S cells. Multinuclear giant cells were seen. There were plasma cells, small lymphocytes, histocytes etc. around the tumor cells (Figure 1).

3. Immunophenotypically, the five cases were CD30 and CD25 (IL-2R) positive but CD15 (LeuM1) negative. All the cases were T cell type, with CD4 and CD8 positive respectively in two cases, and in one case lacking CD4 and CD8 markers (Table 2, Figure 2, 3).

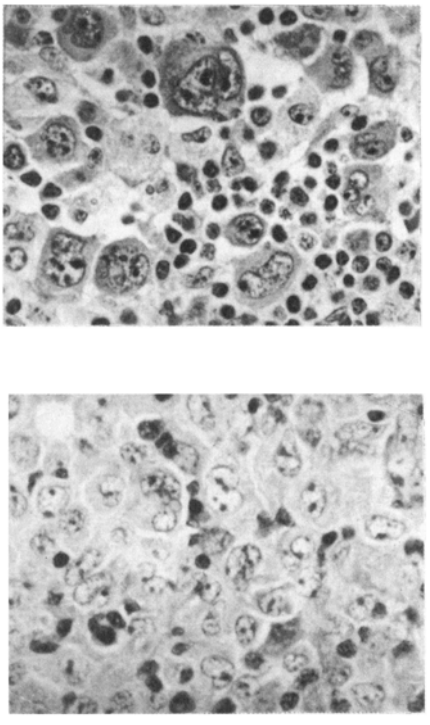

Fig 1. Histologic appearance of a Ki-1 positive NHL showing thatthe tumor cells were relatively large in size, distinct anaplasia and pleomorphism, rich in basophilic or slightly eosinophilic cytoplasm with irregularly shaped nuclei which assumed U-shaped, arc-like, peanut-shaped etc., with prominent nucleoli. Multinucleated giant cells were seen. (A: case 3; B: case 4)

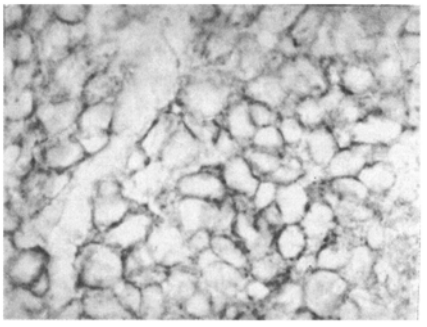

Fig 2. Ki-1 antibody staining of anaplastic large tumor cells. ABC × 400 (case 3)

Table 2. Immunohistochemical results of NHL with Ki-1-positive

No.	Age/Sex	MT1	CD3	CD4	CD8	Ia	CD15	CD25	CD30	CD19	CD20
1	78/M	+	++	-	+	++	-	+++	+++	-	-
2	66/M	++	+++	++	+	+++	-	++	++	±	±
3	47/M	+++	+++	+++	+	+++	-	+++	+++	±	±
4	15/M	+	++	±	±	++	-	+++	+++	-	-
5	60/M	++	++	+	++	++	-	++	++	-	-

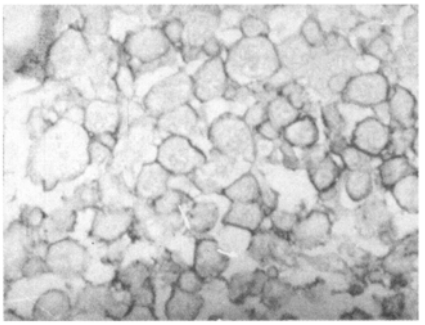

Fig 3. Staining of anaplastic large tumor cells with Pan-T monoclonal antibody MT1. ABC × 400 (case 3)

DISCUSSION

It was reported in 1985 by stein and others the first time that specific antigens Ki-1 of HD and R-S cells were expressed on some cases of NHL, of which with diffused positive ones were called Ki-1 lymphomas or anaplastic large cell lymphomas.[2] The concept of skin lymphoma of six children found by Kadin and so forth in 1986 was same as that of Ki-1 lymphoma discovered by Stein and others.[3] With development of immunology, the reports on Ki-1 lymphoma appeared one by one.[4,5] The five cases in our report were all male. According to documents, primary manifestations were enlargements of superficial lymph nodes in most cases, but enlargements of mediastinal and deeply abdominal lymph nodes and swelling of lymph nodes with skin lesions in some cases. Soft tissues and alimentary canal could also be original.[4,6] Hepato-splenomegaly and bone marrow invasion could be seen in late stage. When first seen, 4 ones of the five patients showed enlargements of superficial lymph nodes, with skin lesions in two patients. Two patients in stage IV with fever, hepato-splenomegaly and bone marrow invasion, whose span-lives were 9 months and 19 months respectively, were dead within the five cases. Although there was no agreement about prognosis of Ki-1 positive lymphoma, it was thought near to high malignancy by the most. It was reported by some people that prognosis of adults was worse than that of children.[3] There was no final conclusion because our cases were a few in number.

From histopathology, the tumor cells were larger with prominent anaplasia and pleomorphism and high malignancy in morphology. Because of their invasions in large quantities into subcapsular sinus, these kinds of lymphomas were often diagnosed as metastatic tumors by mistakes. Some of the tumor cells that looked like the R-S cells were mistaken as HD, however Ki-1 positive NHL would be differentiated from HD by means of obvious heteromorphism of its background cells.

From immunophenotype of the five Ki-1 positive NHL, all the cells were CD30, Ia and CD25 positive but CD15 negative. CD30 had been thought as activated lymphocytic antigen before, but the fact that it might be found in embryoma and gastric plasmacytoma in recent years showed that it was not necessarily activated. It is unknown for the function of Ki-1 antigen and its biological significance. The five cases were all T type, in accordance with the reports.[2,4,6,7] HD and R-S cells had specific immunophenotype, meantime with CD30, CD25 and CD15 antigens, yet any known NHL was not provided with these things.[7] The point that all the Ki-1 positive NHL were CD15 negative was the main differentiation between NHL and HD.

REFERENCES

1. Schwab U, Stein H, Gerders J, et al. Production of a

monoclonal antibody specific for Hodgkin and Sternberg-Reed cells of Hodgkin's disease and a subset of normal lymphoid cells. Nature 1982; 299: 65.

2. Stein H, Mason DY, Gerders J, et al.. The expression of the Hodgkin's disease associated antigen Ki-1 in reactive and neoplastic lymphoid tissue. Blood 1985; 66: 848.
3. Kadin ME, Sako D, Berliner N, et al. Childhood Ki-1 lymphoma presenting with skin lesions and peripheral lymphadenopathy. Blood 1986; 68: 1042.
4. Agnarsson BA, Kadin ME. Ki-1 positive large cell Lymphoma: a morphologic and immunologic study of 19 cases. Am J Surg Pathol 1988; 12: 264.
5. 那须 芳，山边博彦。 Ki-1 阳性リンパ 肿とその周边疾患。病理の临床 1989; 7: 840.
6. Delsol G, Al Saati T, Gatter KC, et al. Coexpression of epithelial membrane antigen (EMA), Ki-1 and interleukin-1 receptor by anaplastic large cell lymphomas. Am J Pathol 1988; 130: 59.
7. Herbst H, Tippelmann G, Anagnostopoulos I, et al. Immunoglobulin and T-cell receptor gene rearrangements in Hodgkin's disease and Ki-1 positive anaplastic large cell lymphoma: dissociation between phenotype and genotype. Leuk Res 1989; 13: 103.