INVESTIGATION OF HISTOPATHOLOGICAL AND IMMUNOHISTOCHEMICAL FEATURES OF PATIENTS WITH NON-HODGKIN LYMPHOMA

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ABSTRACT

Non-Hodgkin's lymphoma is one of the ten most common cancers in Vietnam and in many other countries, ranking fifth in morbidity and sixth in mortality after lung, liver, stomach, colorectal cancer. In the United States, in 2008 there were about 66,000 new cases. According to the statistics of the Vietnam National Cancer hospital for the 10 years from 1979 to 1988, there were 1568 new cases, accounting for 7.6%, ranking fifth in total cancer. ***Objectives:*** To characterize histopathological and immunohistochemical characteristics of non-Hodgkin lymphoma at the Hai Phong Vietnam-Czech friendship Hospital. ***Study subjects:*** Patients diagnosed with non-Hodgkin's lymphoma in the lymph nodes at the Hai Phong Vietnam - Czech friendship Hospital, from 1/2015 to 9/2018. Study method: Descriptive method described through cross-sectional survey. ***Results of the study:*** The most common nodal lesions were nodal metastasis (80.9%), WF7 (54,0%), the WHO classification in 2008, in B-cell lymphoma, the Diffuse large B-cell lymphoma occurred in 80,2% of the patients. In T-cell subtype, peripheral T-cell lymphoma accounted for the highest rate of 40,0%, major cell differentiation (33.4%).

Keywords: *Non-Hodgkin's lymphoma, B cell lymphoma, T cell lymphoma.*

I. INTRODUCTION

Non-Hodgkin's lymphoma is one of the ten most common cancers in Vietnam and in many other countries, ranking fifth in morbidity and sixth in mortality after lung, breast, liver, stomach, colorectal cancer. In the United States, in 2008 there were about 66,000 new cases. According to the statistics of the Vietnam National Cancer hospital for the 10 years from 1979 to 1988, there were 1568 new cases, accounting for 7.6%, ranking fifth in total cancer. Therefore we conduct the study on: "histopathological and immunohistochemical characteristics of non-Hodgkin lymphoma at the Hai Phong Vietnam- Czech friendship Hospital" with the purpose: Comment *histopathological and immunohistochemical characteristics of non-Hodgkin lymphoma* at the Hai Phong Vietnam- Czech friendship Hospital.

II. SUBJECT AND METHOD

2.1. Research site, time, and subject

- Research site: Hai Phong Vietnam-Czech friendship Hospital

- Subject: 156 patients diagnosed with non-Hodgkin lymphoma at the Hai Phong Vietnam- Czech friendship Hospital from January 2015 to September 2018.

- Time: from 1/2015 to 9/2018

2.2. Research method

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2.2.1. Research design

A cross-sectional study was used to conduct the research

2.2.2. Techniques applied in the study

Patients were done lymph node biopsy.

Test samples were processed and analyzed at Hematology - Blood Transfusion center, department of Pathology, Hai Phong Vietnam -Czech hospital and Department of Cytology, National Institute of Hematology - Blood Transfusion.

Collect information: age, gender, site of lesion, classification of WF, classification of WHO 2008;

* Histopathology: The biopsy sample was cut and stained based on Hematoxylin Eosin staining method

* Immunohistochemistry: Use monoclonal antibodies according to immunohistochemical procedure at Hematology-Blood Transfusion center and Pathology department

Panel 1: the minimum panal applied to all non-Hodgkin lymphoma cases to classify the nature of cells, including: LCA, CD20, CD79a, CD43, CD3.

Panel 2: Based on the result of panel 1 and cell morphology to indicate the following markers, which helps to classify subtypes based on WHO classification 2008

2.2.3. Data processing

Data was processed by SPSS 16.0.

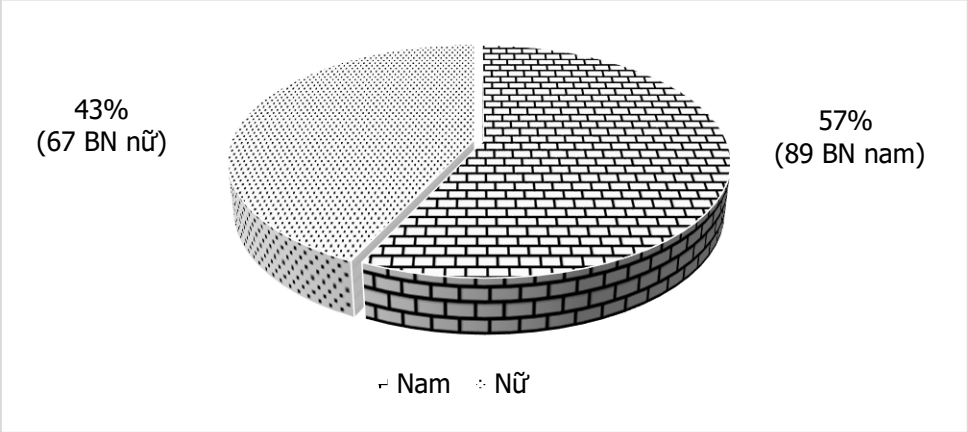
III. RESULT

According to the location of lesion lymph node biopsy, neck lymph node accounted for the highest rate of (82,1%); followed by inguinal lymph nodes with 10,5%; abdominal lymph node accounted for 5,1%; axillary lymph node accounted for 2,3%.

Table 3.1. Distribution of patient by age group

Age group	Quantity	Percentage (%)
<18	6	3,8
18-40	31	19,9
41-60	65	41,7
>60	54	34,6
Total	**156**	**100**

The table shows that 3,8% of patients were below 18 years old; 19,9% patients from 18-40 years old; 41,7% of patients at age 41-60 and 34,6% of patients above 60 years old.

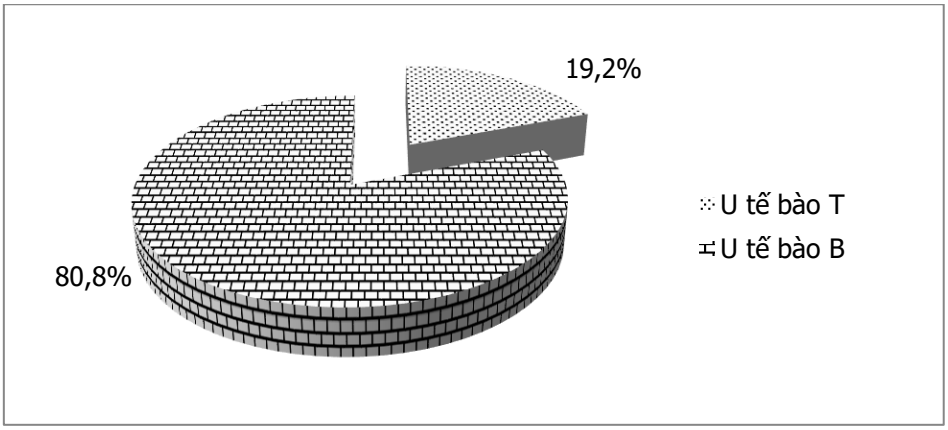


Graph 1: Distribution of patients by gender (male/female = 1,33)

Table 3.2. Distribution of patients by WF

	WF1	WF2	WF3	WF4	WF5	WF6	WF7	WF8	WF9	Total
n	4	2	7	6	8	35	84	7	3	**156**
%	2,5	1,3	4,5	3,8	5,1	**22,4**	**54,0**	4,5	1,9	**100**

Based ob classification of Working Fomulation, the most common lesion was WF7 (54%), followed by WF6 (22,4%), other kinds account for small percentage.



Graph 3.2. Distribution by cell origin

Among 156 patients, 126 patients had B-cell lymphoma (80,8%), 30 patients had T-cell lymphoma (19,2%).

Table 3.3. Distribution of lesion site by cell origin

Position of lesion lymph node	**B cell**		**T cell**		**General percentage**	
	n	**%**	**n**	**%**	**n**	**%**
Neck lymph node	102	80,9	24	80,0	126	80,8
Inguinal lymph nodes	13	10,3	4	13,4	17	10,9
Axillary lymph node	7	5,6	1	3,3	8	5,1
Abdominal lymph node	4	3,2	1	3,3	5	3,2
Total	126	100,0	30	100,0	156	100,0

Neck lymph node accounted for highest proportion (80,8%); followed by inguinal lymph node with 10,9%; Axillary lymph node 5,1%; Abdominal lymph node 3,2%.

Table 3.4. Compare malignancy by WF classification with cell origin

Malignancy level by WF	**B cell (n=126)**		**T cell (n=30)**		**p**
	n	%	n	%	
Low malignancy	15	**11,9**	2	6,7	p<0,05
Average malignancy	109	86,5	21	70,0	p<0,05
High malignancy	2	1,6	7	**23,3**	P<0,01
Total	126	100,0	30	**100,0**	

Based on classification of Working Formulation, average and low malignancy mostly lied in B cell group. T cell group had higher level of malignancy.

Table 3.5. Distribution patients according to WHO 2008

Cell	Type of disease	Quantity	%
B cell	Diffuse large B - cell lymphoma	101	**80,2**
	Follicular lymphoma	14	11,1
	Mantle cell lymphoma	4	3,1
	Small lymphocytic lymphoma (SLL)	3	2,4
	Lymphoplasmacytic lymphoma	1	0,8
	Fringe lymphoma	2	1,6
	Burkitt lymphoma	1	0,8
Total		**126**	**100,0**
T cell	Leukemia in adult	1	3,3
	Peripheral T- cell lymphoma	12	**40,0**
	Angioimmunoblastic T-cell lymphoma	6	20,0
	Large - cell lymphoma	`10	33,4
	NK cell lymphoma	1	3,3
Total		**30**	**100,0**

- In B - cell group, diffuse large B - cell lymphoma accounted for highest proportion (80,2%).

- In T cell group, Peripheral T- cell lymphoma accounted for highest proportion 40,0%.

Table 3.6. Immunohistochemical characteristics according to WHO 2008

Type of disease	n	Frequent signs
Diffuse large B - cell lymphoma	101	CD20 (98/101), CD79a (82/94), BCL2 (51/98)
Follicular lymphoma (FL)	13	CD20 (13/13), CD79a (10/10), CD10 (11/13), BCL2 (12/13)
Mantle cell lymphoma	4	CD20 (3/4), CD79a (3/3), CD5 (3/4), BCL2 (2/4), Cyclin D1 (3/4)
Small lymphocytic lymphoma (SLL)	3	CD20 (3/3), CD79a (1/3), CD5 (2/3)
Fringe lymphoma	2	CD20 (2/2), CD79a (2/2)
Leukemia in adult	2	CD3 (1/2), CD45RO (2/2)
Peripheral T- cell lymphoma, nonspecific	13	CD3 (10/13), CD45RO (9/9)
Angioimmunoblastic T-cell lymphoma	8	CD3 (7/8), CD45RO (6/6)
Large - cell lymphoma	10	CD3 (6/10), CD45RO (6/8), CD30 (10/10), ALK (8/10)

- B cell lymphoma had specific antigens of CD20 and CD79a, which was seen in almost subtypes of disease. Besides, Follicular lymphoma had positive BCL2 in 12/13 cases, CD10 positive in 11/13 cases; Mantle cell lymphoma had CD5 positive in 3/4 cases and Cyclin D1 positive in 3/4 cases; Small lymphocytic lymphoma had CD5 positive in 2/3 cases.

- T cell lymphoma had specific antigens of CD3; CD45RO. In which: Large - cell lymphoma had 100% positive cases with CD30, ALK positive in 8/10 cases, 4 cases of negative CD3.

IV. DISCUSSION

Among 156 patients, average age is 52,1. Patients aged 41-60 account for 41,7% and patients aged above 60 account for 34,6%. Our result is relevant to other researches. The percentage of male is higher than female. According to Nguyen Ba Duc, Do Trung Phan (2005), the rate of male was higher than female (male:female = 2:1) [1]. In our research, this rate is 1,33/1, which is similar to the research of Vu Quang Toan [2].

Non-Hodgkin lymphoma is a group of cancer that arises from in or outside of lymph nodes. According to the study of Nguyen Tuyet Mai on clinical and paraclinical features of non-Hodgkin lymphoma from 2007 to 2011 in hospital K, lymph node lesions accounted for 89.1%, of which head and neck lymph nodes (60%), inguinal lymph nodes (18.2%), axillary lymph nodes (14.5%) and abdominal lymph nodes (34.5%) [4]. In this study, compared to other authors, we found that lesions in the head and neck lymph nodes accounted for a higher proportion (80.9%), while abdominal lymph nodes were much lower (3.2%).).

Among 156 patients, WF7 and WF6 account for the highest rate with 54,0% and 22,4%, respectively. Therefore, the group with average malignancy accounts for the highest rate of 86,5%. However, this rate is lower than that in Bach Quoc Khanh (92,5%) [3] and higher than that in Tran Thanh Tung (59%) [6].

Currently, with the development of immunohistochemistry, WHO 2008 classification is gradually applied in clinical practice in Vietnam. According to our research on cell origin, B-cell lymphoma accounts for higher rate (80,8%) than T-cell lymphoma (19,2%) and higher than the rate of some authors given such as Do Trung Phan (2005): 77,1% [1], Le Dinh Roanh, Nguyen Phi Hung et al (2003): 75,6% [5].

In terms of distribution of lesion according to cell origin: B cell: 80,9% neck lymph node, 10,3% inguinal lymph node, 5,6% axillary lymph node and 3,2% abdominal lymph node. T cell: 80,0% % neck lymph node,13,4% inguinal lymph node, 3,3% axillary lymph node and 3,3% abdominal lymph node. Therefore, at different position, B cell accounts from 80,9% to 3,2% and T cell from 80,0% to 3,3%, there is no difference.

Among B-cell lymphoma, diffuse large B - cell lymphoma accounts for 80,2%, Follicular lymphoma 11,1%, mantle cell lymphoma 3,1%, Small lymphocytic lymphoma 2,4%, Fringe lymphoma 1,6%. This rate is different in researches. In a research by Nguyen Ba Duc, Do Trung Phan (2005): diffuse large B - cell lymphoma accounted for 37,9%, Follicular lymphoma 22,9%, Small lymphocytic lymphoma 7,1%. A research by Tran Thanh Tung (2007) showed that diffuse large B - cell lymphoma accounted for 85% [6].

Among T-cell lymphoma, there is a change in the percentage of diseases. According to Do Trung Phan (2005) and some researches in China, Korea, Canada, peripheral T- cell lymphoma accounted for the highest proportion of 40%. According to Le Dinh Doanh (2004), nonspecific large - cell lymphoma had the highest rate of (46,8%) [5]. Savage et al (2004) [9] carried out a study on 199 peripheral T-cell lymphoma in Canada, which showed that subtype peripheral T-cell lymphoma had the highest rate of 59%, nonspecific large - cell lymphoma 17% and T/NK cell lymphoma…%. In our research, peripheral T-cell lymphoma accounted for

39,2%, followed by nonspecific large - cell lymphoma with 31,4%; Angioimmunoblastic T-cell lymphoma had 21,6%. This difference can be explained: our research only focus on inside lymph nodes; wheres, other researchers focused on lymphoma outside lymphatic system where there are a high percentage of T cell lymphoma.

Currently, immunihistochemistry has become a modern, effective technique for pathologist to diagnose malignant tumors at molecular level. It can be said that the finding and application of this method is a breakthrough in diagnosis of cancers in the late 20th and early 21st century. Our research shows that among T-cell lymphoma, CD20 positive in almost diseases. A study by Zukerberg et al [10] on expression of CD5, CD10, CD23 and CD43 on 56 cases of diffuse B-cell lymphoma with low malignance level, there were difference in 4 subtypes. CD5+ CD10- CD23+ CD43+: expressed in small cell lymphoma; CD5+ CD10-/+ CD23- CD43+: Cellular lymphoma; CD5- CD10+/- CD23-/+ CD43-: Cellular lymphoma/ intracellular; CD5- CD10- CD23-/+ CD43-/+: Fringe lymphoma

When identified, the tumor cells belong to T-cell when positive with common markers: CD3, CD5, CD43, and CD45RO and do not share the same B-cell signature. Subtypes of T-cell lymphoma are classified according to cell morphology and histopathological structure. The study results of Picker et al [11] showed that the rate of losing a common T-cell marker was 33%, the rate of losing two common markers was 24% and the loss of showing three marks was 17%. The percentage of T-cell lymphoma losing 1 or more general markers is 76%. Lymphoblastic lymphoma has a loss rate of 26%. Whereas, our study showed that the immunohistochemical results of most T-cell lymphoma were positive for the CD3 and CD45RO markers. With poorly differentiated large lymphoma, the CD30 is positive in all 10/10 cases, ALK positive in 8/10 cases.

V. CONCLUSION

After studying 156 cases of non-Hodgkin lymphoma at Hai Phong Vietnam-Czech hospital, we draw some conclusions:

- The most common position is neck lymph node (80,8%).
- Based on WF, the most common lesion is WF7 (54,0%).
- Based on WHO 2008, in B-cell group, diffused large B-cell lymphoma has the highest proportion (80,2%). In T-Cell group, peripheral T-cell lymphoma accounts for the highest percentage of 40,0%, followed by poorly differentiated large lymphoma (33,4%).

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