Pediatric Cervical Lymphadenopathy and Head and Neck Masses

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Epidemiology

- 38-45% of normal children will have palpable cervical lymphadenopathy
- 90% of children aged 4-8 years old will present with cervical lymphadenopathy
- These masses can be mistaken for other local and systemic processes
  - Congenital Masses
  - Malignancies
  - Local presentation of systemic disease
- Found by parents and caregivers and demand workup…
Outline and Objectives

1. Cervical lymphadenopathy in children
   - Describe important History and Physical findings including workup of cervical lymphadenopathy
   - Discuss pathogens responsible for acute vs subacute/chronic lymphadenitis
   - Review literature on the common causes and management of lymphadenopathy
   - Review literature on the use of ultrasound and biopsy to aid in diagnosis
   - Summarize a plan for diagnosis and treatment

2. Pediatric Head and Neck Masses
Definitions

• Pathologic Lymph Node
  • >2cm in children is considered abnormal

• Acute Lymphadenopathy
  • < 2 weeks duration

• Subacute Lymphadenopathy
  • 2-6 weeks duration

• Chronic Lymphadenopathy
  • > 6 weeks duration
Pathophysiology

Initial Infection
- URI
- Pharyngitis
- Otitis Media
- Odontogenic infection

Afferent Lymphatic drainage
- Organisms are captured by Macrophages and Dendritic cells
- Presented on MHC molecules

Presentation to T cells
- Proliferation of clonal cells
- Release of cytokines leading to chemotaxis

Activation of B cells
- Immunoglobulin release
- Continued proliferation of immune response

Result in
- Cellular Hyperplasia
- Leukocyte Infiltration
- Tissue Edema
- Vasodilation and Capillary Leak
- Tenderness due to capsule distension
History

• “OLD CARTS” - onset, location, duration, character, aggravating and relieving factors, timing and situation in which the problem is occurring
• Fever, malaise, anorexia, myalgia
• Pain or tenderness of node
• Sore Throat
• URI
• Toothache
• Ear pain
• Insect Bites
• Exposure to animals
• History of travel or exposure to TB
• Immunizations
• Medications
Drug Induced Lymphadenopathy

- Medications
  - Phenytoin
  - Pyrimethamine
  - Allopurinol
  - Phenylbutazone
  - Isoniazide

- Immunizations
  - Smallpox (historically)
  - Live attenuated MMR
  - DPT
  - Poliomyelitis
  - Typhoid fever

**Usually self limited and resolves with cessation of medication or with time in the case of immunization induced LAD**
Physical exam

- **General**
  - Febrile or toxic appearing

- **Skin**
  - Cellulitis, impetigo, rash

- **ENT**
  - Otitis, pharyngitis, teeth, and nasal cavity

- **Neck**
  - Size
  - Unilateral vs Bilateral
  - Tender vs Nontender
  - Mobile vs Fixed
  - Hard vs Soft

- **Lungs**
  - Consolidations suggesting TB

- **Abdomen**
  - Hepatosplenomegaly

- **Extremities**
  - Inguinal and Axillary adenopathy
Differential diagnosis

- Thyroglossal duct cyst
  - Moves with tongue protrusion and is midline
- Dermoid Cyst
  - Midline and often has calcifications on plain films
- Branchial Cleft Cyst
  - Smooth and fluctuant along SCM border
- Laryngoele
  - Enlarges with valsala
Differential diagnosis

- **Hemangioma**
  - Mass is presents after birth, rapidly grows, plateaus, and is red or bluish in color

- **Cystic Hygroma**
  - Transilluminates and is compressible

- **Sternocleidomastoid Tumor**
  - Lymphadenopathy does not present with torticollis

- **Mumps**
  - Mass palpated superior to jaw line
Laboratory workup

- CBC with Differential
- ESR, CRP
- Rapid Streptococcal screen
- Urine VMA
- LDH
Laboratory workup

- Serology
  - EBV
  - CMV
  - Bartonella
  - Toxoplasmosis
  - Syphilis
  - HIV
- PPD placement
Imaging workup

- **CXR**
  - To look for mediastinal lymphadenopathy
- **Ultrasound**
  - To evaluate for or follow progress of an abscess
  - To differentiate benign from malignant
- **CT/MRI**
  - To evaluate for abscess
- **EKG/ECHO**
  - If suspect Kawasaki Disease
- **Biopsy**
  - FNA or Excisional
Etiology of lymphadenopathy

- Acute Infectious
- Subacute/Chronic Infectious
- Malignancy
- Systemic disease/Non-infectious
Infectious Lymphadenopathy
Viral Lymphadenitis

• Most common form of reactive lymphadenopathy
• Common viruses involved:
  1. Adenovirus
  2. Rhinovirus
  3. Coxsackie virus A and B
  4. EBV
Viral Lymphadenitis

- Lymphadenopathy often bilateral, diffuse, non-tender
- Other Signs/Symptoms are consistent with URI
- Management is expectant but they are often biopsied due to slow regression
- Nodal architecture and hillock vascularity are normal on pathologic examination
Suppurative bacterial lymphadenitis

- Staphylococcus aureus and Group A Streptococcus
- Brodsky et al. showed aerobes 67% vs anaerobes 19%
- Common history reveals recent
  - URI
  - Earache
  - Sore Throat/Toothache
  - Skin Lesions
- Management is initially with oral or IV antibiotics depending on severity of infection
Suppurative bacterial lymphadenitis

- If not resolving or getting worse
  - CT with contrast and/or Ultrasound to evaluate for phlegmon/abscess/infiltrate
  - FNA vs Surgical I&D vs Surgical Excision if abscess is identified
Subacute Lymphadenitis

- 2-6 weeks duration
  - Usually seen and treated with antibiotics without improvement
- Parents start to worry and want to know "What is it?"
- Margalith et al. 1995
  - Atypical Mycobacteria
  - Cat Scratch disease
  - Toxoplasmosis
  - EBV and CMV less common
Choi et al 2009 - Archives Otolaryngology-HNS

- Retrospective review of 60 patients <18 y/o with persistent LAD and negative cultures at 48 hours.
- Performed general and specific PCR amplification of surgically excised tissue or abscess contents
- Surgically removed lymph nodes were also sent for permanent staining of specific organisms
- Diagnostic characteristics
  - Mean age of 4.7 years with slight female predominance at 53%
  - Average lymph node size was 3.2 cm
  - Superior cervical chain and submandibular nodes most involved
Choi et al 2009 - Archives Otolaryngology-HNS

- Most common Pathogens
  - Mycobacteria 61.7% of cases and 73% of these were MAI
  - Legionella represented 10% of cases
  - Bartonella represented 10% of cases
  - Unidentified etiology in 18.3% of cases
Method of identification

- Mycobacteria
  - Stain (70%), Culture (86.5%), PCR (81%)

- Bartonella and Legionella
  - PCR (100%), Culture and Gram stain (0%)

Choi et al 2009 - Archives Otolaryngology-HNS
• Results of surgical therapy
  • 90 surgical procedures performed on 60 patients
  • Cure rate was as follows
    • 95% for excisional lymphadenectomy
    • 58% for curettage
    • 23% for incision and drainage
• Conclusions

1. Nontuberculous mycobacterial infections
   • PCR is a rapid way to diagnose causative organisms of LAD as culture can take over 2 weeks for result
   • Surgical excision results in the highest cure rate and is therefore preferred unless the facial nerve or cosmetics are at risk.
   • Simple observation also works if nodes are not suppurative but this leads to protracted course

2. Cat Scratch Disease
   • PCR again is a rapid way to make the diagnosis since serologic studies have low sensitivity and specificity
   • Too small of sample size to determine if surgical vs antibiotics vs observation is superior treatment
   • Surgical treatment is necessary if abscess is identified as reported in 10-20% of casest difference.

Choi et al 2009 - Archives Otolaryngology-HNS
Conclusions

3. Legionella lymphadenitis
   - PCR provides rapid diagnostic benefits as legionella grows on special media
   - Levofloxacin/Moxifloxacin/Azithromicin +/- Rifampin
   - Incision and drainage plus antibiotics showed recurrence in 6/7 patients
   - Surgical excision is recommended but larger sample needed to detect significant difference.

Choi et al 2009 - Archives Otolaryngology-HNS
Atypical Mycobacteria

• #1 cause of subacute disease

• Species involved:
  • *Mycobacterium avium-intracellulare*
  • *Mycobacterium scrofulaceum*

• Develops over weeks to months
Atypical Mycobacteria

- Lymph nodes are tender, rubbery, and may have violaceous discolored skin over the node
- Diagnosis by acid fast stain and culture of material from lymph node (FNA) which can take weeks
- Untreated disease may lead to sinus tract and cutaneous drainage for up to 12 months
- Treatment historically has been surgical excision of involved lymph nodes

**Different from Tuberculous LAD where lymphadenopathy is a more ominous sign of disseminated disease if found in lymph nodes**
Zeharia et al 2008
Pediatric Infectious Disease

• Retrospective review of 92 children with chronic non-TB mycobacterial cervical lymphadenitis
• Parents opted for conservative treatment
• Patients followed for at least 2 years.
• Cultures and PCR used to verify mycobacteria
Zeharia et al 2008
Pediatric Infectious Disease

• Diagnostic Characteristics
  • <4 yrs old and nodal size > 3 cm in 80% of cases
  • Unifocal lymphadenopathy in 90% of cases
  • Submandibular (50%) > Cervical (25%) > Preauricular (10%)
  • Positive PPD >10mm in 85% of cases
  • MAI and M. haemophilum isolated in 90% of cases
Zeharia et al 2008
Pediatric Infectious Disease

Outcomes
- Dominant nodes showed purulent drainage in 97% of patients for 3-8 weeks
- Total Resolution
  - 6 months in 71%
  - 9 months in 98%
  - 12 months in 100%
- No complications other than a skin colored flat scar in the area of drainage at 2 year follow up
Zeharia et al 2008
Pediatric Infectious Disease

• Conclusions

• Previous randomized controlled trials have shown increased benefit of Surgery over Clarithromycin plus Rifabutin

• Surgical Therapy Complication rates of 10-28%
  • Large incision with poor cosmetic result
  • Fistula formation and prolonged wound drainage
  • Repeat surgical procedures for recurrence
  • Secondary *S. aureus* wound infections
  • Transient or permanent facial nerve paralysis

• Therefore expectant management is recommended, however a randomized study comparing surgery and observation is needed
Cat scratch disease

- Species involved:
  - Bartonella Henselae
- Age <20, M>F,
- 90% have had exposure to cat bite or scratch
- Can take up to 2 weeks to develop
Cat scratch disease

- Tender LAD are usually present however, fever and malaise are mild and present in <50% of patients (Twist)
- Diagnosis with serology for antibodies or PCR
- Historically management has been expectant with antibiotics reserved for rare cases with complicated courses (Windsor 2001)
- Antibiotics always given to immunocompromised patients to prevent disseminated disease

**Other less common zoonotic causes are tularemia, brucellosis, and anthracosis.**
Bass et al. 1998-Pediatric Infectious Disease

- Prospective Randomized Double Blinded Placebo controlled trial
- 29 patients randomized to Azithromycin x 5days vs Placebo (14 and 15 respectively)
- Lymph node volume calculated until total lymph node volume was less than 20% original value
Bass et al. 1998-Pediatric Infectious Disease

• Results
  • Azithromycin group showed 50% success rate at 30 days
  • placebo group showed only 7% success (p<0.02)
• After 30 days however the rate or degree of resolution was not significantly different between groups
Conclusions

Antibiotic therapy is indicated to rapidly decrease node size within the first 30 days.

Antibiotic therapy should be considered in all patients, especially those who are immunocompromised and at increased risk for disseminated disease.

Suppurative lymphadenitis occurs in 10% of patients from previous reports, but surgical drainage is rarely necessary.
Toxoplasma gondii

• Mechanism
  • Consumption of undercooked meat
  • Ingestion of oocytes from cat feces
• Symptoms
  • Malaise, fever, sore throat, myalgias
  • 90% have cervical lymphadenitis
• Diagnosis by serologic testing
• Complications include
  • myocarditis
  • pneumonitis
• Risk of TORCH infection to fetus
• Treatment with pyrimethamine or sulfonamides
Infectious mononucleosis - EBV

- Epidemiology
  - 50% seropositive by age 5
  - 90% seropositive by age 25
- Signs/Symptoms
  - Fever
  - Exudative pharyngitis
  - Painless generalized lymphadenopathy
  - Axillary LAD and Splenic enlargement increase likelihood
  - 50% lymphocytosis with >10% Atypical lymphocytes on peripheral smear is suggestive Diagnosis
Infectious mononucleosis - EBV

- Positive monospot test
- Serum heterophile Antibody definitive
  - 60% positive at 2 weeks while 90% are positive at 1 month
- Treatment is expectant and supportive
- Tonsillar hypertrophy can become bad enough to produce airway obstruction and you may need to place nasopharyngeal tube and start high dose steroids
- Do not give amoxicillin as patients will develop an iatrogenic rash in 80% of patients.
- No sports for 8 weeks to prevent splenic injury and rupture
Chronic lymphadenopathy

- >6 weeks
- Subacute pathogens frequently implicated
- Risk of Malignancy increased
  1. Neuroblastoma
  2. Rhabdomyosarcoma
  3. Leukemia/Lymphoma
Chronic lymphadenopathy

• Supraclavicular (Ellison 1999) and posterior triangle adenopathy (Putney 1970) are at increased risk for malignancy.

• Almost all patients receive biopsy at this point

• Excisional biopsy often needed to obtain enough tissue for diagnosis

• Management is usually a referral a medical oncologist given the age group and most common cancers identified
Non-Infectious Lymphadenopathy
Kawasaki Disease

- Lymphomucocutaneous Disease

- Five Characteristics of Disease (4/5 for diagnosis)
  - Fever >5 days
  - Cervical lymphadenopathy (usually unilateral)
  - Erythema and edema of palms and soles with desquamation of skin
  - Nonpurulent Bilateral Conjunctivitis
  - Strawberry Tongue
Kawasaki Disease

- Complications
  - Coronary artery aneurysms
  - Coronary artery thromboses
  - Myocardial infarction

- Treatment
  - IVIG and Aspirin

**Be sure to get Echo and EKG if Kawasaki disease is suspected**
Rosai - Dorfman

- Massive, painless, bilateral cervical adenopathy
- Benign condition
- Generalized proliferation of sinusoidal histiocytes
- First decade of life with 2M:1F
Rosai - Dorfman

- Associated signs and symptoms
  - Fever
  - Neutrophilic leukocytosis
  - Polyclonal hypergammaglobulinemia
  - Most patients will get a biopsy given the large adenopathy
- Characteristic biopsy showing sinus expansion with histiocytes and phagocytosed lymphocytes (Foucar 1990)
- Treatment is supportive and most patients have spontaneous regression
Langerhans Cell Histiocytosis

- Eosinophilic Granuloma
  - Solitary bone, skin, lung, or stomach lesions
- Hands-Schuller-Christian Disease
  - Diabetes Insipidus, Exophthalmos, Lytic bone lesions
- Letterer-Siwe disease
  - Life threatening multisystem disorder
  - 50% 5 year survival
Langerhans Cell Histiocytosis

• 1/3 of patients will have background LAD
• Histopathology shows normal lymph node architecture but increase sinusoidal Langerhan’s cells, macrophages, and eosinophils
• Treatment with topical steroids, oral steroids, and even chemoradiation therapy
Role of Ultrasound (Ahuja et al. 2005)

- No radiation exposure
- Good for following the progress of an abscess
- Differentiate Reactive vs Malignant nodes
- **Reactive**
  - <1 cm
  - Oval (S/L ratio <0.5cm)
  - Normal hilar vascularity
  - Low resistive index with high blood flow
Role of Ultrasound (Ahuja et al. 2005)

- Malignant
  - >1 cm
  - Round (S/L ratio >0.5cm)
  - No echogenic hilus
  - Coagulative necrosis present
  - High resistive index with low blood flow
  - Extracapsular spread
- Sensitivity 95% and Specificity 83% for differentiating reactive vs metastatic lymph nodes
FNA – Fine Needle Aspirate

- Minimally invasive
- Low morbidity
- Not as reliable in children as in adults so you can only trust FNA if it is positive (Twist 2000)
- Chau et al. 2003
  - Evaluated FNA of 289/550 patients referred with LAD
  - Sensitivity 49% and Specificity of 97%
  - False negative rate of 45%
  - 83% of false negatives were lymphomas
Excisional Biopsy

• Gold standard for diagnosis

• Consider if FNA is inconclusive or if FNA is negative but your suspicion for malignancy is high

• You must excise the largest and firmest node that is palpable and must remove the node with the capsule intact (Twist 2000)
Pediatric neck masses

History
Physical exam

Congenital
Suspected:
- Branchial cleft cyst
- Cystic hygroma
- Dermoid
  MRI/CT
  Consider surgical excision

Acquired
Suspected:
- Thyroglossal cyst
  Ultrasound
  Consider surgical excision

Infectious/Inflammatory
Go to B

Suspected malignancy
- CBC with diff
- Chest radiograph
- MRI/CT
- Oncology consult
  Consider surgical excision

Malignancy
- Hodgkin disease
- Other lymphoma
- Rhabdomyosarcoma
- Neuroblastoma
  No malignancy
  Consider other diagnosis

A
Infectious/Inflammatory

Suspected: inflammatory
- Kawasaki disease
- Sinus histiocytosis
- Drug induced
- Sarcoidosis

Suspected: viral
- CBC/diff
- EBV, cat scratch, toxicology titers
- PPD

Suspected: bacteria
- CBC/diff
- EBV, cat scratch, toxicology titers
- PPD

Suspected: atypical mycobacteria
- Go to C

Treat with oral antibiotics
- Good response
- Observe or surgical excision
- Poor response

Treat with oral antibiotics
- Good response
- Needle aspiration MRI/CT
- Poor response
- IV antibiotics
Suspected atypical mycobacteria

PPD

Treat with anti-Tbc chemotherapy

Trial of oral antibiotics/anti-Tbc chemotherapy

Good response

Poor response

Surgical excision
Thank you for listening