

Lymphadenopathy

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Attending physician

Disclosures/Objectives

- Nothing to disclose
- No discussion of off-label medications
- Objectives:
 - Etiology and DDX of lymphadenopathy
 - When to be worried and what to do if you are



Disclosures/Objectives



Case 1: Patient HZ

- 18-year-old female previously healthy
- 3 months prior to presentation developed left submandibular LAD treated with 2 courses of oral antibiotics: Good resolution of adenopathy
- 1 month later developed left posterior auricular LN that did not respond to antibiotics
- 2 weeks PTA noted left supraclavicular LN
- All nodes non tender, no erythema or warmth
- No constitutional symptoms except a 10-pound intentional weight loss

Case 1: Patient HZ

Case 2: Patient MZ

- 7-year-old male previously healthy
- 3-4 day history of neck pain
- Increasing L post cervical LN
 - 1 prominent node (2 x 3 cm)
 - multiple other local LN
- Denies URI symptoms, travel, constitutional symptoms
- Indirect exposure to mature cats

Case 2: Patient MZ

LN structure and function

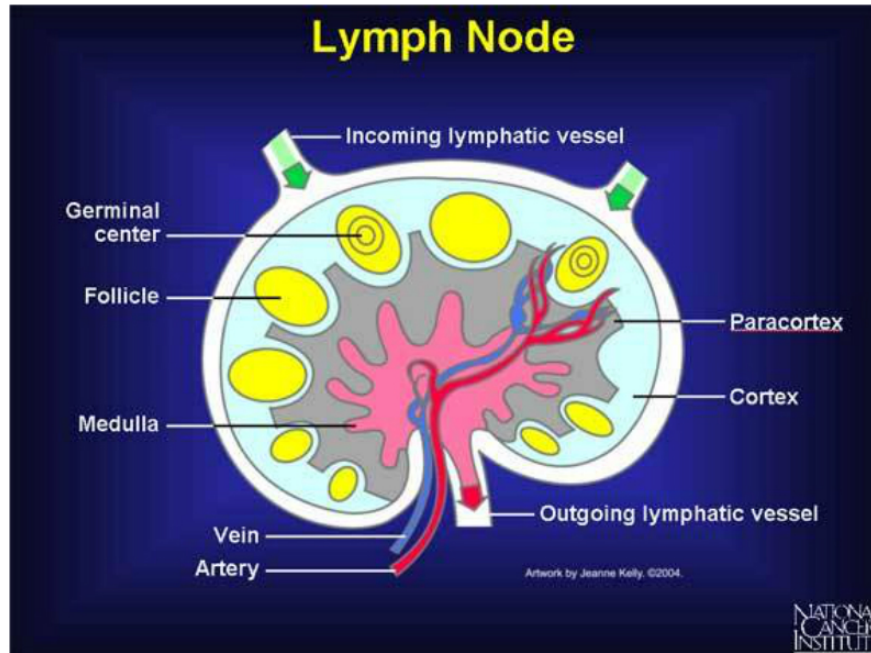


Image: NCI

- Sinus:
 - Filters antigens from extracellular fluid
- Cortex:
 - Follicles: B cell proliferation
 - Interfollicular zone: T cell differentiation and proliferation
- Medulla:
 - Immunoglobulin secretion

LN structure and function

Pathophysiology of LAD

- LAD very common in pediatrics
 - Est. 38-45% children have palpable LAD¹
- Usually benign, self limited
- Proliferation of intrinsic lymphocytes
 - Due to local inflammatory reaction
 - Infection of node itself
- Infiltration of nodal tissue
 - Primary or metastatic malignancy
 - Autoimmune disorders, storage diseases, etc.

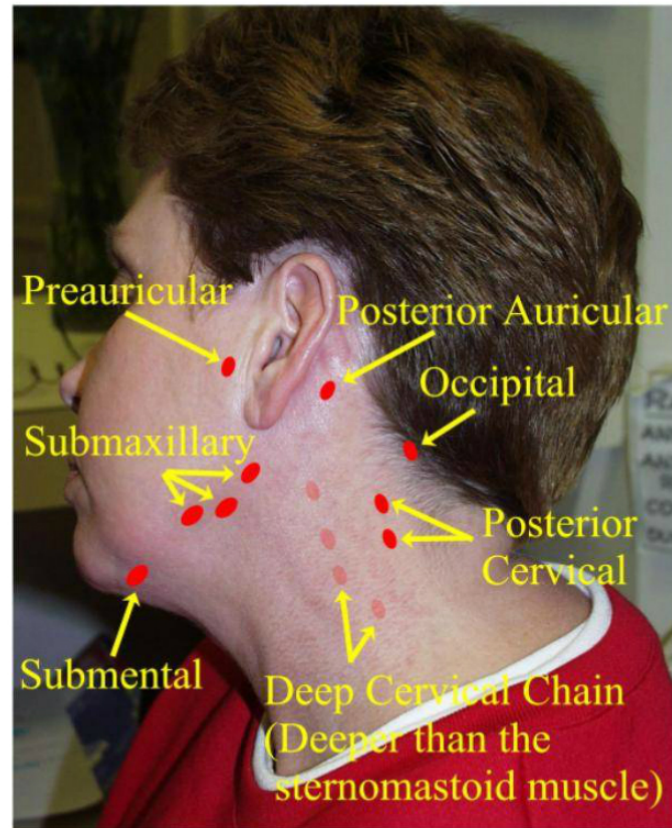
¹ Larsson, et al 1994



Pathophysiology of LAD

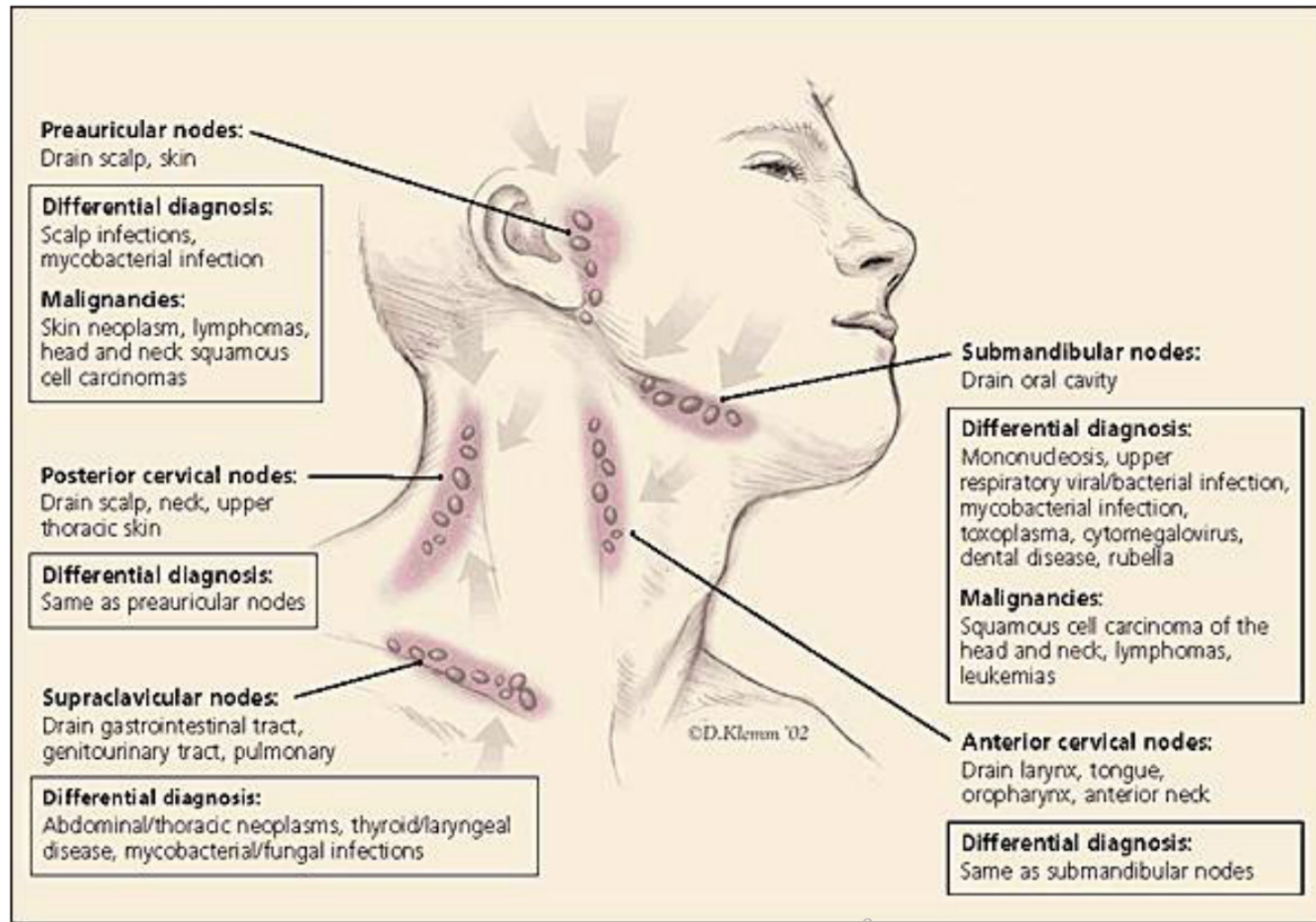
Anatomy and LN regions

- Occipital
- Preauricular
- Submaxillary/submental
- Cervical
- Supraclavicular
- Mediastinal
- Axillary
- Epitrochlear
- Inguinal
- Iliac
- Popliteal
- Abdominal
- Pelvic



Anatomy and LN regions

Regions and Differential Dx



Incidence

- One of the most common PE findings in pediatrics
- Changes with age
 - Significant number of newborns have palpable LAD (usually very small, < 0.5 cm)
 - Peaks in school-age children
 - Decreases during adolescence and adulthood



Incidence



Approach to LAD: History

- Age of patient
- Duration of adenopathy
 - acute <3-4 weeks, chronic >4-6 weeks
- Associated symptoms
 - Fever
 - Fatigue, malaise, weight loss, night sweats
 - Infections, ill contacts, skin lesions
 - Travel, pet exposure
 - Trauma
 - Medications/drugs, sexual activity

Approach to LAD: History

Approach to LAD: Exam

- General appearance of patient
- Distribution of LAD: local vs. generalized
- Size: Normal up to 1-1.5 cm depending on age and location
- Texture
 - Soft vs. firm, matted
 - Mobile vs. fixed
 - Tender, warm vs. non tender
- Location
- Pulmonary, abdominal, +/-skin exams key



Approach to LAD: Exam

Adenopathy (that's not)

- Congenital malformations may be confused w/ lymphadenopathy
- May enlarge with trauma or infection
- Often painless masses seen after birth
- Cystic hygroma
- Branchial cleft anomalies
 - May be bilateral
- Thyroglossal duct cyst
- Epidermoid cysts
- Neonatal torticollis
- Hemangioma
- Laryngocele

Adenopathy (that's not)

Differential Diagnosis

- Infection
- Autoimmune
- Storage diseases
- Medications
- Vaccinations
- Malignancy
- Histocytosis
- Immunodeficiency
- Miscellaneous
 - Kawasaki
 - Kikuchi
 - Rosai-Dorfman
 - Castleman's
 - ALPS

Differential Diagnosis

DDx: Infection

Viral	Bacteria	Mycobacterial	Protozoa	Fungal
EBV/CMV	Staph A. Grp A Strep	TB	Toxoplasmosis	Histio
Flu/HHV-6 adeno	Anaerobic	MAI	Malaria	Coccidio
Measles Rubella	Bartonella			Crypto
HIV Hep B	Tularemia			Aspergillus

DDx: Infection

DDx: Autoimmune/Storage disorders

- JRA, especially during the acute phase
- SLE
- Serum sickness
- Niemann-Pick
 - Sphingomyelin/lipids accumulate in spleen, liver, lymph nodes and CNS
- Gaucher
 - Increased glucosylceramide in spleen, lymph nodes and bone marrow

DDx: Autoimmune/Storage disorders

DDx: Medications/Vaccines

- Phenytoin
 - Regional or generalized LAD with maculopapular rash, fever, HSM, jaundice and anemia
 - Resolves after drug discontinued
- Other drug reactions associated with fever, rash, arthralgia and eosinophilia
- Rarely with vaccines
 - MMR, DTaP, varicella, polio, BCG
 - Historically with smallpox vaccine

DDx: Medications/Vaccines

DDx: Histiocytosis

- Langerhans cell histiocytosis (LCH)
 - May present in infancy/early childhood
 - Often associated with distinctive rash
- Hemophagocytic syndromes (HLH)
 - Sporadic or familial forms
 - Assoc. with massive HSM, increased ferritin, etc.
- Rosai Dorfman
 - Generalized proliferation of sinusoidal histiocytes
 - Massive, painless, bilateral cervical LAD
 - Benign course, presents in first decade of life



DDx: Histiocytosis



DDx: Immunodeficiency and Miscellaneous

- Autoimmune lymphoproliferative syndrome (ALPS)
 - p/w cytopenias, often thrombocytopenia
- Kawasaki
 - Fever >5 days
 - cervical LAD (unilateral)
 - edema/erythema of palms/soles, skin desquamation
 - Bilateral conjunctivitis
 - Strawberry tongue

DDx: Immunodeficiency and Miscellaneous

DDx: Miscellaneous, cont.

- Castleman's syndrome
 - Benign adenopathy, often neck and chest
- Sarcoidosis
 - Rare in childhood, consider in adolescents
- Kikuchi Disease
 - Necrotizing lymphadenitis
 - Benign disorder in young Japanese females
 - Fever, malaise, arthralgia, weight loss, night sweats
 - Occasional heptosplenomegaly

DDx: Miscellaneous, cont.

DDx: Malignancy

- Leukemia
 - Diffuse adenopathy, cervical and other sites
 - 2/3 ALL pts, 1/3 AML pts
 - Nodes may be small(ish) but more numerous and firm than usual
 - Signs/symptoms of systemic disease
 - Usually, but not always, accompanied by cytopenias and abnormal WBC differential



DDx: Malignancy



DDx: Malignancy, cont.

- Lymphoma (Hodgkin's and Non-Hodgkin's)
 - Lymph nodes tend to be larger (>3 cm)
 - Often more firm, matted, non mobile
 - May be localized or in multiple, often contiguous LN chains
 - Mediastinal mass may be present
 - HD may have a more indolent presentation
 - NHL tends to have a more acute onset of symptoms

DDx: Malignancy, cont.

DDx: Malignancy, cont.

- Metastatic solid tumors
 - Neuroblastoma
 - Nasopharyngeal carcinoma
 - Rhabdomyosarcoma
 - Thyroid carcinoma
- Often head and neck primary
 - Except NBL (posterior mediastinum)
- Nodes may be rock hard



DDx: Malignancy, cont.



To worry or not...

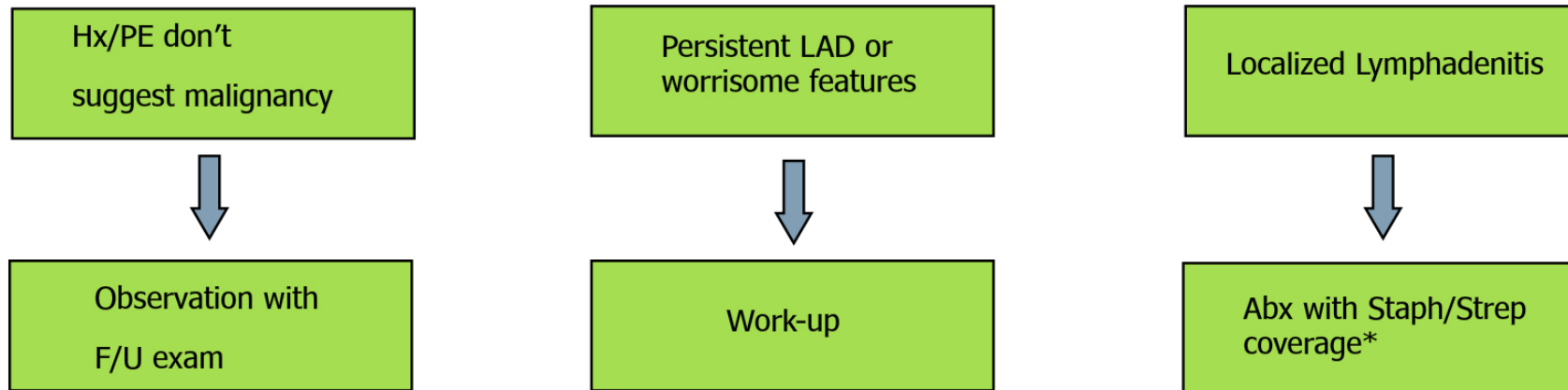
- N=126 over 3 years
 - N=98 with LAD
 - Localized in >50%
 - Most in head/neck
 - N=75 with benign dz
 - 2/3 reactive
 - 1/3 infection
 - N=23 with malignancy
 - Supraclavicular, generalized, nodes>3cm and elevated LDH
- N=457 over 8 years
 - N=346 benign
 - N=111 malignant
 - 50% "acute"; 50% chronic
 - Almost all "acute" pts were benign
 - Of malignant, more likely:
 - >3cm, >4 weeks, generalized, supraclavicular and abnl labs/X-ray

Yaris et al. *Clinical Pediatrics*, 2006.

Oguz et al. *Pediatric Hematol Oncol*, 2006

To worry or not...

...that is the question.



- *T/C cat scratch eval.
- If MAI suspected, need complete excision.
- If no response or persists for 6 weeks without identification of an infection, biopsy is warranted.



...that is the question.

OK, I'm worried. Now what?

- Laboratory evaluation
 - CBC with manual differential
 - ESR +/- CRP
 - CMP, LDH/uric acid
 - t/c EBV, CMV, HIV, B. henselae antibody
- Chest X-ray
- Ultrasound vs. CT (with contrast)
- PPD
- Open LN biopsy (NO fine needle aspiration)
- Bone marrow aspirate/biopsy



Ok, I'm worried. Now what?

So, what happened to our patients?

- Case 1:
 - PMD ordered CT neck, chest
 - Stage IV Hodgkin's lymphoma
- Case 2:
 - Referred for oncology consult
 - LN seemed to improve over 2-3 weeks, however still present on ultrasound of neck
 - LN biopsy reactive with evidence of EBV in node (despite negative EBV serology)

So, what happened to our patients?

Conclusion: LAD Red Flags

- Size
 - Over 2-3 cm
- Duration
 - Over 3-4 weeks without adequate explanation
- Texture
 - Firm, matted, non-mobile, non-tender
- Location
 - Supraclavicular (pathologic until proven otherwise)
- Signs of systemic illness

Conclusion: LAD Red Flags

Questions?

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Send an email: choprefonco@email.chop.edu

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Questions

