OVERVIEW OF LYMPHOMA

Lymphoma is a cancer that develops in the lymph system

Two Types of Lymphoma
- Non-Hodgkin Lymphoma
- Hodgkin Lymphoma
**OVERVIEW OF LYMPHOMA**

**Non-Hodgkin Lymphoma (NHL)**
- Everything that is not Hodgkin Lymphoma
  - Burkitt
  - Diffuse Large B-cell
  - Primary Mediastinal B-cell
  - Lymphoblastic
  - Anaplastic Large cell
  - Other rare lymphomas
- Malignant proliferation of cells of lymphocytic origin
  - Derived from B-cell and T-cell Lineages

**Hodgkin Lymphoma (HL)**
- Classic Hodgkin Lymphoma
  - Nodular Sclerosis
  - Mixed Cellularity
  - Lymphocyte predominant
  - Lymphocyte depleted
- Nodular Lymphocyte predominant

**Epidemiology**
- Higher incidence of NHL at younger age.
- HL incidence increased in adolescence

**NON-HODGKIN LYMPHOMA**
- Diverse collection of Malignant neoplasms derived from both mature and immature lymphoid cells of either B-cell or T-cell origin
- Includes all of the malignant lymphomas that are not classified as Hodgkin lymphoma.
How I think about these compares to developmental milestones in pediatrics and where it goes wrong

**Immature** (infants, toddlers, adolescents)

**Mature** (adults)

Remember this all happens in the lymph system, not the bone marrow

**Immature**
- T-Cell
- B-Cell

- Easy to remember because they are nearly identical to Pre-B cell/T-Cell ALL.
  - Only difference is the amount of bone marrow disease
  - <25% bone marrow disease

**Mature**
- Does not typically involve the bone marrow
- Think of these as disease outside the bone marrow (not a rule, just easier to classify mentally)

Epidemiology

Pediatric non-Hodgkin lymphomas are more common in younger children, males, and Caucasians
### Predisposing Factors
- Genetic abnormalities/Immune function:
  - Examples: CVID, agammaglobulinemia, SCID, Wiskott-Aldrich syndrome, ALPS
- Post-Transplant:
  - Post-solid organ transplant, or post bone marrow transplant with T-cell depleted marrow
- Infection:
  - HIV, EBV

### Clinical Presentation
- Each subtype varies (type, location)
- Orthopnea, wheezing, cough, dyspnea
- SVC syndrome
- Abdominal pain, ascites, acute abdomen, intussusception
- Adenopathy
- Rarely CNS symptoms
- 70% present with advanced stage disease
- 25% have anterior mediastinal mass

### Work up for suspicion of lymphoma
- Physical Exam
- CT of the affected region
- CBC with diff
- CMP
- Ferritin
- LDH
- ESR

### If concerns, next steps is biopsy
- **Excisional node biopsy is key!!!**
  - Do not get a fine needle biopsy

### Few histo-path pictures
- Burkitt = Starry Night (Van Gogh)
- Dark purple are the burkitt cells and macrophages are the stars
Non-Hodgkin Lymphoma

- Few histo-path pictures

Treatment
- Surgery
- Chemotherapy
- Radiation
- Immunotherapy

Prognosis

- Burkitt
  - 70-80% EFS
- Lymphoblastic
  - 60-90% EFS
- DLBCL
  - 80-90% EFS
- ALCL
  - 70-75% EFS

EFS = Event free survival

Hodgkin Lymphoma

- Named after Thomas Hodgkin (1798-1866)
  - January 10, 1832 Hodgkin described observations on several cadavers
  - The name stuck

Pediatric Lymphoma: Subtypes Simplified

<table>
<thead>
<tr>
<th>T cell derived</th>
<th>B cell derived</th>
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<tbody>
<tr>
<td>Immature</td>
<td>T-lymphoblastic</td>
</tr>
<tr>
<td>Mature</td>
<td>Anaplastic Large Cell</td>
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<tr>
<td></td>
<td>Diffuse Large B cell</td>
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HODGKIN LYMPHOMA

- Hodgkin lymphoma is characterized by progressive enlargement of the lymph nodes
- Has a predictable pattern of spread by extension to contiguous lymph nodes
- Derived from a neoplastic clone originating from B-cells in lymph node germinal centers.

Predisposing Factors
- Genetics:
  - Family members with Hodgkin Lymphoma increase the risk of developing disease.
  - Parent = 4x higher risk
  - Sibling = 7x higher risk (brothers 6x, sisters 8x)
  - Monozygotic twins = 99x higher risk
- Immune Function:
  - Examples: ALPS, ITP, AIHA, HIV, nephrotic syndrome
- Infection:
  - EBV
- Socioeconomic status (SES):
  - Lower SES has increased risk of Hodgkin Lymphoma in younger age
  - Higher SES has increased risk of Hodgkin Lymphoma in older age

Clinical Presentation (most common to least common)
- Painless swelling of one or more lymph nodes (rarely painful)
- Any lymph node chain
- **Supraclavicular lymphadenopathy is lymphoma until proven otherwise**

Clinical Presentation:
- Splenomegaly
- B-Symptoms:
  - >10% unintentional weight loss
  - Night Sweats (Soaking sheets/blankets)
  - Fever
  - Pruritis
  - Shortness of breath
  - EtOH induced pain.

Work up for suspicion of Lymphoma
- Physical Exam
- CT of the affected region
- CBC with diff
- CMP
- Ferritin
- LDH
- ESR

If concerns, next steps is biopsy
- **Excisional node biopsy is key!!!**
  - Do not get a fine needle biopsy
**HODGKIN LYMPHOMA**

- Two major Subtypes
  - Classical Hodgkin Lymphoma
  - Nodular Lymphocyte Predominant Hodgkin Lymphoma

1. Nodular Sclerosis
2. Mixed Cellularity
3. Lymphocyte-deplete
4. Lymphocyte-rich

**Pathology**

- Malignant cell of classic Hodgkin lymphoma is the Reed Sternberg cell ("owl’s eye appearance")

**HODGKIN LYMPHOMA**

- Classical Hodgkin Lymphoma
  - A pathologic distinction/diagnosis

**HODGKIN LYMPHOMA**

- Nodular Lymphocyte Predominant Hodgkin Lymphoma

**Pathology Distinctions:**

- Hodgkin Lymphoma
  - CD15+
  - CD30+
  - CD45-

- Nodular Lymphocyte Predominant Hodgkin Lymphoma
  - CD15-
  - CD30-
  - CD45+
**HODGKIN LYMPHOMA**

- Treatment
  - Surgery
  - Chemotherapy
  - Radiation
  - Immunotherapy

**PROGNOSIS**

- Overall good prognosis
- >85%
- Depends on stage

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**CASE REPORTS**

**CASE #1**

- 8 year old male presents to PCP's office with 2 week history of enlarged cervical lymph nodes and a fever. Also has congestion and runny nose.
- PMHx: Negative
- FHx: Negative
- SHx: Lives on a farm with animals

**CASE #1**

- PE: Bilateral cervical lymphadenopathy (LAD) noted, painful upon exam
- Well appearing, no other acute concerns on physical exam

**CASE #1**

- What are the next steps?
  - Observation?
  - Antibiotics?
  - Labs?
  - Scans?
  - Refer to Peds Heme/Onc?
  - Excisional node biopsy?
CASE #2

- 10 year old male presents to PCP’s office with 2 week history of enlarged cervical lymph nodes and a fever. Also has congestion and runny nose.
- PMHx: Negative
- FHx: Negative
- SHx: Lives on a farm with animals

PE: Right sided cervical lymphadenopathy (LAD) noted, painful upon exam
- Scratches over the right arm, otherwise well appearing on exam

What are the next steps?
- Observation?
- Antibiotics?
- Labs?
- Scans?
- Refer to Peds Heme/Onc?
- Excisional node biopsy?

CASE #3

- 3 year old thin male presents to PCP’s office with 2 week history of enlarged cervical lymph nodes
- PMHx: Negative
- FHx: Negative
- SHx: Lives on a farm with animals

PE: Bilateral posterior cervical lymphadenopathy (LAD) noted, not painful upon exam, well appearing, no other acute concerns on physical exam
- No weight loss, fevers or night sweats

What are the next steps?
- Observation?
- Labs?
- Scans?
- Refer to Peds Heme/Onc?
- Excisional node biopsy?
CASE #3

- 2 week follow up, lymph nodes are the same size, no changes otherwise
- Next steps?
  - Observation?
  - Labs?
  - Scans?
  - Refer to Peds Heme/Onc?
  - Excisional node biopsy?

CASE #3

- Labs show the following
  - WBC = 8
  - Hgb = 12
  - Platelets = 259
  - Ferritin = 60
  - ESR = 1
  - LDH = 200

CASE #3

- Next steps?
  - Observation?
  - Labs?
  - Scans?
  - Refer to Peds Heme/Onc?
  - Excisional node biopsy?

CASE #4

- 13 year old male presents to PCPs office with 2 week history of enlarged cervical lymph nodes, congestion, cough
  - PMHx: Negative
  - FHx: Negative
  - SHx: Negative

CASE #4

- PE: Left anterior cervical lymphadenopathy (LAD) noted, not painful upon exam, nasal congestion, no other acute concerns on physical exam
  - 10 lb weight loss,
  - No fevers or night sweats

CASE #4

- What are the next steps?
  - Observation?
  - Antibiotics?
  - Labs?
  - Scans?
  - Refer to Peds Heme/Onc?
  - Excisional node biopsy?
CASE #4

- Labs show the following
  - WBC= 8
  - Hgb= 12
  - Platelets= 259
  - Ferritin= 60
  - ESR= 26
  - LDH=350

- Now what?
- Pivotal Point in management
  - Non-painful LAD
  - Weight loss
  - Slightly elevated inflammatory markers
  - Pressure from family to do something
- Antibiotics?
- Steroids?
- CT Scan?

CASE #4

- Steroids are part of the treatment regimen of Lymphoma
- Patient will initially get better, lymph nodes will get smaller
- The lymph nodes will return and be more resistant to therapy
- DON'T give steroids for enlarged lymph nodes if lymphoma may be on the differential diagnosis

CASE #5

- 13 year old male presents to PCP's office with 2 week history of progressively enlarging left sided cervical lymph nodes, hoarse voice and fevers, 20 lb unintentional weight loss.
- PMHx: Negative
- FHx: Negative
- SHx: negative

CASE #5

- PE: Left sided cervical lymphadenopathy (LAD) noted, not painful upon exam
- Oropharyngeal exam is negative no tonsillar enlargement
- Has a hot potato voice when speaking

- What are the next steps?
- Observation?
- Antibiotics?
- Labs?
- Exams:
- Refer to Peds Heme/Onc?
- Excisional node biopsy?
CASE #5

- You bring the patient in to review labs:
  - WBC= 8
  - Hgb= 12
  - Platelets= 259
  - Ferritin= 60
  - ESR= 26
  - LDH=350
  - Potassium level = 6
  - Uric Acid = 9

- Look in his mouth again and notice the left tonsil is now quite enlarged

CASE #5

- What are the next steps?
  - Observation?
  - Antibiotics?
  - Labs?
  - Scans?
  - Refer to Peds Heme/Onc?
  - Excisional node biopsy?

CASE #5

- Rapidly growing lymph nodes, signs of tumor lysis (elevated potassium, uric acid)
- This is Burkitt Lymphoma until proven otherwise
- Burkitt can double in size every 24 hours. This is an oncologic urgency/emergency

CASE #6

- 13 year old male presents to PCP’s office with 2 week history of intermittent abdominal pain and 20 lb unintentional weight loss.
  - PMHx: Negative
  - FHx: Negative
  - SHx: negative

CASE #6

- PE: Abdominal pain with tenderness in the right lower/right mid abdomen

CASE #6

- What are the next steps?
  - Observation?
  - Antibiotics?
  - Labs?
  - Scans?
  - Refer to Peds Heme/Onc?
  - Excisional node biopsy?
CASE #6
- Ultrasound shows intussusception at the ileocecal junction, also noted a mass in this region
- **Refer to Peds Heme/Onc**
- This is a “common” presentation of Burkitt Lymphoma

CASE #7
- 13 year old male presents to PCP’s office with 2 week history of a lump in the armpit and 20 lb unintentional weight loss, and soaking night sweats.
- PMHx: Negative
- FHx: Negative
- SHx: negative

CASE #7
- PE: Diffuse adenopathy noted: left cervical, left axillary, and inguinal. Splenomegaly noted

CASE #7
- What are the next steps?
- **Observation?**
- **Antibiotics?**
- **Labs?**
- **Scans?**
- Refer to Peds Heme/Onc?
- Excisional node biopsy?

CASE #8
- 13 year old male presents to PCP’s office with 2 week history of progressively enlarging right sided painless mass above the clavicle.
- PMHx: Negative
- FHx: Negative
- SHx: negative

CASE #7
- Once adenopathy is confirmed on scans consult pediatric surgery for **whole lymph node excisional biopsy**
- **DO NOT** get a fine needle aspirate of a lymph node
  - If needle samples part of lymph node that is not affected, this will delay diagnosis.
**CASE #8**

- **PE:** Right supraclavicular lymph node noted

**CASE #8**

- **What are the next steps?**
  - Observation?
  - Antibiotics?
  - Labs?
  - Scans?
  - Refer to Peds Heme/Onc?
  - Excisional node biopsy?

**CASE #9**

- **SUPRACLAVICULAR LYMPH ADENOPATHY** is Hodgkin Lymphoma until proven otherwise!

**CASE #9**

- 12 year old male presents to PCP's office with 2 week history of fatigue, difficulty breathing when laying down at night, cough and shortness of breath when climbing stairs.
  - **PMHx:** Negative
  - **FHx:** Negative
  - **SHx:** Negative

**CASE #9**

- Next steps?
  - Observation?
  - Labs?
  - Scans?
  - Refer to Peds Heme/Onc?
  - Excisional node biopsy?

**CASE #9**

- Labs show the following
  - WBC: 2
  - Hgb: 9
  - Platelets: 57

- **CXR:** Mediastinal mass and a possible pericardial effusion
**CASE #9**

- This is a classic presentation of T-cell lymphoma
- This is a medical emergency with pending airway/cardiovascular collapse.
- Try not to have the patient lay flat, or sedate them for any procedures.

**REVIEW**

- There are two main classifications of Lymphoma
  - Non-Hodgkin Lymphoma
  - Hodgkin Lymphoma
- Varying clinical presentation but most have
  - Painless adenopathy
  - Progressively enlarging

- Supraclavicular LAD = Hodgkin Lymphoma
- Never give steroids if concerns for lymphoma
- Always safe to get labs and scans and close observation
- If concerning adenopathy and patient stable, refer for whole lymph node excisional biopsy.
- If any rapidly progressing adenopathy, airway compromise, mediastinal masses, refer to peds heme/onc

**WORKS CITED**

1. ASPHO 2019 Board Review Course 2019
2. Song, Joo Y., ASH, imagebank.hematology.org