PEDIATRIC LYMPHOMA

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OUTLINE

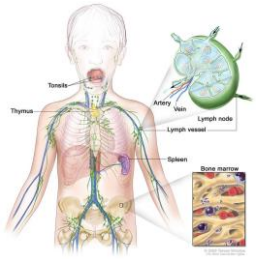
- Overview of Lymphoma
- Classification of Lymphoma
- Clinical Presentation
- Work up
- Case Review

GOALS

- Understand there are different types of lymphoma
- How lymphoma presents
- How to diagnose lymphoma
- When to refer to our team

OVERVIEW OF LYMPHOMA

Lymphoma is a cancer that develops in the lymph system



OVERVIEW OF LYMPHOMA

- 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 Lineage

Hodgkin Lymphoma (HL)

- Classic Hodgkin Lymphoma
  - Nodular Sclerosing
  - Mixed Cellularity
  - Lymphocyte predominant
  - Lymphocyte depleted
- Nodular Lymphocyte predominant

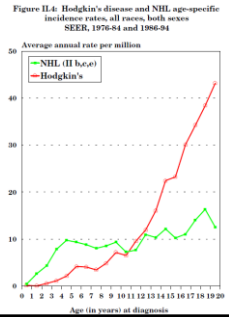
OVERVIEW OF LYMPHOMA

Pediatric Lymphoma: Subtypes Simplified

	T cell derived	B cell derived
Immature	T-lymphoblastic	B-lymphoblastic
Mature	Anaplastic Large Cell	Burkitt Diffuse Large B cell Hodgkin

OVERVIEW OF LYMPHOMA

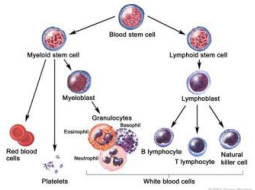
- Epidemiology
  - Higher incidence of NHL at younger age.
  - HL incidence increased in adolescence



NON HODGKIN LYMPHOMA

NON-HODGKIN LYMPHOMA

- Diverse collection of Malignant neoplasms derived from both mature and immature lymphoid cells of either B-cell or T-cell orgin
  - Includes all of the malignant lymphomas that are not classified as Hodgkin lymphoma.



NON-HODGKIN LYMPHOMA

Pediatric Lymphoma: Subtypes Simplified

	T cell derived	B cell derived
Immature		
Mature		

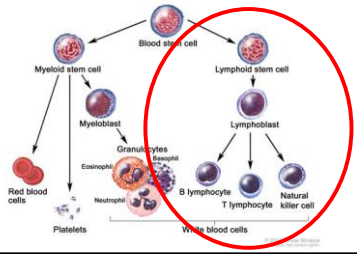
NON-HODGKIN LYMPHOMA

Pediatric Lymphoma: Subtypes Simplified

	T cell derived	B cell derived
Immature	T-lymphoblastic	B-lymphoblastic
Mature	Anaplastic Large Cell	Burkitt Diffuse Large B cell

NON-HODGKIN LYMPHOMA

- How I think about these compares to developmental milestones in pediatrics and where it goes wrong



Immature (infants, toddlers, adolescents)

Mature (adults)

NON-HODGKIN LYMPHOMA

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

	T cell derived	B cell derived
Immature	T-lymphoblastic	B-lymphoblastic
Mature	Anaplastic Large Cell	Burkitt Diffuse Large B cell Hodgkin

Immature (infants, toddlers, adolescents)

Mature (adults)

NON-HODGKIN LYMPHOMA

	T cell derived	B cell derived
Immature	T-lymphoblastic	B-lymphoblastic

- 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

NON-HODGKIN LYMPHOMA

- 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)

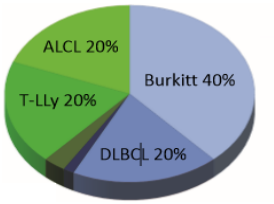
	T cell derived	B cell derived
Mature	Anaplastic Large Cell	Burkitt Diffuse Large B cell

NON-HODGKIN LYMPHOMA

- Epidemiology

Pediatric non-Hodgkin lymphomas are more common in younger children, males, and Caucasians

NON-HODGKIN LYMPHOMA



NON-HODGKIN LYMPHOMA

- 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

NON-HODGKIN LYMPHOMA

- 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

NON-HODGKIN LYMPHOMA

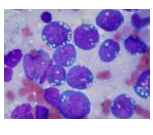
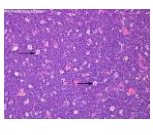
- Work up for suspicion of lymphoma
  - Physical Exam
  - CT of the affected region
  - CBC with diff
  - CMP
  - Ferritin
  - LDH
  - ESR

NON-HODGKIN LYMPHOMA

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

NON-HODGKIN LYMPHOMA

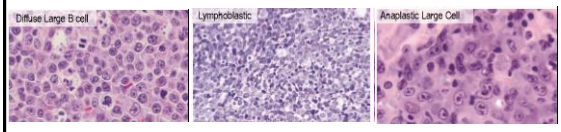
- Few histo-path pictures
  - Burkitt = Starry Night (Van Gogh)


- Dark purple are the burkitt cells and macrophages are the stars

NON-HODGKIN LYMPHOMA

- Few histo-path pictures



NON-HODGKIN LYMPHOMA

- Treatment
  - Surgery
  - Chemotherapy
  - Radiation
  - Immunotherapy

PROGNOSIS

- Burkitt
  - 70-90% EFS
- Lymphoblastic
  - 80-90% EFS
- DLBCL
  - 85-90% EFS
- ALCL
  - 70-75% EFS

EFS= Event free survival

HODGKIN LYMPHOMA

HODGKIN LYMPHOMA

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

HODGKIN LYMPHOMA

Pediatric Lymphoma: Subtypes Simplified

	T cell derived	B cell derived
Immature	T-lymphoblastic	B-lymphoblastic
Mature	Anaplastic Large Cell	Burkitt Diffuse Large B cell Hodgkin

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.

HODGKIN LYMPHOMA

- 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 increase risk of Hodgkin Lymphoma in older age

HODGKIN LYMPHOMA

- 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***

HODGKIN LYMPHOMA

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

HODGKIN LYMPHOMA

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

HODGKIN LYMPHOMA

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

HODGKIN LYMPHOMA

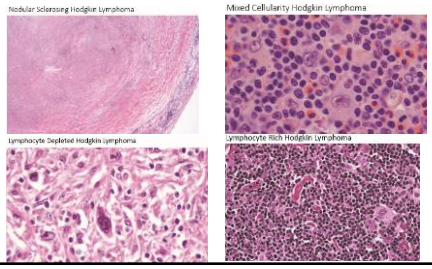
- Two major Subtypes
  - Classical Hodgkin Lymphoma
  - Nodular Lymphocyte Predominant Hodgkin Lymphoma

HODGKIN LYMPHOMA

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

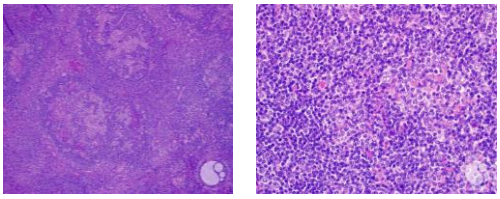
HODGKIN LYMPHOMA

- Classical Hodgkin Lymphoma
  - A pathologic distinction/diagnosis



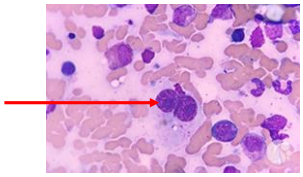
HODGKIN LYMPHOMA

- Nodular Lymphocyte Predominant Hodgkin Lymphoma



HODGKIN LYMPHOMA

- Pathology
- Malignant cell of classic Hodgkin lymphoma is the Reed Sternburg cell ("owl's eye appearance)



HODGKIN LYMPHOMA PATHOLOGY DISTINCTIONS:

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

HODGKIN LYMPHOMA

- Treatment
  - Surgery
  - Chemotherapy
  - Radiation
  - Immunotherapy

PROGNOSIS

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

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

CASE #2

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

CASE #2

- 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

CASE #3

- 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

CASE #3

- 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

- Now what?

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

CASE #4

- 13 year old male presents to PCP's 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

CASE #4

- 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 a 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

CASE #5

- What are the next steps?

- Observation?
- Antibiotics?
- Labs?
- Scans?
- 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 #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

- 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 #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 #8

- **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: Medistinal 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
  - Progressivey enlarging

REVIEW

- 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

REVIEW

- We are always on call to help guide management in children with concerns of lymphoma.
- Do not ever hesitate to call

WORKS CITED

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2. Song, Joo Y., ASH, imagebank.hematology.org
3. Lanzkowsky et al, Lanzkowsky's manual of pediatric hematology oncology, 6th edition, 2016.