Lymphoma: The Basics

Dr. Douglas Stewart
Objectives

• What is lymphoma?
• How common is it?
• Why does it occur?
• How do you diagnose it?
• How do you manage it?
• How do you follow patients after treatment?
What is Lymphoma?

- A cancer of cells in the lymphocyte lineage
  - Cancer: uncontrolled growth, invasion, spread
  - Lymphocyte: a WBC, important in the immune system
- Lymphoma is not a single disease
  - Subtypes behave and respond differently
Lymphocytes

- B-cells develop in the bone marrow and influence the immune system by helping cells recognize infection.


- NK (natural killer) cells destroy viruses and cancers.
Function of the Lymph System
Lymph Node

Diagram labels:
- primary lymphoid follicle
- afferent lymphatic vessel
- para cortical area (mostly T cells)
- secondary lymphoid follicle (mostly B cells)
- germinal center
- cortex
- medullary cords (macrophages and plasma cells)
- medullary sinus
- artery
- vein
- efferent lymphatic vessel
- marginal sinus
How common is it? In 2017:

**Lymphoma Types**

**Hodgkin**
- 1,000 new cases/yr
- Relative 5-year survival 85%
- Leading cancer age 15-29

**Non-Hodgkin**
- 8,300 new cases/yr
- Relative 5-year survival 66% but varies greatly by subtype

**Chronic lymphocytic leukemia**
- 2,200 new cases/yr
- 7-10 year survival for most
Increasing age is a risk factor for NHL
Why does it occur?

- Environmental:
  - Chemicals: bioactive solvents, pesticides

- Viruses
  - HTLV-1, EBV, HCV, HHV-8, HIV

- Dysfunction of the Immune System
  - Immunodeficiency (congenital, HIV, Organ Tx)
  - Chronic stimulation of damaged system
    - Chronic autoimmune disease
      - RA, SLE, Sjogren’s, Celiac D, thyroiditis
  - Infections
    - Helicobacter Pylori chronic gastritis
Clinical Presentation of Lymphoma

• **Lumps:**
  - Lymph nodes: neck, axilla, groin, abdominal mass
  - Organs: skin, thyroid, testis, liver, spleen

• **Organ dysfunction or discomfort**
  - Stomach, lung, liver, brain
  - Bone marrow (cytopenias): infection, bleeding, fatigue

• **Obstruction of tubular organ or vessel**
  - Bronchus: cough, shortness of breath (SOB)
  - Superior Vena Cava: face swelling, SOB, headache
  - Intestine: pain, vomiting, constipation, bleeding
  - Ureter: uremia (n/v, malaise, confusion, dyspnea)

• **“B” Symptoms:** fever, night sweats, weight loss (pruritus)
Clinical Presentation of Lymphoma
Clinical Presentation of Lymphoma
Clinical Presentation of Lymphoma
Current Lymphoma Classification
WHO – 2016 Revision

There are over 60 types of lymphoma.

Hodgkin lymphoma
   Classical Hodgkin lymphomas (4)
   Nodular lymphocyte predominant Hodgkin lymphoma (1)

Mature B-cell neoplasms (41 types)

Mature T-cell & NK-cell neoplasms (27 types)
## Common Types of Lymphoma

### B-Cell Lymphomas

- **Indolent**
  - Follicular
  - Small Lymphocytic /CLL
  - Marginal Zone
    - MALT or Nodal
  - Lymphoplasmacytic

- **Aggressive**
  - Diffuse Large B-Cell (DLBCL)
  - Hodgkin
  - Burkitt (BL)
  - Intermediate betw HL/DLBCL
  - Mantle Cell
  - Post-transplant Lymphoproliferative Disorder

### T-Cell Lymphomas

- **Indolent**
  - Mycosis Fungoides & Sezary Syndrome-CTCL
  - 1º Cutaneous CD30+ ALCL
  - Lymphomatoid Papulosis

- **Aggressive**
  - Peripheral T-cell: NOS
  - Anaplastic Large cell
  - Angioimmunoblastic
  - Nasal NK/T cell
  - Enteropathy-type T-cell
  - γδ Hepatosplenic T-cell
  - Adult T-cell Leuk/Lymphoma
  - Precursor T-Lymphoblastic
The different lymphomas originate at different levels of lymphocyte maturation.

**B Cell Cancers by Cell Development**

- **Cell Stage**
  - Stem Cell
  - Precursor B-Cell
  - Immature B-Cell
  - B-Cell Before Antigen Exposure
  - B-Cell After Antigen Exposure
  - Antibody Producing B-Cell

- **Malignancy**
  - acute lymphocytic leukemia (ALL)
  - lymphoblastic lymphoma/leukemia
  - Precursor B-lymphoblastic lymphoma / leukemia
  - Small Non-Cleaved Cell Lymphoma (Burkitt's/Non-Burkitt's) (Possibly)
  - Chronic Lymphocytic Leukemia (CLL)
  - Small Lymphocytic Lymphoma
  - Follicular Lymphomas
  - Large Cell Lymphoma
  - Immunoblastic Lymphoma
## Distinguishing lymphomas by clinical behaviour

<table>
<thead>
<tr>
<th>Indolent NHL or CLL</th>
<th>Aggressive NHL or HL</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Slow growth</td>
<td>• Rapid growth</td>
</tr>
<tr>
<td>• Often asymptomatic</td>
<td>• Often symptomatic</td>
</tr>
<tr>
<td>• Long natural history possible</td>
<td>• Fatal in months (if untreated)</td>
</tr>
<tr>
<td>• Incurable with standard therapy</td>
<td>• Potential for cure with standard therapy</td>
</tr>
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</table>
Approach to Lymphoma Management

• **Establish Diagnosis**
  - Adequate tissue biopsy
  - Pathology review: IHC, Flow, Genetics

• **Determine Stage**
  - History & physical exam (B sx, ECOG, Age)
  - Blood tests: CBC, LDH, creatinine, LFTs
  - Imaging: CT scan Chest/Abdomen/Pelvis
  - Bone Marrow Asp/Bx

• **Develop Treatment Plan**
  - multidisciplinary input, standard/experimental options

• **Ensure Appropriate Follow-Up**
  - early detection/management of relapse or toxicities
Lymphoma Diagnosis

• Pathological diagnosis requires:
  • morphology (architecture)
  • IHC stains
  • Flow Cytometry
  • Genetics (FISH)

• Therefore,
  • **Fine needle biopsy is NOT good enough**
  • **Incisional or excisional surgical biopsy sent for lymphoma protocol is essential**
    • CT guided **CORE** needle biopsy may be adequate
Lymphoma Classification

- Morphology
- Immunohistochemistry
- Cytogenetics
- (gene expression profiling)
• "A" means that you have no “B” symptoms
• "B" reported fever, night sweats, & weight loss = ‘B’ symptoms
• "E" parts of your body other than the lymph nodes are involved
### CLL Staging – Rai Staging System

<table>
<thead>
<tr>
<th>Rai stage</th>
<th>Risk</th>
<th>lymphocytes</th>
<th>RBC</th>
<th>Platelets</th>
<th>Lymph nodes enlarged?</th>
<th>Spleen enlarged?</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>low</td>
<td>high</td>
<td>normal</td>
<td>normal</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>1</td>
<td>intermediate</td>
<td>high</td>
<td>normal</td>
<td>normal</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>2</td>
<td>intermediate</td>
<td>high</td>
<td>normal</td>
<td>normal</td>
<td>maybe</td>
<td>yes</td>
</tr>
<tr>
<td>3</td>
<td>high</td>
<td>high</td>
<td>low</td>
<td>normal</td>
<td>maybe</td>
<td>maybe</td>
</tr>
<tr>
<td>4</td>
<td>high</td>
<td>high</td>
<td>low</td>
<td>low</td>
<td>maybe</td>
<td>maybe</td>
</tr>
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</table>
With all of the information we are now able to formulate a treatment plan and discuss prognosis.

Initial Evaluation:
Specific Histologic Sub-type
Extent of disease
General health status of patient

Treatment Plan
Prognosis
Goals of treatment

- Cure
- Prolongation of life
- Prolongation of remission
- Control of symptoms (palliation)

➢ Typically, the greater the goal, the greater the potential toxicity
Treatment plan

• Partnership between patient and health care team

• Role of the health care providers:
  • Identify potential treatment goals
  • Discuss treatment options
  • Inform about advantages/disadvantages of options

• Role of the patient
  • State priorities regarding risk vs benefit
  • Make the ultimate decision
## Initial Lymphoma Treatment

<table>
<thead>
<tr>
<th>Lymphoma</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>Diffuse Large B-Cell</td>
<td>Rituximab+CHOP +/- IFRT</td>
</tr>
<tr>
<td>Follicular</td>
<td>IFRT or WW vs BendaR→R x2yr</td>
</tr>
<tr>
<td>Hodgkin’s Disease</td>
<td>ABVD +/- IFRT</td>
</tr>
<tr>
<td>Marginal Zone, nodal</td>
<td>BendaR→R x2yr</td>
</tr>
<tr>
<td>Gastric MALT</td>
<td>Hp PAC vs IFRT</td>
</tr>
<tr>
<td>Mantle Cell</td>
<td>RChemo-AutoSCT or BR then Rx2yr</td>
</tr>
<tr>
<td>Peripheral T-Cell, NOS</td>
<td>CHOP→AutoSCT</td>
</tr>
<tr>
<td>Anaplastic Large T-cell</td>
<td>CHOP</td>
</tr>
<tr>
<td>Precursor T-Lymphoblastic</td>
<td>ALL-like regimen vs AlloSCT</td>
</tr>
<tr>
<td>Mycosis Fungoides</td>
<td>Topicals, Electron Beam</td>
</tr>
<tr>
<td>Small Lymphocytic/CLL</td>
<td>FCR vs BR vs CBL-O vs Ibrutinib</td>
</tr>
<tr>
<td>Burkitt</td>
<td>R-CODOX-M / IVAC</td>
</tr>
<tr>
<td>PTLD</td>
<td>Rx4→RCHOP, ↓ immune suppress(^n)</td>
</tr>
<tr>
<td>HIV Associated Lymphoma</td>
<td>R-CHOP + HAART + ABx</td>
</tr>
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HIV Associated Lymphoma
How to Estimate Lymphoma Prognosis?

- Diagnostic subtype
- Stage: limited vs advanced
- Prognostic Index Scores (Age, Stage, LDH, Hb, & others)
- Biomarkers
  - DLBCL: p53, C-MYC, BCL-2, GCB vs non-GCB COO
  - MCL: Ki-67
  - ALCL: ALK-1
- Treatment Administered
  - Dictated by other health issues, esp dysfunction of:
    - Heart, Lung, Liver, Kidney, Brain
Components of Follow-Up

- Detection of cancer relapse/progression
- Detection/support for treatment complications
- Early detection of new primary cancers
- Monitoring for the long-term and late physical and psychological effects.