REVIEW PAPER

LARGE CELL ANAPLASTIC LYPMHOMA VERSUS HODGKIN'S DISEASE - DIFFICULTIES IN THE DIAGNOSIS */

Kaczmarek-Kanold M, Stefańska K, Trejster E, Kołecki P, Wróbel G, Sopyło B, Stańczak E

Polish Children's Leukemia/Lymphoma Study Group Poznań, Wrocław, Warszawa.

Received 3 September 1998; revision received 8 April 1999; accepted 26 May 1999.

Key words: lymphomas in children; LCAL; HD.

ABSTRACT

During the last 5 years in the Polish Children's Leukemia/Lymphoma Study Group (7 centers) 241 children with Hodgkin's Disease and 14 children with Large Cell Anaplastic Lymphoma were treated.

In 5 of them we had problems with differential diagnosis.

Immunohistochemical tests :
- CD30 positive, CD15 positive, LCA negative allowed us to change the diagnosis from Large Cell Anaplastic Lymphoma to Hodgkin's Disease (one child) and
- CD30 positive, CD15 negative from Hodgkin's Disease to Large Cell Anaplastic Lymphoma (four children).

All children achieved remission after changing the protocol of chemotherapy.

INTRODUCTION

Large cell anaplastic lymphoma - LCAL appears in children in 8-12% of Non-Hodgkin's Lymphomas-NHL: (Murphy 1994). The clinical symptoms characteristic for Hodgkin's Disease-HD as well as for LCAL and normal histopathological examination could cause a problem in differential diagnosis.

We present here observations made in the Polish Children's Leukemia/Lymphoma Study Group – PCLLSG.

MATERIALS AND METHODS

In the years 1993-1997 in seven centers of the PCLLSG 241 children with HD and 14 with LCAL were treated. We sent questionnairs to all centers applying to children who had caused problems in differential diagnosis between HD and LCAL. We asked about initial symptoms, diagnosis and treatment. We also asked about results of immunohistochemical tests and final diagnosis. We were interested in the interval between the initial and final diagnosis.

The histopathological diagnosis was based on the microscopic examination of lymph nodes (mediastinal tumor or peripheral lymph nodes). In the years 1993-1995 we had no technical possibilities to perform immunohistochemical tests in all centers. Therefore properly prepared material was sent to the selected centers. It concerned all doubtful cases (in the routine investigation - HE (Hematoxlin-Eozin)). At present, in all cases of lymphomas immunohistochemical tests are performed simultaneounsly with routine histopathological examinations. However, in children with the diagnosis of neoplasms we could not wait for the results of immunohistochemical tests. Therefore, we began the treatment typical for HD or LCAL. Children with HD underwent chemotherapy MVPP (mechlorethamine, vinblastine, procarbasine, prednisone) and B-DOPA (bleomycine, dacarbasine, oncovin, prednisone, adriamycyne) combined with involved field radiotherapy (Balwierz 1994). All patients with LCAL were treated according to LCAL-93 protocol based on NHL-BFM 90 protocol (Reiter 1994).

Immunohistochemical tests, CD15, CD30 and LCA, were performed, according to the instructions of producers (Novocastra, Dako, Biker).

RESULTS

In the five-year period mentioned above we found in the PCLLSG 5 children in whom we had difficulties with diagnosis. Lack of remission after initial therapy and the results of

*/ Supportet by Grant KBN 4 PO 5E 13914

Initials	Symptoms			Initial diagnosis	Initial treatment	Immunohistochemical tests			Diagnosis was changed after:	Final diagnosis
	MT	LE	CS			CD 15	CD 30	LCA		
A. M.	+	+	–	LCAL	preface cycles A, B, A AA	pos.	pos.	neg.	3 months	HD II^0 hist.
A. G.	+		+	HD III^0 hist.	cycles B–DOPA, MVPP, B–DOPA	neg.	pos.	–	2 months	LCAL
Sz. A.	–	+	+	HD IV^0 hist.	cycle B–DOPA	neg.	pos.	–	2 weeks	LCAL
B. P.	+	–	–	HD II^0 hist.	cycle B–DOPA	neg.	pos.	–	2 weeks	LCAL
T. W.	+	+	+	HD II^0 hist.	cycle B–DOPA	neg.	pos.	–	2 weeks	LCAL

Table 1. Detailed data.

Abbreviations

MT – mediastinal tumor

LE – enlargment of peripherial lymph nodes

CS – constitutional symptoms

immunohistochemical tests obtained later made us change the diagnosis and the therapy. The detailed data is shown in tab.1.

After initial therapy only partial remission was achieved in two children (with initial diagnosis of HD) probably after administration of corticosteroids. In two patients lack of remission and in one case progression of the disease were observed.

In all but one child second chemotherapy according to LCAL-93 protocol was performed. In a patient with the final diagnosis of -HD the treatment consisted of cycles MVPP/B-DOPA and radiotherapy.

All children achieved remission after changing the protocol of chemotherapy. Two of them have remained in the first remission 12 and 27 months. Relapse was observed in three children. One of them died because of the progression of the disease. Two children are still in the second remission, one after autologous bone marrow transplantation.

DISCUSSION

In all the discussed children mediastinal tumor was observed. In 60% of cases it appears in HD together with enlargment of peripheral lymph nodes. In 4-6% a mediastinal tumor is diagnosed as an isolated symptom (Armata, 1995). But mediastinal tumor is also typical for LCAL (Rubie, 1994). Likewise constitutional symptoms : such as fever and loss of weight can be similar (Pilerii, 1995). Histopathological examination should be decisive. However also in such cases difficulties can appear. Large cells with large nucleus and large nucleous characteristic for LCAL can resemble Hodgkin's cells and Reed-Sternberg cells. Fibrosis can also appear in LCAL and HD-nodular sclerosis.

It is therefore sometimes impossible even for an experienced oncologist and pathologist to make a differential diagnosis between LCAL and HD based only on clinical symptoms and routine histopathological examination.

Finding out an antigen Ki-1 (CD30) by Stein in 1985 made it possible to diagnose the type of large cell lymphoma (Stein, 1985; Goldbrunner, 1996). Therefore it is necessary to use modern immunohistochemical methods as supplement to basic methods in histopathological examinations. These examinations should be performed in all neoplasms in children according to the recommendation of the International Society of Pediatric Oncology (Societe Internationale d'Oncologie Pediatrique - SIOP)

CD30 positive and CD15 negative reactions allow us to diagnose LCAL (Stein, 1985). Differentiation between both discussed neoplasms is very important because of different protocols of chemotherapy. Clinical observations, sensitivity to chemotherapy and the dynamics of the disease are often helpful in the diagnosis.

Cases presented by us indicate how important immunohistochemical examinations are in coexistance with clinical observations.

REFERENCES

Armata J. Jeszcze w sprawie wcześniejszego rozpoznania choroby Hodgkina. Ped.Pol. (1995); 70: 199-204.

Balwierz W, Armata J, Depowska T, Ochocka M, Newecka-Samól T, Koczyński A, Sońta-Jakimczyk D, Janik-Moszant A, Bogusławska-Jaworska J, Pisarek J, Radwańska U, Kaczmarek-Kanold M, Rokicka-Milewska R, Sopyło B, Rola E, Gadomski A, Kołakowska-Mrozowa B, Kowalczyk J, Skomra S. Wyniki chemioterapii skojarzonej z miejscowym napromienianiem dzieci z chorobą Hodgkina. Raport Polskiej Grupy Pediatrycznej ds. Leczenia Białaczek i Chłoniaków. Ped.Pol. (1994); 69: 721-728.

Goldbrunner R, Warmuth-Metz M, Tonn J. Primary Ki-1 - positive T-cell lymphoma of the brain - an agressive subtype of lymphoma. Surg. Neurol. (1996); 46: 37-41.

Murphy S. Pediatric lymphomas: recent advances and commentary on Ki-1 positive anaplastic large cell lymphomas on childhood. Ann. Oncol. (1994); supl.1, 5: 31-33.

Pileri S, Picecaluga A, Poggi S, Sabattini E, Piccaluga P, De-Vivo A, Falini B, Stein H. Anaplastic large cell lymphoma: update of findings. Leuk. Lymphoma (1995); 18: 17-25.

Reiter A, Scharppe M, Tiemann M. Succesful treatment strategy for Ki-1 anaplastic large cell lymphoma of childhood: a prospective analysis of 62 patients enrolled in three consecutive Berlin-Frankfurt-Münster Group Studies. J. Clin. Oncol. (1994); 12: 899-908.

Rubie H, Gladieff J, Robert A, Gaubert I, Huguet F, Rochax P, Pein F, Michel G, Hoerni B, Sommelet D Childhood anaplastic large cell lymphoma Ki-1 (CD30) : clinic, pathologic features of 19 cases. Med. Pediatr. Oncol. (1994); 22: 155-161.

Stein H, Mason D, Gerdes J. The expression of the Hodgkin's disease associated antigen Ki-1 reactive and neoplastic lymphoid tissue. Blood (1985); 66: 848-858.