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# Clinical and age peculiarities of non-Hodgkin's lymphomas with primary involvement of lymph nodes

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## Abstract

**Background:** Non-Hodgkin's lymphomas (NHLs) are a heterogenous group of malignant tumors developing from the lymphoid tissue and having a wide range of clinical manifestations and varied evolution and prognosis.

**Material and methods:** We have studied the clinical peculiarities of 228 patients of different age groups with NHLs and a primary involvement of lymph nodes.

**Results:** The frequency of the lymph nodes primary involvement has constituted 37.6%. It has been established that NHLs most frequently had their primary onset in the peripheral lymph nodes (61.8%), less frequently – in the abdominal (23.3%) and mediastinal (14.9%) ones. NHLs most frequently begin their development in the peripheral lymph nodes, first in patients over 60 years old (84.6%), in the abdominal lymph nodes – in children (57.2%), in the mediastinum – in children and people aged between 19 and 39 (48.2%).

**Conclusions:** Children develop only aggressive NHL forms, these forms also predominate in adults. Aggressive NHLs in adults have been most often diagnosed in the patients having the primary tumor focus location in the mediastinal and abdominal lymph nodes. The frequency of indolent NHLs is higher in the cases with the primary involvement of the peripheral lymph nodes, the patients' age being over 60. Metastases in the bone marrow have most frequently been recorded in NHL patients with the primary involvement of peripheral lymph nodes (53.5%). The involvement of CNS has taken place most frequently in the patients with NHLs, having the onset in the abdominal (34.4%) and mediastinal (30.0%) lymph nodes.

**Key words:** non-Hodgkin's lymphomas, lymph nodes, age.

## Introduction

Non-Hodgkin's lymphomas (NHLs) are a heterogenous group of malignant tumors, developing from the lymphoid tissue and having a wide range of clinical manifestations and varied evolution and prognosis. NHL is one of the most widely spread diseases of hemopoietic system. It represents 4-5% in the structure of malignant tumors and has lately shown a tendency to grow [1, 2, 3, 4].

The onset of NHLs may occur in any organ or tissue but most frequently they primarily develop in the lymph nodes [5, 6, 7, 8]. There has been an obvious progress in researching the NHLs in the recent years with regard to immunology, cytogenetics, molecular biology [9, 10, 11, 12, 13, 14]. But only some limited researches show that NHL prognosis also depends on the location of primary NHLs [15, 16, 17]. These conclusions point to the necessity of a differential study of NHLs and an obligatory assessment of the disease development regarding the NHL primary location.

From the above mentioned it can be concluded that the study of NHLs with the involvement of the lymph nodes, which are the most frequent primary NHL localizations, is clinically actual.

**The purpose** of this work is to study the frequency and clinical peculiarities of NHLs with the primary involvement of lymph nodes in respect to patients' age.

## Material and methods

The clinical characteristics have been studied in 228 NHL patients with the primary involvement of the lymph nodes, their age ranging from 2 to 84 years old.

In all the cases the diagnosis has been confirmed morphologically.

The degree of the tumor process spread in the organism has been determined according to the International Clinical Classification (ICC) approved in Ann-Arbor, USA in 1971. In staging the tumor process and distinguishing the zones of initial metastases and in NHL generalization we have used the following: clinical, radiologic, ultrasonic examinations, a bone marrow puncture, the trepanobiopsy with marrow histological study, the endoscopic and radiologic examinations of the gastro-intestinal tract, fibroepipharyngoscopy.

To assess the patients' survival, the *life-table* method has been used in which the survival limits according to Kaplan-Meier have been formed.

## Results and discussion

The primary involvement of lymph nodes has been detected in 228 out of 606 patients with NHLs, what has made up 37.6% (tab. 1). A higher frequency of NHLs with primary involvement of lymph nodes has been observed in children (47.1%). Approximately the same frequency of NHL onset in the lymph nodes has been noted in the patients aged 19-39 and over 60 (38.9% and 39.4% respectively). Less frequently NHLs have had their primary development in the lymph nodes in the patients aged between 40 and 59(27.7%).

**Table 1**

**Distribution of NHL patients with primary involvement of lymph nodes according to the age**

| Age | Total number of patients | NHL patients with primary involvement of lymph nodes | |
|---|---|---|---|
| | | Absolute number of the patients | % |
| 0-18 | 119 | 56 | 47.1 |
| 19-39 | 108 | 42 | 38.9 |
| 40-59 | 181 | 52 | 27.7 |
| > 60 | 198 | 78 | 39.4 |
| Total | 606 | 228 | 37.6 |

Most frequently the peripheral lymph nodes have been primarily affected (61.8%), most rarely – the abdominal and mediastinal ones (23.3 and 14.9% respectively) (tab. 2). However, it should be mentioned that the primary involvement of the abdominal lymph nodes (57.2%) has been pre-

**Table 2**

**Distribution of NHL patients with the primary involvement of lymph nodes according to the location of primary tumor focus and age**

| Location of the primary tumor focus | Number of the patients | Frequency % | Age | | | |
|---|---|---|---|---|---|---|
| | | | 0-18 Absolute (%) | 19-39 Absolute (%) | 40-59 Absolute (%) | > 60 Absolute (%) |
| Peripheral lymph nodes: | 141 | 61.8 | 13 (23.3) | 26 (61.9) | 36 (69.2) | 66 (84.6) |
| Antiauricular | 3 | 1.3 | - | 2 (4.8) | - | 1 (1.3) |
| Submandibular | 10 | 4.3 | - | 3 (7.1) | 1 (1.9) | 6 (7.7) |
| Cervical | 70 | 30.8 | 12 (21.4) | 10 (23.8) | 16 (30.8) | 32 (41.0) |
| Supraclavicular | 11 | 4.8 | - | 1 (2.4) | 3 (5.8) | 7 (8.9) |
| Axillary | 23 | 10.1 | - | 4 (9.5) | 11 (21.1) | 8 (10.3) |
| Inguinal | 24 | 10.5 | 1 (1.8) | 6 (14.3) | 5 (9.6) | 12 (15.4) |
| Mediastinal lymph nodes | 34 | 14.9 | 11 (19.6) | 12 (28.6) | 6 (11.5) | 5 (6.4) |
| Abdominal lymph nodes | 53 | 23.3 | 32 (57.2) | 4 (9.5) | 10 (1.9) | 7 (9.0) |
| Total | 228 | 100 | 56 (100) | 42 (100) | 52 (100) | 78 (100) |

dominant in children, and the peripheral lymph nodes have more frequently affected the adults over 60 years old (84.6%). NHLs with the onset in the peripheral lymph nodes, both in children and adults, most frequently have begun developing in the cervical lymph nodes. NHLs with the onset in the mediastinum have been most frequent in children and people aged 19-39 (19.6% and 28.6% respectively) (tab. 2).

The above shows that the frequency of different lymph nodes involvement is different depending on the age.

The morphological verification of the diagnosis indicates that children have developed only aggressive forms of NHLs; these have been also predominating in adults. Still, it can be mentioned that the number of patients with indolent NHL forms increases with age. Indolent NHL forms have most frequently occurred in the patients aged over 60 and their number has been approximately the same as that of the aggressive forms (tab. 3).

**Table 3**

**Distribution of NHL patients with the primary involvement of lymph nodes according to the age and morphological variants**

| Age | Number of patients | Morphological variants | | |
|---|---|---|---|---|
| | | Aggressive Absolute (%) | Indolent Absolute (%) | Unidentified Absolute (%) |
| 0-18 | 56 | 56 (100) | - | - |
| 19-39 | 42 | 33 (78.6) | 7 (16.7) | 2 (4.7) |
| 40-59 | 52 | 30 (57.7) | 20 (38.5) | 2 (3.8) |
| > 60 | 78 | 37 (47.4) | 34 (43.6) | 7 (9.0) |
| Total | 228 | 156 (68.4) | 61 (26.8) | 11 (4.8) |

After studying the frequency of morphological NHL variants according to the primary tumor focus in the lymph nodes we have determined that the aggressive variants predominate and do not depend on the primary location. Most of the patients with the primary NHL location in the mediastinal and abdominal lymph nodes have developed aggressive NHLs (91.3% and 86.8%, respectively). Indolent NHL frequency has been higher in patients with NHLs beginning in the peripheral lymph nodes (37.6%) (tab. 4).

Thus, the frequency of aggressive and indolent NHL cases varies according to the age and the primary tumor focus location in different groups of lymph nodes. Only aggressive NHLs have been recorded in children and these have predominated in adults as well. The aggressive NHLs in adults have been predominantly diagnosed in the patients having the primary tumor focus location in the mediastinal and abdominal lymph nodes. The indolent NHL frequency has been higher in the patients over 60 years old and in the cases with the tumor primary location in the peripheral lymph nodes.

In accordance with the ICC more than half of the patients (61.4%) have been assessed by generalized tumor stages (III and IV) which have predominated in children, patients aged 40-59 and over 60 (60.7%, 71.1% and 68.0% respectively). Only in the group of patients aged 19-39 in 61.9% of cases NHLs have been diagnosed to be in the local stages of development (tab. 5).Most frequently the initial tumor stages of development, especially stage I, have been determined in NHL patients with primary involvement of the peripheral lymph nodes (tab. 6).

The symptoms of general intoxication have been recorded in 100 (43.8%) cases. Frequently the symptoms of general intoxication have been present in NHL patients with primary

**Table 4**

**Distribution of NHL patients with the primary involvement of lymph nodes according to morphological variant and primary tumor focus location**

| Primary tumor focus location | Number of patients | Morphological variants | | |
|---|---|---|---|---|
| | | Aggressive Absolute (%) | Indolent Absolute (%) | Unidentified Absolute (%) |
| Peripheral lymph nodes | 141 | 79 (56.0) | 53 (37.6) | 9 (6.4) |
| Mediastinal lymph nodes | 34 | 31 (91.3) | 2 (5.8) | 1 (2.9) |
| Abdominal lymph nodes | 53 | 46 (86.8) | 6 (11.3) | 1 (1.9) |
| Total | 228 | 156 (68.4) | 61 (26.8) | 11 (4.8) |

**Table 5**

**Distribution of NHL patients with the primary involvement of lymph nodes according to the clinical stage and age**

| Age | Number of the patients | Clinical stage | | | |
|---|---|---|---|---|---|
| | | I Absolute (%) | II Absolute (%) | III Absolute (%) | IV Absolute (%) |
| 0-18 | 56 | 7 (12.5) | 15 (26.8) | 9 (16.1) | 25 (44.6) |
| 19-39 | 42 | 10 (23.8) | 16 (38.1) | 7 (16.7) | 9 (21.4) |
| 40-59 | 52 | 8 (15.4) | 7 (13.5) | 10 (19.2) | 27 (51.9) |
| > 60 | 78 | 9 (11.5) | 16 (20.5) | 18 (23.1) | 35 (44.9) |
| Total | 228 | 34 (14.9) | 54 (23.7) | 44 (19.3) | 96 (42.1) |

Table 6

**Distribution of NHL patients with the primary involvement of lymph nodes according to the clinical stage and primary focus location**

| Primary tumor focus location | Number of patients | Clinical stage | | | |
|---|---|---|---|---|---|
| | | I Absolute (%) | II Absolute (%) | III Absolute (%) | IV Absolute (%) |
| Lymph nodes: | | | | | |
| Peripheral | 141 | 29 (20.6) | 30 (21.2) | 29 (20.6) | 53 (37.6) |
| Mediastinal | 34 | 1 (2.9) | 9 (26.5) | 4 (11.8) | 20 (58.8) |
| Abdominal | 53 | 4 (7.5) | 15 (28.3) | 11 (20.8) | 23 (43.4) |
| Total | 228 | 34 (14.9) | 54 (23.7) | 44 (19.3) | 96 (42.1) |

involvement of mediastinal (91.2%) and abdominal (70.4%) lymph nodes. Less frequently the general intoxication symptoms have been recorded in the patients with NHL primary focus in the peripheral lymph nodes (21.9%). The character of the intoxication symptoms has been different; NHL cases with the primary involvement of mediastinal and peripheral lymph nodes have been predominantly accompanied by fever, while for the patients with NHLs, having their onset in the abdominal lymph nodes, the loss of weight has been characteristic.

Regardless of the location of the primary tumor focus and the patients' age, in most of the cases (72.1%), NHLs have been spread onto the sentinel lymph nodes and subsequently onto the more distant ones.

Extra nodal foci have developed in liver (42.6%), bone marrow (39.3%), spleen (28.2%), central nervous system (CNS) (17.9%), soft tissue (17.2%), pulmonary tissue (12.4%) and pleura (14.5%). Only rarely other organs and tissues have been involved in the process of generalization.

The frequency of metastases in the liver, spleen, soft tissue, pulmonary tissue and other organs and tissues has been low and has not correlated with the NHL primary focus location and the patients' age, while the involvement of bone marrow and CNS in the process of NHL generalization has varied according to the tumor primary focus location, the morphological variant and the age.

The involvement of bone marrow has been diagnosed more frequently in the patients with NHL onset in the peripheral lymph nodes (53.5%) and has been established in all age groups, predominating in the group of patients aged between 40 and 59 (65.2%) and in indolent NHL cases (77.3%). In NHL cases with primary involvement of the abdominal and mediastinal lymph nodes the bone marrow has been less often affected and has constituted 39.3% and 30.0% respectively.

In mediastinal NHLs the metastases in the bone marrow have developed in the patients under 40, primarily in children (63.7%) in the NHL aggressive variants. In NHL patients with primary involvement of the abdominal lymph nodes the bone marrow has been predominantly affected in patients over 50 years old (71.4%) and only in the indolent NHL variants.

The involvement of the CNS has most frequently developed in NHLs with the primary involvement of abdominal (34.4%) and mediastinal (30.0%) lymph nodes. Very rarely the metastases in the CNS have been recorded in the patients with NHL onset in the peripheral lymph nodes (2.8%) and only in children – in 50.0% of cases. The CNS involvement has not been recorded in the above group of adult patients.

In NHL patients with the primary involvement of the abdominal and mediastinal lymph nodes the metastases in the CNS have predominantly developed in children (90.9% and 54.5% respectively).

In the NHL adults with the primary involvement of the abdominal lymph nodes the metastases in the CNS have occurred very rarely, only in one patient aged 29 (4.7%). In mediastinal NHLs the involvement of the CNS has been recorded in 25.0% of patients aged up to 40.

From the above it can be concluded that the prevention of CNS involvement should be carried out not only in all the children with NHL onset in the lymph nodes, no matter where the location of the primary tumor focus is, but also in the adults under 40 years old with mediastinal NHLs.

The general survival period of more than 5 years in patients with the primary involvement of lymph nodes has been 36.9% of cases. The survival figures have been higher in the patients with the primary involvement of the peripheral lymph nodes (46.8%), being followed by those referring to the patients having NHL onset in the abdominal lymph nodes (36.4%). In the patients with mediastinal NHLs the general survival period of 5 years has been very rare and has constituted only 5.8%.

These data indicate an aggressive NHL evolution in the cases with the primary involvement of mediastinal lymph nodes.

The emphasized clinical peculiarities of NHLs with the primary involvement of lymph nodes will enrich the general knowledge about this disease and will contribute to the optimization of the diagnosis and treatment conduct.

## Conclusions

1. The frequency of NHLs with the primary involvement of lymph nodes is 37.6%.

2. Most frequently NHLs primarily develop in the peripheral lymph nodes (61.8%), less frequently – in the abdominal (23.3%) and mediastinal (14.9%) lymph nodes.

3. NHL onset in the peripheral lymph nodes most frequently occur in the patients over 60 years old (84.6%),

in the abdominal lymph nodes – in children (57.2%), in the mediastinum – in children and patients aged 19-39 (48.2%).

4. Children develop only aggressive NHL variants, which also predominate in adults. Aggressive NHLs in adults have been predominantly diagnosed in the patients having the primary tumor focus location in the abdominal and mediastinal lymph nodes. The indolent NHL frequency has been higher in case of primary involvement of peripheral lymph nodes in patients aged over 60.

5. The frequency of metastases in the bone marrow and CNS has been dependent on the location of NHL primary focus, morphological variant and age.

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# Functional recovery of retina after photo stress is accelerated by trans-cranial cerebellar stimulation in patients with diabetic retinopathy

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**Abstract**

**Background:** The characteristics of visual evoked potentials (VEP) have been studied in diabetic patients with and without diabetic retinopathy.

**Material and methods:** The magnetic impulses (2.0 Tl at the height of impulse) have been delivered to the cerebellar surface trans-cranially, using Neuro-MS/D, (Russian Federation), and the VEP have been registered every 20 seconds from the moment of the photo stress during one minute.

**Results:** An increase of the latency period and a reduction of the VEP amplitude have been recorded in the period following the exposure of the macular part of the retina to the photo stress. The VEP characteristics have been restored to the initial level at 74.3 $\pm$ 3.1 seconds from the photo stress moment in the control group, while in the diabetic patients with and without retinopathy this index has been 131.7 $\pm$ 10.2 and 86.5 $\pm$ 5.5 seconds respectively. In the presence of cerebellar trans-cranial magnetic stimulations (2.0 Tl, 40 impulses) the VEP amplitude depression has been less pronounced, and the restoration period of the VEP characteristics shortened to 90.5 $\pm$ 6.8 seconds in the patients with diabetic retinopathy.

**Conclusions:** 1. Retinopathy development is linked to a prolonged VEP latency period (P100), lowering N75-P100 amplitude, as well as to the enlargement of the recovery period of the retina's functional capacity in patients suffering from the diabetes mellitus in the presence of photo stress. 2. The cerebellar trans-cranial magnetic stimulation facilitates a quicker recovery of the retina's functional capacity in response to the photo stress in the diabetic patients with retinopathy. 3. The periodical cerebellar trans-cranial stimulations may be considered as a prevention method as well as a treatment method of diabetic retinopathy.

**Key words**: diabetic retinopathy, visual evoked potential, trans-cranial magnetic stimulation.