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Contribution of Immunohistochemistry in the Diagnosis of Lymphomas

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Abstract

Objective: Making the interest of using immunohistochemistry clear in addition to histological test in the diagnosis of lymphomas. **Methods**: This is a retrospective study from January 2011 to June 2013 involving 18 cases of lymphomas collected in the teaching hospitals of Treichville and Yopougon. **Results**: 1) 38.88% diagnosis of LMNH B large-cell in histology against 38.88% LDGCB with IHC. 2) 11.11% diagnosis of LMNH small cell in histology against 11.11% with IHC. 3) 5.55% diagnosis of T lymphoma in histology against 27.77% diagnosis of T lymphoma with IHC. 4) 5.55% diagnosis of follicular lymphoma in histology against 11.11% diagnosis of LF with IHC. 5) 11.11% diagnosis of Burkitt lymphoma in histology against 5.55% diagnosis of LB with IHC. 6) 5.55% diagnosis of medullary hypoplasia in histology against 5.55% diagnosis of Hodgkin's disease. Our results confirm the contribution of immunohistochemistry in the diagnosis of lymphomas in addition to histological test. This is striking, especially as there is 27.77% of T lymphoma with immunohistochemistry against only 5.55% with histology.

Keywords

Lymphomas, Immunohistochemistry, Histology, WHO Classification

1. Introduction

The term lymphoma refers to anatomo-clinical entities that are a tumor proliferation of lymphoid tissue characterized by the multiplication of an abnormal

lymphocyte clone. We distinguish Hodgkin's disease from non-Hodgkin's lymphomas.

The diagnosis is based on the multidisciplinary morphological analysis: which is interested in the size of the cell (small cell in low-grade or large-cell LMNH in high-grade LMNH) and the architecture of the immunological sampling: searching for the presence of Ag on cell membranes, and cytogenetics: searching for chromosomal abnormalities (t(11, 14) in mantle NHNH, t(14, 18) in follicular LMNH) and/or molecular: searching for proto-oncogene.

The morphological study may prove to be insufficient for diagnosis in the case of poorly differentiated tumor or remodeled tumor (necrosis) or low tumor cell sampling as well as the nature of the B or T lymphomatous cell involving the use of immunohistochemistry. To determine monoclonality with the presence of an immunoglobulin light chain, immunohistochemistry makes it possible to establelish a precise phenotype with the identification of B or T lymphocyte nature or Natural-killer cells. Our study aims at showing the contribution of immunohistochemistry in the diagnosis of non-Hodgkin lymphoma in our working conditions.

2. Patients and Methods

This was a descriptive retrospective and analytical study conducted in the clinical hematology department of the teaching hospitals of Yopougon and Treichville between January 2011 and June 2013.

This study involved patients diagnosed with non-Hodgkin's lymphoma; the patients in whom the diagnosis was confirmed by histological analysis and who had undergone an immunohistochemical analysis were selected.

The sampling was systematic random, including 18 patients for whom immunohistochemistry was performed. Patients with non-Hodgkin lymphoma and who did not go through an immunohistochemistry test were excluded from the study.

The data was collected using a survey form that was prepared, specifying for each patient epidemiological, clinical, histological and immunohistochemical data. These data were collected from medical records (age, gender, occupation).

The clinical variables studied were the type of affection (ganglionic or extra ganglionic) and the general signs: (fever, weight loss, profuse sweat).

The proposed diagnosis was established after the histological study carried out in the laboratory of anatomical pathology and this histological study consisted in the recording of the sample, verification of the good fixation of the sample, macroscopic examination of the sample (weighing, measuring and cutting), dehydration of the components, the paraffin impaction of the components, carrying out microtome cutting, lamellas staining after heating to deparaffinize them and finally the assembly of the lamellas for the interpretation.

The diagnosis chosen was that obtained after the immunohistochemical study, which consisted in demonstrating Ag *in situ* on cell or tissue preparations using

labeled Ac. It applied to samples that were fixed and included in paraffin as well as to frozen tissues. These samples corresponded to the tissues that had already been examined in histology.

3. Results

The general characteristics (epidemiological and clinical) are presented in Table 1 and biological in Table 2.

Out of the 18 patients, the average age of the study population was 41 years with extremes of 4 and 73 years. The study population was composed of 12 women and 6 men with a sex ratio of 0.5. The reason for consultation is dominated by adenopathies in more than 88% cases. Most of our patients consulted at a stage III and IV of ANN ARBOR (66.67%). More than 66.7% of the studied population had a sign of biological evolution. Most of the patients in our study were at an extensive stage of their disease.

This data are illustrated in Table 1, Figure 1, Tables 2-5.

As regard the comparation between histological analysis and immunohistochemical analysis, we found one cas of lymphoma T at histological analysis against five cas of lymphoma T at immunohistochemical analysis.

These data were presented in Tables 6-8.

4. Discussion

Different observation led us to the following comments:

Table 1. Distribution of population by age.

Age	Number	Percentage
0 - 15	02	11.11
16 - 30	05	27.78
31 - 45	02	11.11
46 - 55	03	16.67
>55	06	33.33
Total	18	100

Table 2. Distribution of population by occupation.

Occupation	Number	Percentage
Housewife	04	22.2
Pupil/Student	04	22.2
Farmer	04	22.2
Public/private worker	03	16.7
Informal sector	03	16.7
Total	**18**	**100**

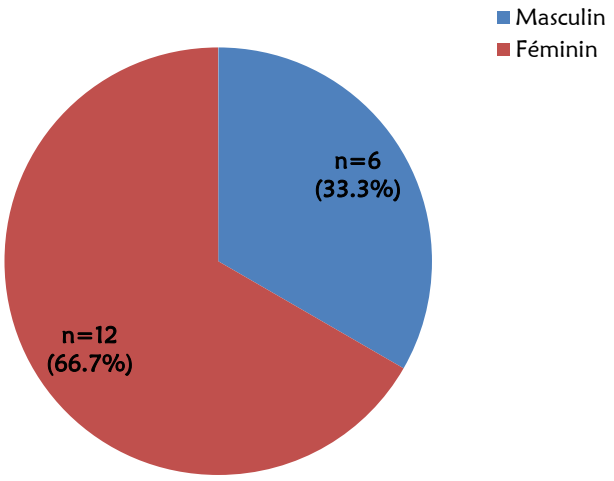

Figure 1. Distribution of population by sex.

Table 3. Distribution of population according to the reason for consultation.

Reason for consultation	Number	Percentage
Fever	10	55.6
Weight loss	12	66.7
Adenopathy	16	88.9
Asthenia	11	61.1
Other (pruritus, cavum mass…)	9	50

Table 4. Distribution of population through the ANN ARBOR stage.

ANN ARBOR Stage	Number	Percentage
Stage I	03	16.67
Stage II	03	16.67
Stage III	07	38.88
Stage IV	05	27.78
Total	**18**	**100**

Table 5. Distribution of population through the biological evolution stage.

Biological evolution stage	Number	Percentage
Yes	12	66.7
No	06	33.3
Total	**18**	**100**

4.1. For Epidemiology

About 50% of the sampled population was aged over 40 and this observation matches with documentation revealing that lymphoma is observed at any age but especially after 40 years [1] [2] [3].

Table 6. Distribution of the population according to the anatomo-pathological result.

Anatomo-pathological	Number	Percentage	Affected person
Diffuse NHL B with Large cell	07	38.9	Cases 1, 4, 6, 7, 9, 10, 11
Small cell diffuse Lymphoma	04	22	Cases 2, 3, 5, 15
BURKITT Lymphoma	02	11.1	Cases 8, 12
Centrocytical and Centroblastic Diffuse NHL	01	5.6	Case 18
Lymphoma T	01	5.6	Case 13
Subcutaneous nodule	01	5.6	Case 14
Mixed Follicular Lymphoma	01	5.6	Case 16
Medullary hypoplasia	01	5.6	Case 17
Total	18	100	

Table 7. Distribution of the population according to the immunohistochemistry result.

Immunohistochemistry	Number	Percentage	Antibodies
Large cell diffuse Lymphoma B	07	38.9	CD20+CD3−CD30−AE1/AE3−
Small cell DLBCL B	03	16.6	CD20+CD15−
Follicular Lymphoma	01	5.6	CD20+CD5−CD10+BCL2+
Lymphoma T	05	27.7	CD3+CD34-CD5+CD30−BCL2+
Hodgkin's disease	01	5.6	CD20+CD30+CD3−
Burkitt	01	5.6	CD20+CD3−BCL2+
Total	**18**	**100**	

Table 8. Spreading of population base on histologic and immunohistochemistry diagnosis.

Sickness cases	histology	IHC
Case of 1, 4, 6, 7, 9, 10	Dual LMNH with large diffuse B-cell	LDGCB
Case of 8	Burkitt Lymphoma	LDGCB
Case of 2, 15	Diffuse small LMNH cell	Diffuse small cell Lymphoma
Case of 3	Diffuse small cell Lymphoma	T Lymphoma
Case of 11	Diffuse Large B-cell Lymphoma	T Lymphoma
Case of 13	T Lymphoma	T Lymphoma
Case of 14	S/C Nodule	T Lymphoma
Case of 18	diffuse centrocytic and centroblastic LMNH	T Lymphoma
Case of 17	Medullar hypoplasia	Hodgkin Diseases
Case of 16	Follicular Lymphoma	follicular Lymphoma
Case of 5	Small cell LMNH	follicular Hyperplasia
Case of 12	Burkitt Lymphoma	Burkitt Lymphoma

In our sampled group most affected gender was women (66.7%) over men (33.3%) with a sex ratio of 0.5 contrary to what is described in the documentation describing a sex ratio of 1, 3 to 2 in favor of the man. this could be justified by our very selective and reduced sample.

Over 60% of our sampled population were housewives, farmers and students.

4.2. Clinical Explanation

The clinical picture was mainly characterized by adenopathy infection in more than 88% cases followed by weight loss in 66.7% cases and fever in more than 55% of cases. Patients were diagnose stage III and IV of ANN ARBOR in more than 60% cases which represent the most advanced stage of the disease and matches with most authors that we read [1] [2] [4] [5].

4.3. Diagnostic Explanation (Histology and Immunohistochemistry)

4.3.1. DLBCL

1) From histologic aspect

7 patients were diagnose with histological diagnosis of large-cell non-Hodgkin's B-cell lymphoma (case 1, case 4, case 6, case 7, case 9, case 10, case 11).

LDGCB is defined as a diffuse proliferation of large B lymphomatosis cells, of which nucleus is at least twice larger than the nucleus of a normal lymphocyte or larger than the one of a macrophage.

About the centroblastic variant, the cell population is mainly composed of a range of medium to large elements with a rounded nucleus and clear chromatin bearing two to four nucleoli classically contiguous to the nuclear membrane. The cytoplasm is scanty and discreetly basophilic and often, cells of which nuclei have incisions melts to it.

The histological aspect from our study matches with description reported in documentation [5] [6] [7].

2) From IHC aspect

The immunohistochemistry examination confirmed the LDGCB diagnosis with 7 patients (case1, case 4, case 6, case 7, case 8, case 9, case 10) and positive Antibodies CD20+CD3−CD30−AE1/AE3.

The IHC performed as part of study confirmed the LDGC diagnosis with 7 patients by specifying the nature B proliferations.

4.3.2. Small Cell LMNH (Centrocytic) with Small Malt Cell

1) From histologic aspect:

The histological diagnosis of non-Hodgkin's small cell lymphoma was performed over 4 patients (case 2, case 3, cases 5 and 15).

Diffuse lymphoma with small Malt cell, centrocytic and small cell B.

The histological description matches with documentation.

2) From IHC Aspect

Diffuse lymphoma was diagnose to 2 cases (case 2 and case 15) with CD20+CD15− and residual CD3 and refute to 2 cases (case 3 and case 5)

Case 3 = CD3+CD34−CD5+BCL2+CD30

IHC helped correct small cell NHL histological diagnosis of 2 patients [5] [6] [7].

4.3.3. Follicular Lymphoma

1) From histologic aspect:

Follicular lymphoma has been diagnose to one patient (Case 16).

Most of the time, tumor proliferation architecture is nodular, made of follicles with ill-defined contours and closely contiguous to each other.

The microscopic description matches with observation made on our patient.

2) From IHC aspect:

IHC analysis confirmed the diagnosis of follicular lymphoma: CD20+CD5−CD10+BCL2+ [8] [9].

4.3.4. T Lymphoma

1) From histologic aspect

The histological diagnosis of T-cell lymphoma has been issued to a patient (case 13). The morphological aspect is often characteristic and displaying a fading architecture with a diffuse polymorphic proliferation.

In our sample group, histological aspect has not been described.

2) From IHC aspect:

the IHC analysis confirmed the histological diagnosis with CD3+CD5+BCL2, CD20 residual CD34−CD30.

In addition, the IHC analysis allowed the correction of histological diagnosis in cases 3, 11, 14 and 18 all referring to CD3+, CD5+, BCL2+CD34−CD30− where T lymphomas proliferation has been recorded [9] [10] [11].

4.3.5. Hodgkin's Disease

1) From histologic aspect

The histology led to diagnose bone marrow hypoplasia to a patient (case 17).

2) From IHC aspect

On the said patient, the IHC analysis has rather enabled the diagnosis of a Hodgkin's disease with the positive antibodies, CD20+, CD30+ and CD3− [11] [12].

4.3.6. Burkitt's Lymphoma

1) From histologic aspect

Histological analysis diagnosed Burkitt's lymphoma to 2 patients, cases 8 and 12.

Microscopic analysis showed lymphoblasts with adenogram over 5%.

2) From IHC aspect

The immunohistochemical analysis confirmed the diagnosis of Burkitt's lymphoma in one patient (case 12), CD20+CD3-BCL2+ and refute the diagnosis

to another patient (case 8) CD20+CD3−CD30−AE1/AE3− [12] [13].

5. Conclusion

Results from our analysis confirm that the contribution of immunohistochemistry in the diagnosis of lymphomas associated with histological examination is fundamental, mainly as only immunohistochemistry can be used to diagnose T lymphomas. From this point of view, immunohistochemistry results reveal the 27.77% prognostic of T lymphocytes impact in immunohistochemistry, compared with only 5.55% of immunohistochemistry in histology.

This work indeed shows the important role of IHC in the diagnosis of lymphoid haemopathies [lymphoma] alongside morphological cytological and anatomo-pathological analyzes. They are all complementary and their request must be part of a logical approach with collaboration between biologists and practitioners.

In addition, equipment and training of our laboratory staff in modern diagnostic techniques is essential to ensure not only a good patient care but a minimization of the cost of examinations that will no longer need to be shipped.

Conflict of Interest

There is no conflict of interest regarding this publication.

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