Lymphoma Overview

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Overview

- What is lymphoma?
- How common is lymphoma?
- Who gets lymphoma?
- What is the general approach to a lymphoma patient?
- What general kinds of treatment are available?
What is lymphoma?

Lymphoma is a family of blood cancers that comes from cancerous lymphocytes:

- **B-cells**: Lymphocytes normally fight viruses, bacteria, fungi, and foreign organisms.
- **T-cells**: Lymphocytes travel in the lymphatic system.
- **NK-cells**: These cells can grow in lymph nodes (nodal sites) or outside the lymph nodes (extranodal sites).
The Lymphatic System: where the cells of the immune system work and travel

- We have a lot of “lymphoid tissue” in our bodies
- Lymph nodes are normal
- Lymph nodes normally enlarge and become painful with infection

Lymphoma often grows in lymphoid tissues
- “nodal” = growing in a lymph node
- “extranodal” = growing outside of a lymph node
# How Common is Lymphoma?

## Estimated New Cases

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>174,650</td>
<td>268,600</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>116,440</td>
<td>111,710</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>78,500</td>
<td>67,100</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>61,700</td>
<td>61,880</td>
</tr>
<tr>
<td>Melanoma of the skin</td>
<td>57,220</td>
<td>39,260</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>44,120</td>
<td>37,810</td>
</tr>
<tr>
<td><strong>Non-Hodgkin lymphoma</strong></td>
<td>41,090</td>
<td>33,110</td>
</tr>
<tr>
<td>Oral cavity &amp; pharynx</td>
<td>38,140</td>
<td>29,700</td>
</tr>
<tr>
<td>Leukemia</td>
<td>35,920</td>
<td>26,830</td>
</tr>
<tr>
<td>Pancreas</td>
<td>29,940</td>
<td>25,860</td>
</tr>
<tr>
<td>All sites</td>
<td>870,970</td>
<td>891,480</td>
</tr>
</tbody>
</table>

- **Male**: 41,090 new cases/year
- **Female**: 33,110 new cases/year

### Table Notes

**Hodgkin and non-Hodgkin lymphoma affect both genders, all ages, all races**

~74,000 new cases/year

662,789 people living with lymphoma
Age at Diagnosis for Hodgkin and Non-Hodgkin Lymphoma

The graph illustrates the age at diagnosis for Hodgkin (HD) and Non-Hodgkin Lymphoma (NHL) cases per 100,000 population. The y-axis represents cases per 100,000, while the x-axis indicates age at diagnosis in years. The data shows an increased trend in the number of cases as age increases, with a notable peak for NHL after the age of 70.
Who gets lymphoma?

• Increasing age
• Abnormalities of the immune system
  – Inherited
  – Related to treatment of another condition
  – Acquired (HIV)
• Viruses
  – Hepatitis B and C
  – Human herpes virus 6
• Exposure to certain chemicals
• Bacteria
  – Helicobacter pylori
Non-Hodgkin Lymphoma occurs worldwide but is more common in developed countries.

**Trends in Incidence, USA**

- 83% increase in age-adjusted incidence between 1975-2008

**International Variation**

Slide courtesy of Dr. Brian Chiu

cancer.uchicago.edu
General approach to patient with lymphoma

- **DIAGNOSIS**: What does the patient have?
- **STAGING**: How much disease does the patient have?
- **PROGNOSIS**: How will the patient do?
### How is lymphoma diagnosed?

**TISSUE IS THE ISSUE**

<table>
<thead>
<tr>
<th></th>
<th><strong>PRO</strong></th>
<th><strong>CON</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fine needle aspirate</strong></td>
<td>• can distinguish lymphoma from other cancers</td>
<td>• Unable to give architectural detail</td>
</tr>
<tr>
<td></td>
<td>• Quick, easy, office-based</td>
<td>• Insufficient for most prognostic tests</td>
</tr>
<tr>
<td><strong>Core needle biopsy</strong></td>
<td>• Can be done in hard to reach places (stomach, spinal cord)</td>
<td>• Unable to give architectural detail</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Insufficient for most prognostic tests</td>
</tr>
</tbody>
</table>
| **Incisional or excisional biopsy** | • Gold standard  
|                         | • Allows architectural evaluation                                     | • May be more invasive                                                  |
|                         | • Allows tests for prognosis                                            | • May require surgery and anesthesia                                   |
|                         | • Can be used for research                                             |                                                                         |
Relative sizes of biopsy material
Excisional lymph node biopsy
There are more than 80 types of lymphoma:

- Different subtypes are present in varying percentages:
  - Mantle cell (6%)
  - Follicular (25%)
  - Burkitt (2.5%)
  - Diffuse large B cell (DLBCL) (30%)
  - T and NK cell (12%)
  - Other subtypes (9%)
  - Small lymphocytic (7%)
  - MALT-type marginal-zone B cell (7.5%)
  - Nodal-type marginal-zone B cell (<2%)
  - Lymphoplasmacytic (<2%)
There are many ways to slice the “lymphoma pie”
How do we make sense of all these lymphoma types? Look at “expected clinical behavior”….

- Low grade/indolent lymphoma:
  1. Slow growing
  2. Incurable
  3. More common in elderly

- Intermediate grade/aggressive lymphoma:
  1. Fast growing
  2. Potentially curable
  3. Occurs in all age groups

- High grade/highly aggressive lymphoma:
  1. Very fast growing
  2. Some are highly curable

- Mantle cell lymphoma?
- T-cell lymphomas?
General approach to patient with lymphoma

What does the patient have?

How much disease does the patient have?

How will the patient do?

DIAGNOSIS

STAGING

PROGNOSIS
Ann Arbor Staging: Stage I

Factors That Influence Treatment

Stage I

- Localized disease
- Single lymph node region
- Single organ outside of the lymph nodes

Courtesy of The Leukemia & Lymphoma Society.
Factors That Influence Treatment

Stage II

- Two or more lymph node regions near to each other
Ann Arbor Staging: Stage III

Factors That Influence Treatment

Stage III

- Two or more lymph node regions in different parts of the body
Ann Arbor Staging: Stage IV

Factors That Influence Treatment

Stage IV

- Widespread disease
- Multiple organs
- With or without lymph node involvement
What are “B symptoms”?

• Three classic B symptoms:
  – Fevers
  – Night sweats
  – Unintentional weight loss more than 10% of body weight

• Other parts of staging:
  – E: extranodal
  – X: bulky (> 10 cm in size)
  – S: spleen is involved

• Other symptoms that can happen with lymphomas:
  – Itching
  – Pain with alcohol intake
  – Fatigue
Imaging: an important part of staging

**CT Scans**
(Computed tomography)
- Gives STRUCTURAL information
- Allows measurements

**PET Scans**
(positron emission tomography)
- Gives METABOLIC information
- Shows intensity of activity

Neither test is SPECIFIC for lymphoma
Both tests require at least one centimeter of disease
Other types of initial tests that may be needed

- Bone marrow biopsy
  - Looks at the function of the bone marrow where all red cells, white cells and platelets are produced
  - Used less commonly than before
- Spinal tap (also called lumbar puncture)
  - Evaluates the fluid surrounding the brain and spinal cord
- Fertility preservation
  - Should be discussed with all patients of childbearing age
  - Consultation with specialists may be needed
- Echocardiogram or MUGA test
  - Performed to determine the heart’s function before using certain chemotherapy treatments
- Pulmonary function tests
  - A test to evaluate the lung’s capacity to extract oxygen from the air
General approach to patient with lymphoma

- **What does the patient have?**
  - **DIAGNOSIS**

- **How much disease does the patient have?**
  - **STAGING**

- **How will the patient do?**
  - **PROGNOSIS**
Types of prognostic assessments

• Laboratory
  – LDH (lactate dehydrogenase)
  – B2M (beta-2 microglobulin)

• Clinical
  – IPI (International Prognostic Index)
  – FLIPI (Follicular Lymphoma International Prognostic Index)
  – MIPI (Mantle cell International Prognostic Index)

• Biological
  – Immunohistochemistry (protein analysis)
  – Cytogenetics, FISH (chromosome analysis)
  – Gene expression profiling
IPI (International Prognostic Index): diffuse large B-cell lymphoma

- Age > 60 years
- Performance status > 1
- LDH abnormal
- Stage 3 or 4 disease
- More than one “extranodal” site
Why do patients have different outcomes?

Why do patients have different outcomes?

GENE SIGNATURES

Two molecular subtypes with disparate outcomes

Understanding biology identifies targets

PI3K
BCL6
BCR signaling
SYK
…and MANY more

TYPES OF TREATMENT
Therapy and lymphoma cells

Chemotherapy drugs

Antibodies, Kinase inhibitors

Target microenvironment

immunotherapy

Slide courtesy of Arnold Freedman
How do chemotherapy drugs work?

- Attack dividing cells
- Damage DNA
- Incorporate into DNA

Collateral effects:
- Hair loss
- Bone marrow
- Nails
- Nerves
How does radiation work?

- Radiation attacks DNA in both normal and malignant cells.
- **SIZE** and **dose** of radiation field affect side effects.
- Role of radiation in lymphoma is shifting.
Monoclonal antibodies: a special type of protein made by B cells and plasma cells

- Light chain
- Heavy chain
- Variable region
- Antigen binding region
How do antibodies kill lymphoma cells?

- Direct killing
- Deliver a targeted payload
- Recruit or activate immune cells
- Punch holes in cell

Slide courtesy of Arnold Freedman
What are signaling pathways?

- Cascade of events inside a cell
- Usually cause cancer cells to grow and stay alive
- Can be targeted
- Some cancer cells are “addicted” to certain pathways
Signaling pathways: tell cancer cells what to do

Targeted drug

Protein 1

Protein 2

Protein 3

grow
divide
invade
spread
Immunomodulatory agents: seed vs. soil

Anti-cancer drug

Cancer cell

FDC

T-cell

T-cell

T-cell

T-cell

T-cell

T-cell

T-cell

T-cell
Immunotherapy, Stem cell transplant, CAR-T

• Harness the immune system to kill lymphoma cells
• Can use drugs (immunotherapy)
• Can use stem cells (stem cell transplant)
• Can use manipulated T-cells (CAR-T therapy)

Come to Immunotherapy Plenary Session on Sunday!!
Summary: Lymphoma Overview

• A complex family of blood cancers
• A good biopsy is CRITICAL for management
• We are just beginning to understand why lymphomas develop
• Staging and prognosis are important parts of the overall management
• There are MANY new treatments that are based on better science

Listen, learn, absorb and ask questions
Thank you!