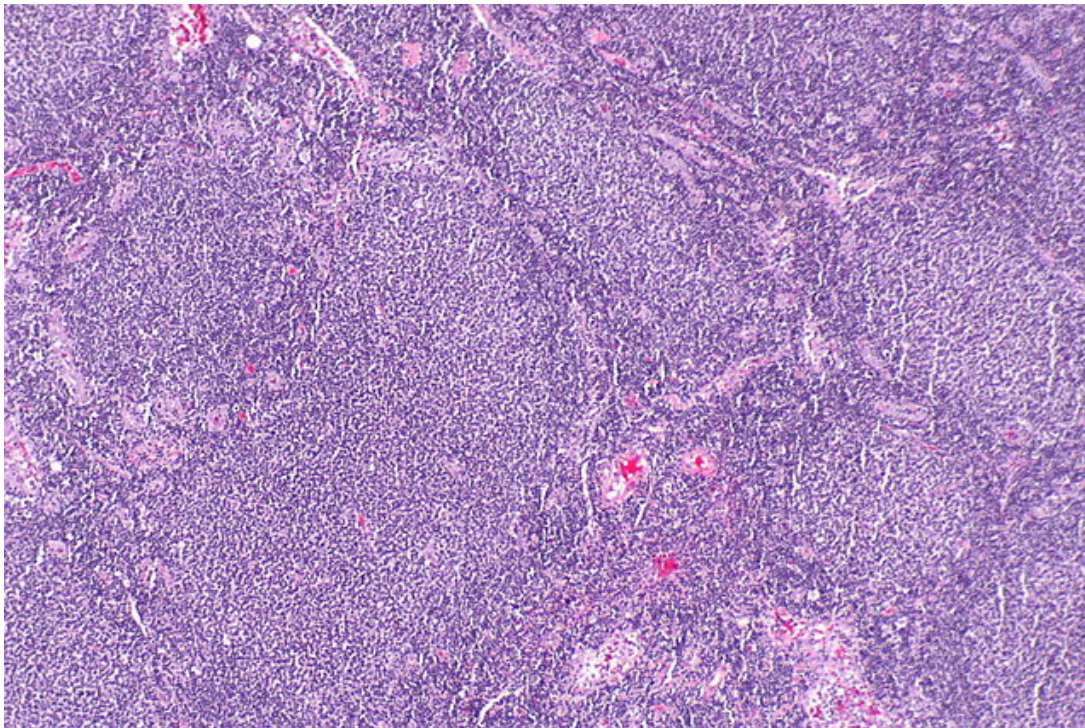


Follicular Lymphoma — Diagnosis and Survival Rate

[See online here](#)

There are two types of lymphoma - Hodgkin lymphoma (Hodgkin disease) and non-Hodgkin lymphoma (NHL). Follicular lymphoma (FL) belongs to the second group. It is a slow-growing B-cell lymphoma, and the second most common subtype of NHL; it most often occurs due to chromosomal translocation $t(14;18)$ causing *BCL2* gene rearrangement. Most of the patients with FL are asymptomatic; hence, they remain undiagnosed for years, and it is usually detected in the advanced stages.



Definition and Background

Follicular lymphoma (FL) is a B-cell tumor and the second most common subtype of non-Hodgkin lymphoma (NHL). It is characterized by slow growth (the most indolent one), and most of the patients remain asymptomatic for years before a diagnosis of FL is made.

Epidemiology of Follicular Lymphoma

Follicular lymphoma accounts for approximately 35% of all cases of NHL in the United States, with an estimated incidence of 3.18 cases per 100,000 people. The incidence increases with age, and the median age at diagnosis is 60 years. It is uncommon in

children and adolescents.

The incidence of FL is equal in males and females, but there are ethnic and racial variations. FL is twice as common in whites as in blacks. The incidence of FL is low in China and Japan.

Pathogenesis of Follicular Lymphoma

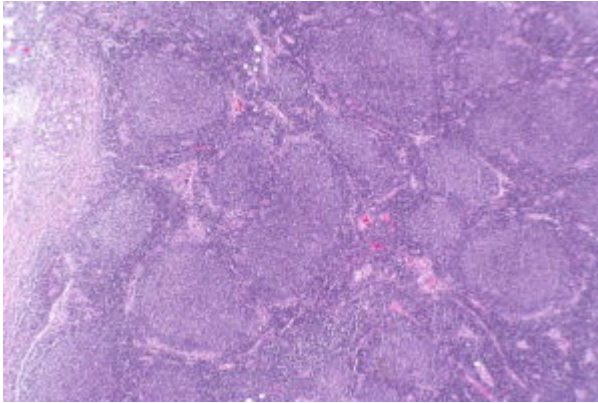


Image: "Micrograph showing a small B-cell lymphoma compatible with follicular lymphoma. H&E stain. Related images FL - very low mag. FL - low mag. FL - intermed. mag. FL - high mag. FL - very high mag. FL - BCL2 - low mag. FL - BCL2 control - low mag." by Nephron. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

The lymph nodes in follicular lymphoma have a nodular growth pattern, consisting of closely packed nodules varying in size and shape. These nodules contain a mixture of centrocytes (small- to medium-sized cells with elongated nuclei) and centroblasts (large cells with round or oval nuclei).

The majority of patients with FL have a chromosomal translocation, t(14;18), which results in gene rearrangement and overexpression of B-cell leukemia/lymphoma 2 (*BCL2*) oncogene. The *BCL2* oncogene blocks apoptosis (programmed cell death) leading to prolonged cell survival.

Etiology of Follicular Lymphoma

A number of risk factors have been implemented as etiologic agents for FL, but most have not been validated in independent studies. The risk factors include various immunocompromised conditions (HIV/AIDS), infections (viral, bacterial, fungal), chemical exposure (benzene, pesticides, herbicides, hair dyes, drugs, toxins), obesity and autoimmune diseases.

Clinical Features of Follicular Lymphoma

The follicular lymphoma frequently presents with chronic, painless, waxing and waning, lymphadenopathy commonly in the cervical, axillary or femoral regions. The mediastinal, hilar and abdominal lymph nodes are also often involved. Apart from enlarged lymph nodes, these patients may have constitutional symptoms (labeled as **B-symptoms**), such as:

- Drenching night sweats
- Fever (>38 C)

- Unintentional weight loss (> 10% in the last six months)

The other common clinical features of FL are:

- Breathlessness, chest pain, cough
- Abdominal pain and distention
- Pain in bones
- CNS involvement
- Pallor (signs of anemia)
- Purpura, petechiae or ecchymoses (signs of thrombocytopenia)
- Palpable thyroid mass
- Abdominal mass
- Testicular mass
- Pleural effusion
- Skin lesions

Diagnosis of Follicular Lymphoma

The hallmark of follicular lymphoma is enlarged non-tender, firm, and rubbery lymph nodes. FL is accurately diagnosed after histopathological examination of an enlarged lymph node. About one-half of all patients have hepatosplenomegaly. The following investigations help in determining the diagnosis, general health status, and prognosis of the patient:

Laboratory studies

- Complete blood counts (may show pancytopenia or isolated decreased blood cell lines due to bone marrow involvement)
- Quantitative analysis of immunoglobulins
- Bone marrow cytology and bone marrow histology
- LDH, β^2 -microglobulin
- Cytogenetics (FISH, PCR) for (14;18) in order to distinguish FL from other indolent types of NHL
- Flow cytometry: The presence of follicular dendritic cell markers (e.g., CD21, CD23) can aid in the diagnosis of FL.
- Biopsy of affected nodes; in the areas where access to the nodes is difficult, a CT-guided needle aspiration biopsy

Imaging studies

- CT scan of the neck/thorax/abdomen/pelvis
- Positron emission tomography (PET) in higher grades of the malignant process

Grading of Follicular Lymphoma

Follicular lymphoma is composed of closely packed nodules that have a mixture of centrocytes (small- to medium-sized cells) and centroblasts (large cells). The centroblasts are often smaller in number. The World Health Organization (WHO) has classified FL into different grades on the basis of the number of centroblasts.

Grading	Definition
1	0 - 5 centroblasts per hpf

2	6 - 15 centroblasts per hpf
3	>15 centroblasts per hpf

Reference:

<https://www.biooncology.com/pathways/b-cell/follicular-lymphoma-nhl/follicular-lymphoma-diagnosis.html>

Staging of Follicular Lymphoma

Follicular lymphoma is staged, like other non-Hodgkin lymphomas, by the Ann-Arbor classification.

Stage	Criteria
I	Involvement of a single lymph node region (I/N), or of a single or localized extranodal site (I/E)
II	Involvement of two or more lymph node regions on the same side of the diaphragm (II/N), or involvement of an extranodal site or organ (II/E) and one or more lymph node regions on the same side of the diaphragm (II/N/E)
III	Involvement of two or more lymph node regions on both sides of the diaphragm (III/N), or involvement of localized extranodal foci and affected lymph nodes on both sides of the diaphragm (III/E or III/N/E)
IV	Diffuse or disseminated involvement of one or more extralymphatic organs, with or without lymph node involvement

Table:

<https://www.onkopedia-guidelines.info/en/onkopedia/guidelines/follicular-lymphoma/@@view/html/index.html>

Prognosis of Follicular Lymphoma

The follicular lymphoma international prognostic index is used to predict the prognosis of patients with FL. It consists of the following five risk factors:

- > 4 affected lymph node regions
- Lactate dehydrogenase > normal
- Age > 60 years
- Ann-Arbor stage III or IV
- Hemoglobin <12g/dl

The 10-year survival rate depends upon the presence of a number of these risk factors.

Number of Risk Factors	Risk of Relapse	10-Year Survival Rate in %
0 - 1	Low	62 - 71
2	Intermediate	48 - 51
3 - 5	High	34 - 36

Table: <https://www.onkopedia-guidelines.info/en/onkopedia/guidelines/follicular-lymphoma/@@view/html/index.html>

Management of Follicular Lymphoma

Early stages of FL (Stages I and II) are successfully treated with administration of radiotherapy, and patients do not require hospitalization. Rituximab as monotherapy is another option in low-grade FL (mediates target-cell lysis).

Front-line immunochemotherapy

The frontline immunochemotherapy for FL consists of:

- Alkylating agents (inhibit cell growth and proliferation)
- Antimetabolites (block the pathway required for the targeted cells)
- Anthracyclines (inhibit DNA synthesis)
- Vinca alkaloids (interfere with mitotic cycle)
- Corticosteroids (induce lymphocytic effect and alter a body's immune reaction to the abnormal stimuli)

Bone marrow transplantation is efficient in non-advanced stages of the disease.

Review Questions

The correct answers can be found below the references.

1. A 67-year-old woman complains of enlarged lymph nodes in her neck and underarms. Her body temperature is 39°C. She is drowsy and sweaty, and there are pallor and dryness of the skin. The patient is breathless and complains of dizziness and chest pain. The CBC reveals anemia and decreased platelets. The biopsy of the neck node indicates >15 centroblasts per HPF. Follicular lymphoma is the primary diagnosis. What stage of FL can be diagnosed in this patient according to the result of a histological examination?

- A. Grade 1
- B. Grade 2
- C. Grade 3
- D. Grade 3A
- E. Grade 3B

2. The highest risk of relapse of FL is in the presence of...

- A. 0 - 1 risk factors
- B. 1 - 2 risk factors
- C. 3 - 4 risk factors
- D. 5 risk factors
- E. None

3. A 59-year-old white farmer was diagnosed with follicular lymphoma stage 2 a week ago. There were 13 centroblasts per HPF in the histological study of biomaterial obtained from the cervical lymph node, and a CT scan revealed two affected nodes above the diaphragm. What is the treatment strategy for this stage of FL?

- A. Radiotherapy, watch and wait strategy.
- B. Monotherapy with Rituximab, watch and wait strategy.
- C. Bone marrow transplantation, watch and wait.
- D. Radiotherapy and further bone transplantation.
- E. None of the above.

References

[Follicular Lymphoma](#) via lymphoma.org

[Follicular lymphoma: a historical overview](#) via ncbi.nlm.nih.gov

[B-Cell Lymphoma](#) via emedicine.medscape.com

[Follicular Lymphoma](#) via onkopedia-guidelines.info

[Follicular Lymphoma Management Overview](#) via emedicine.medscape.com

[Cytologic differential diagnosis of follicular lymphoma grades 1 and 2 from reactive follicular hyperplasia: cytologic features of fine-needle aspiration smears with Pap stain and fluorescence in situ hybridization analysis to detect t\(14;18\)\(q32;q21\) chromosomal translocation](#) via ncbi.nlm.nih.gov

[Follicular lymphoma - treatment and prognostic factors](#) via ncbi.nlm.nih.gov

Correct answers: 1C, 2D, 3A

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Notes