Pediatric Cervical Lymphadenopathy

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One focus. One purpose. Your child.

Children’s Hospital of Michigan
I have nothing to disclose.
Objectives

1) Define pediatric lymphadenopathy
2) Understand the workup of pediatric lymphadenopathy
3) Understand the differential diagnosis of pediatric lymphadenopathy
4) Discuss the unusual causes of pediatric lymphadenopathy
5) Discuss health disparities in pediatric otolaryngology
Lymphadenopathy aka Lymphadenitis (inflammatory nature)

- Lymphadenopathy: lymph nodes > 1 cm
  - > 2 mm supraclavicular
  - > 5 mm preauricular
- Incidence of palpable adenopathy
  - 62% age 3 weeks to 6 months
  - 52% age 7-23 months
  - 41% age 2-5 years
  - All less than 16mm and not supraclavicular
- 40% of healthy children have palpable lymphadenopathy
- Mills 1983
  - 100% of patients aged 4-10 who had recurrent tonsillitis had palpable adenopathy
vast majority- benign self-limiting condition
- cancer occurs at a rate lower than 1%
- >25% of malignant pediatric cancers involve the head and neck regions
History

- Duration?
  - Since birth?
  - Recurrence?
- Fluctuation of size?
- Pain, Erythema?
- Infectious symptoms (sore throat, URI?)
- Rashes, arthralgias?
- Fever, night sweats, unexplained weight loss, easy bruising, fatigue?
- Treatment attempted?
  - Which antibiotics?
- Recent animal (cat) or travel exposure?
Physical exam

- Location
  - Supraclavicular nodes are more likely to be malignant
  - Posterior- drain from the scalp
    - Mononucleosis
  - Submandibular
    - Atypical mycobacterium
- Size
- Unilateral versus bilateral
  - Midline neck masses usually not adenopathy
- Quality
  - Firm, matted, rubbery, fluctuant, mobility, tender, warm, erythematous, overlying skin changes
- Neck range of motion
<table>
<thead>
<tr>
<th>Region</th>
<th>Drainage areas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Submental</td>
<td>Bottom lip, floor of mouth, skin of cheeks</td>
</tr>
<tr>
<td>Submandibular</td>
<td>Mouth, lips, tongue, submandibular gland, cheek</td>
</tr>
<tr>
<td>Preauricular</td>
<td>Anterior and temporal scalp, anterior ear canal and pinna, conjunctiva, parotids</td>
</tr>
<tr>
<td>Postauricular</td>
<td>Temporal and parietal scalp</td>
</tr>
<tr>
<td>Occipital</td>
<td>Posterior scalp</td>
</tr>
<tr>
<td>Upper, middle and</td>
<td>Tongue, tonsils, larynx, oropharynx, anterior neck, scalp, lower ear canal,</td>
</tr>
<tr>
<td>lower cervical</td>
<td>parotid</td>
</tr>
<tr>
<td>Posterior cervical</td>
<td>Scalp and neck</td>
</tr>
<tr>
<td>Supraclavicular</td>
<td>Mediastinum, lungs, abdomen</td>
</tr>
</tbody>
</table>

Chang et al, 2020
Differential

- Infectious
- Immunologic
- Malignancy
- Miscellaneous
## Etiologies of Pediatric Cervical Lymphadenopathy: A Systematic Review of 2687 Subjects

<table>
<thead>
<tr>
<th>Etiology</th>
<th>No. of Patients</th>
<th>Prevalence Rate (% of Total)</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonspecific diagnosis</td>
<td>1822</td>
<td>67.8</td>
<td>66 - 69.6</td>
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<tr>
<td>Epstein-Barr virus</td>
<td>238</td>
<td>8.86</td>
<td>7.81 - 9.96</td>
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<tr>
<td>Malignant</td>
<td>126</td>
<td>4.69</td>
<td>3.92 - 5.52</td>
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<tr>
<td>Granulomatous</td>
<td>109</td>
<td>4.06</td>
<td>3.34 - 4.83</td>
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<tr>
<td>Cytomegalovirus</td>
<td>108</td>
<td>4.02</td>
<td>3.31 - 4.79</td>
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<tr>
<td>Group A/β Hemolytic Streptococcus</td>
<td>78</td>
<td>2.9</td>
<td>2.3 - 3.57</td>
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<tr>
<td>Rubella</td>
<td>46</td>
<td>1.71</td>
<td>1.26 - 2.23</td>
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<tr>
<td>Toxoplasmosis</td>
<td>32</td>
<td>1.19</td>
<td>0.816 - 1.63</td>
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<tr>
<td>Abscess</td>
<td>28</td>
<td>1.04</td>
<td>0.694 - 1.46</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>22</td>
<td>0.819</td>
<td>0.514 - 1.19</td>
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<tr>
<td>Cat scratch disease</td>
<td>17</td>
<td>0.633</td>
<td>0.369 - 0.966</td>
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<tr>
<td>Kawasaki disease</td>
<td>14</td>
<td>0.521</td>
<td>0.285 - 0.826</td>
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<tr>
<td>Sarcoidosis</td>
<td>10</td>
<td>0.372</td>
<td>0.179 - 0.635</td>
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<tr>
<td>Scaphylococcal pharyngitis</td>
<td>8</td>
<td>0.298</td>
<td>0.129 - 0.536</td>
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<tr>
<td>Streptococcal tonsillitis</td>
<td>7</td>
<td>0.261</td>
<td>0.105 - 0.486</td>
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<tr>
<td>Phlegmons</td>
<td>6</td>
<td>0.223</td>
<td>0.082 - 0.434</td>
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<tr>
<td><em>Mycoplasma pneumonia</em></td>
<td>3</td>
<td>0.112</td>
<td>0.023 - 0.269</td>
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<tr>
<td>Parvovirus B19</td>
<td>2</td>
<td>0.0744</td>
<td>0.00902 - 0.207</td>
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<tr>
<td>Familial Mediterranean fever</td>
<td>2</td>
<td>0.0744</td>
<td>0.00902 - 0.207</td>
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<td>AIDS</td>
<td>2</td>
<td>0.0744</td>
<td>0.00902 - 0.207</td>
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<tr>
<td>Dermatomyositis</td>
<td>2</td>
<td>0.0744</td>
<td>0.00902 - 0.207</td>
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<tr>
<td>Streptococcal pneumoniae</td>
<td>1</td>
<td>0.0372</td>
<td>0.000943 - 0.137</td>
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<tr>
<td>Rosai-Dorfman disease</td>
<td>1</td>
<td>0.0372</td>
<td>0.000943 - 0.137</td>
</tr>
<tr>
<td>Kikuchi-Fugimoto disease</td>
<td>1</td>
<td>0.0372</td>
<td>0.000943 - 0.137</td>
</tr>
<tr>
<td>PFAPA syndrome</td>
<td>1</td>
<td>0.0372</td>
<td>0.000943 - 0.137</td>
</tr>
<tr>
<td>Lymphomatoid papillomatosis</td>
<td>1</td>
<td>0.0372</td>
<td>0.000943 - 0.137</td>
</tr>
</tbody>
</table>
Blood work

- CBC with diff
- Erythrocyte sedimentation rate (ESR)
- C-Reactive protein (CRP)
- Uric Acid, Lactate dehydrogenase (LDH)
  - Indicative of high cell turnover
- Liver and kidney function testing
  - Multisystem involvement
- Bartonella, EBV, cytomegalovirus, TB, toxoplasmosis, and HIV
Imaging

- Concerning ultrasonography features
  - Round shape
  - Narrow or absent hilum
  - Irregular borders
  - Cystic necrosis
- Chest x-ray
  - Mediastinal widening
  - Hilar adenopathy
  - Evaluate for TB
Infection likely-treat
CONCERNING FEATURES

- >2 cm
- Increase in size over 2-3 weeks
- No improvement/size decrease in 4-6 weeks
- Supraclavicular
- Hard/fixed/matted
- Non-tender
- Fever > 1 week
- Weight loss, petechiae, night sweats, hepatosplenomegaly
- Abnormal blood counts or CXR
FNA

- Sensitivity as low as 67%
  - Depends on cytopathologist
  - Variable reports across studies
    - Up to 57% exclusion rate due to inadequate specimen
- 92-100% specificity
- Up to 20% nondiagnostic
- Up to 39% still require surgery for diagnosis
- FNA in young children often requires sedation
- Beneficial for carcinoma (adults)
  - Less accurate in low grade lymphoma
- Cutting needle biopsy?
Tissue biopsy

- Persistent symptoms for more than 4-6 weeks
- Steady increase in size over 2 to 3 weeks
- Greater than 2 cm
- Concerning features on US or CT
- Send for
  - Histology (fresh)
  - Gram stain
  - Bacterial culture
  - Acid-fast bacilli
  - Fungal culture
- >3 cm – 75% malignant (Srouji 2004)
Excisional biopsy

- Gold standard
- Risks:
  - Bleeding, pain, scarring, infection, hematoma, seroma, injury to surrounding structures
    - CN VII, XI, XII
  - Anesthesia
- Limited literature
  - Most reflects patients who had concerning signs/symptoms and needed biopsy
  - Up to 27% of biopsies are malignant
    - Varies based on referral practice/other pathologies present
Cervical lymph node biopsies in the evaluation of children with suspected lymphoproliferative disorders: Experience in a tertiary pediatric setting

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- 111 met inclusion criteria
- Median age higher in malignant group 11 (0-16) vs 14 (2-18)
- Median age Hodgkin Lymphoma was 15 (3-18)
- Median age Non Hodgkin Lymphoma 20 (2-16)
- Fever and tenderness more common in benign group
- No difference between groups for fever and night sweats
- Most common location was level V (benign and malignant)
Labs
- LDH elevated in both groups
  - Higher in benign group
- CRP elevated in both groups
  - Higher in malignant group
- ESR elevated in both groups
- Mean RBC, WBC and platelets within normal range

Imaging
- Malignant- more necrosis and surrounding edema (not significant)
- Long axis length 40.8 mm (malignant) vs 28.7 mm (benign)
- Mediastinal nodal involvement
  37/49 malignant vs 2/36
Table 3
Summary of diagnostic imaging available for review in the benign and malignant groups.

<table>
<thead>
<tr>
<th>Imaging Modality</th>
<th>Benign Group Total Cohort = 56n (%)</th>
<th>Malignant Group Total cohort = 55n (%)</th>
<th>p-valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neck Ultrasound</td>
<td>45 (80.4%)</td>
<td>24 (43.6%)</td>
<td>N/A</td>
</tr>
<tr>
<td>CT Neck</td>
<td>21 (37.5%)</td>
<td>41 (74.5%)</td>
<td>N/A</td>
</tr>
<tr>
<td>Chest x-ray</td>
<td>35 (62.5%)</td>
<td>47 (85.5%)</td>
<td>N/A</td>
</tr>
<tr>
<td>CT Chest</td>
<td>1 (1.8%)</td>
<td>9 (16.4%)</td>
<td>N/A</td>
</tr>
<tr>
<td>Ultrasound Characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shape</td>
<td>Ovoid: 25 (55.6%)</td>
<td>Ovoid: 10 (41.7%)</td>
<td>0.272</td>
</tr>
<tr>
<td>Round</td>
<td>20 (44.4%)</td>
<td>Round: 14 (58.3%)</td>
<td></td>
</tr>
<tr>
<td>Smooth</td>
<td>5 (11.1%)</td>
<td>Smooth: 2 (8.3%)</td>
<td>0.933</td>
</tr>
<tr>
<td>Lobulated</td>
<td>25 (55.6%)</td>
<td>Lobulated: 13 (54.2%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>15 (33.3%)</td>
<td>Other: 9 (37.5%)</td>
<td></td>
</tr>
<tr>
<td>Echogenicity</td>
<td>Heterogeneous: 18 (40.0%)</td>
<td>Heterogeneous: 9 (37.5%)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Hyperechoic</td>
<td>26 (57.8%)</td>
<td>Hyperechoic: 15 (62.5%)</td>
<td></td>
</tr>
<tr>
<td>Hypoechoic</td>
<td>1 (2.2%)</td>
<td>Hypoechoic: 0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>Necrosis</td>
<td>None: 17 (30.3%)</td>
<td>None: 5 (20.8%)</td>
<td>0.090</td>
</tr>
<tr>
<td>Calcification</td>
<td>None: 44 (97.8%)</td>
<td>None: 23 (95.8%)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Border</td>
<td>Sharp: 21 (46.7%)</td>
<td>Sharp: 8 (33.3%)</td>
<td>0.285</td>
</tr>
<tr>
<td>Hhilum Echogenicity</td>
<td>24 (53.3%)</td>
<td>Ill-Defined: 16 (66.7%)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Normal</td>
<td>4 (8.9%)</td>
<td>Normal: 2 (8.3%)</td>
<td></td>
</tr>
<tr>
<td>Abnormal</td>
<td>33 (73.3%)</td>
<td>Abnormal: 18 (75.0%)</td>
<td></td>
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<tr>
<td>Absent</td>
<td>8 (17.8%)</td>
<td>Absent: 4 (16.7%)</td>
<td></td>
</tr>
<tr>
<td>Vascularity</td>
<td>Normal: 0 (0.0%)</td>
<td>Normal: 0 (0.0%)</td>
<td>0.171</td>
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<tr>
<td>Peripheral</td>
<td>5 (11.1%)</td>
<td>Peripheral: 6 (25.0%)</td>
<td></td>
</tr>
<tr>
<td>Central</td>
<td>16 (35.6%)</td>
<td>Central: 6 (25.0%)</td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>20 (44.4%)</td>
<td>Both: 11 (45.8%)</td>
<td></td>
</tr>
<tr>
<td>Not Available</td>
<td>4 (8.9%)</td>
<td>Not Available: 0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>No Flow</td>
<td>10 (22.2%)</td>
<td>No Flow: 1 (4.2%)</td>
<td></td>
</tr>
<tr>
<td>Surrounding Edema</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long Axis Length (mean, SD)</td>
<td>28.7 ± 10.5 mm</td>
<td>40.8 ± 13.4 mm</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Short Axis Length (mean, SD)</td>
<td>13.8 ± 6.2 mm</td>
<td>19.0 ± 4.5 mm</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Ratio of Long to Short Axis (mean, SD)</td>
<td>0.92 ± 0.41</td>
<td>0.94 ± 0.28</td>
<td>0.832</td>
</tr>
<tr>
<td>Parameter</td>
<td>Sensitivity</td>
<td>Specificity</td>
<td>AUC</td>
</tr>
<tr>
<td>--------------------------------------------------</td>
<td>-------------</td>
<td>-------------</td>
<td>------</td>
</tr>
<tr>
<td>Age $\geq$ 11 years(^a)</td>
<td>0.76</td>
<td>0.56</td>
<td>0.66</td>
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<tr>
<td>Suspected Mediastinal Nodal Enlargement (Chest X-Ray or CT when available(^b))</td>
<td>0.76</td>
<td>0.94</td>
<td>N/A</td>
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<tr>
<td>Lymph Node Long Axis $\geq$ 31.5 mm(^a)</td>
<td>0.88</td>
<td>0.64</td>
<td>0.79</td>
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<tr>
<td>Lymph Node Short Axis $\geq$ 14.5 mm(^a)</td>
<td>0.88</td>
<td>0.71</td>
<td>0.82</td>
</tr>
<tr>
<td>Benign Pathological Diagnosis</td>
<td>Number</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>---------------------------------------------------</td>
<td>--------</td>
<td>-----</td>
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<tr>
<td>Reactive^a</td>
<td>23</td>
<td>41.1</td>
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<tr>
<td>Kikuchi-Fujimoto Disease</td>
<td>16</td>
<td>28.6</td>
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<tr>
<td>Granulomatous Lymphadenopathy</td>
<td>9</td>
<td>16.1</td>
<td></td>
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<tr>
<td>Progressive Transformation of Germinal Centers</td>
<td>2</td>
<td>3.6</td>
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<tr>
<td>Benign cyst</td>
<td>1</td>
<td>1.8</td>
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<tr>
<td>Chronic Inflammatory</td>
<td>1</td>
<td>1.8</td>
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</tr>
<tr>
<td>Extensive granulomatous inflammation</td>
<td>1</td>
<td>1.8</td>
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<tr>
<td>Neuroblastoma, reactive lymph node hyperplasia^b</td>
<td>1</td>
<td>1.8</td>
<td></td>
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<tr>
<td>Lymphadenitis</td>
<td>1</td>
<td>1.8</td>
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<tr>
<td>Rosai Dorfman Disease</td>
<td>1</td>
<td>1.8</td>
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<tr>
<td><strong>Malignant Pathological Diagnosis (n = 55)</strong></td>
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<tr>
<td>Hodgkin Lymphoma</td>
<td>41</td>
<td>74.5</td>
<td></td>
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<tr>
<td>Lymphoblastic Lymphomas/Leukemias</td>
<td>8</td>
<td>14.5</td>
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<tr>
<td>Anaplastic Large Cell Lymphoma</td>
<td>3</td>
<td>5.5</td>
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<tr>
<td>Large B Cell Lymphoma</td>
<td>2</td>
<td>3.6</td>
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<tr>
<td>Spindle Cell Neoplasm</td>
<td>1</td>
<td>1.8</td>
<td></td>
</tr>
</tbody>
</table>

^a Reactive</br>^b Neuroblastoma, reactive lymph node hyperplasia
Increased suspicion for lymphoma

- Presentation as a teenager
  - Reactive adenopathy is common in younger children
- Prolonged duration
- High rate of growth
- B symptoms (present in up to 40% of patients with Hodgkin lymphoma)
  - Also seen in reactive adenopathy
Diving deeper into the differential
Differential: Reactive adenopathy

- Secondary to viral infection (most common)
  - History of viral prodrome
  - Tender
  - Unilateral or bilateral
  - Resolves with resolution of the viral illness
    - Adenovirus, rhinovirus, RSV, parainfluenza, influenza, many more
  - Acute, Subacute or chronic viral causes
    - Fever, fatigue, tender bilateral, often posterior nodes
    - Epstein-Barr (EBV), Cytomegalovirus (CMV), Human immunodeficiency (HIV)
      - Pharyngitis with EBV
Bacterial lymphadenitis

- 2nd most common cause
- *Staphylococcus aureus*, group B strep (neonates), group A strep, anaerobic
- Timing: days to week of fever with enlarging neck swelling
- **Concern for bacterial when symptoms worsening 4-7 days**
  - Viruses typically resolve
- Exam:
  - Limited neck range of motion
  - Firm and tender swelling
  - Possible overlying erythema
  - **Fluctuance only noted in 25% of abscessed nodes**
Bacterial lymphadenitis treatment

- Clindamycin, Amoxicillin/clavulanate, or macrolides (oral)
  - More than 50% are *S aureus* or *S pyogenes*
  - 1% anaerobic
  - 2% acid-fast bacilli
- Clindamycin or Ampicillin/sulbactam (IV)
- Vancomycin and ceftriaxone if initial treatment ineffective
- **If no response in 48-72 hours, consider abscess**
  - Ultrasound-user dependent and variable
  - If equivocal: CT with contrast or MRI
Submental abscess

8 month old with 3 day history of fever and submental swelling
Denies recent illness other than slight runny nose
No other risk factors
Tx: I&D with Clindamycin
Parapharyngeal abscess
Retropharyngeal abscess

Underwent transoral drainage
GAS + cultures

One focus. One purpose. Your child.
Abscessed nodes

- Small 1 x 1 x 1 cm may not need drainage
- Intermediate (~1.5-2 cm) may resolve
  - Appropriate to observe if child is stable
Subacute or chronic

- *Bartonella* (Cat scratch)
- Toxoplasmosis
- other viral (CMV, HIV, EBV)
- Mycobacterial
- Lyme Disease
- Ehrlichiosis
- Rocky Mountain Spotted Fever
- Consider malignancy
Bartonella henselae

- Granulomatous infection
- Often transmitted by scratch or bite of cat
  - May occur immediately or several weeks/months after injury
- Painless and fluctuant neck mass
- Serologic testing for B. henselae
- Treatment:
  - Azithromycin (1st line)
    - May consider Clarithromycin, Ciprofloxacin, or Sulfamethoxazole/trimethoprim
  - Consider surgical excision if no improvement
Atypical Mycobacterial Infections

- Often children age 1-5
- Organism found in soil
- Usually submandibular or parotid areas
- Enlarge weeks to months, but may be rapid
- Often afebrile
- Nodes are large, nontender, indurated, possibly fluctuant
- **Violaceous skin changes**
- Sinus tracts
- Purified protein derivative (PPD)
  - May be weakly positive but often negative
- FNA (Caution)

Rosenberg 2014
Mycobacterium Smagmatis
Atypical mycobacterial infection

- Complete surgical excision (95% cure rate) versus medical management (66% cure rate)
- Pathology
  - Necrotizing granulomatous lesion
  - Positive stain for acid-fast bacilli
- I&D may result in chronically draining fistula
- If structures (ie facial nerve) at risk, consider curettage
- Medical management (dual therapy with macrolide and antimycobacterial agent) clarithromycin and rifampin (hepatotoxicity, body fluid or tooth discoloration)/ethambutol (optic neuritis)
  - 12 weeks
Scrofula (*Mycobacterium tuberculosis*)

- Typically children >5
- TB exposure
- Unilateral or bilateral, firm, non tender, often fixed
- May have fever or systemic symptoms
- May occur anywhere but often supraclavicular
- PPD or QunatiFERON-TB Gold
- 28-71% have abnormal CXR
- FNA (Caution)
- Excisional biopsy may be required
- I&D may result in chronically draining fistula
- Treatment: medical management
Toxoplasmosis

- *Toxoplasma gondii*
  - Common protozoan in cat feces or undercooked meat (from infected animal)
- Asymptomatic or flu-like illness
- Nontender, non-suppurative lymphadenopathy
- Blood PCR for antibody testing (IgM, IgG)
- Treatment:
  - Combination of pyrimethamine, sulfadiazine, leucovorin
- Typically resolves in 4-6 weeks
Noninfectious/Other causes
Malignancy

- Primary or metastatic
- Before age 6
  - Non-Hodgkin’s lymphoma
  - Rhabdomyosarcoma
  - Neuroblastoma
- After age 6
  - Hodgkin lymphoma (Reed-Sternberg cells)
- History
  - Fevers, night sweats, weight loss, easy bleeding/bruising, fatigue
- Common metastatic disease
  - Papillary thyroid CA
  - Nasopharyngeal CA
Malignancy

- Physical exam
  - Firm, matted down, non tender
  - Bilateral nodes less concerning than unilateral?
Other Causes
Kikuchi-Fujimoto Disease (KFD)

- Histiocytic necrotizing lymphadenitis
- Benign and self limiting
- Lymphadenopathy (may or may not be tender), **fever**, fatigue, rash (30% of patients), arthralgia, malaise
- May have night sweats, weight loss, hepatosplenomegaly
- Older children >7, adolescents, young adults
- More common in women
- Most cases occur in Asia but is worldwide
- Underdiagnosed
  - Often mistaken as viral infection
- Pathogenesis unknown (Viral?, Autoimmune?)
Kikuchi-Fujimoto Disease (KFD) Workup

- Labs
  - Variety of results
  - LDH may be elevated
  - 25-58% have Leukopenia
  - 2-5% have Leukocytosis
- Ultrasound and/or CT
- Excisional biopsy is gold standard for diagnosis
Kikuchi-Fujimoto Histologic Features

- Necrosis with apoptotic cells in central core
- **No neutrophils or eosinophils**
- Histiocytes (with **crescentic nuclei**), activated T-lymphocytes, **plasmacytoid dendritic cell** in periphery
- CD8 positive lymphocytes
- CD68 positive histiocytes
  - Contrast to B-cell lymphoma which stain CD20 positive
- **Myeloperoxidase expression can help differentiate from T-cell lymphoma**
KFD associations

- Autoimmune disease
  - Systemic lupus erythematosus (SLE) (approximately 13% of cases)
    - KFD may predispose the patient to SLE
    - Study by Baenas et al 2016
      - 30% KFD prior to SLE
      - 47% simultaneous occurrence
      - 23% KFD after diagnosis of SLE
  - Grave’s disease
    - 4 case reports of disseminated intravascular coagulopathy (DIC) with KFD
      - Do not imply a causal relationship
KFD Treatment/Prognosis

- Self limited
- NSAIDs for fever or tenderness
- Steroids if severe tenderness
- Most cases resolve in 6 months
- May be beneficial to monitor for SLE
- ESR monitoring may be beneficial
- Slight increased risk of malignancy or autoimmune disease
- 3-4% may recur (may be years later)
  - Optimal management of recurrence uncertain
  - Case reports of hydroxychloroquine use
PFAPA

- Periodic fever
  - lasting 3-5 days; occurring every 2-8 weeks
  - Diagnostic criteria: at least 5 episodes

- Aphthous stomatitis
  - 50% of patients

- Pharyngitis
  - Over 90% of patients

- Adenitis (cervical)
  - 53-94% of patients
  - Bilateral anterior chain
    - 2-3 cm in size
    - Mildly tender
PFAPA

- Most common periodic fever syndrome in kids
- 90% appear by age 5
- Complete resolution between episodes
- Normal growth and development
- Prodrome to fever attacks
  - ~60% of patients
  - fatigue, headache, abdominal pain, or irritability
- Most cases have spontaneous resolution 3-6 years after onset
- Familial clustering
PFAPA treatment

- Antibiotics generally not effective
- nonsteroidal anti-inflammatory drugs (NSAIDs)
- Cimetidine
  - Daily
  - May decrease the severity and frequency of fever episodes
  - 25% of patients may experience complete remission
- Prophylactic colchicine
  - may increase the time interval between fever episodes
  - May not lead to remission
- Corticosteroids
  - abortive treatment for fevers
  - 1 x prednisone at 1-2 mg/kg at the onset of the fever episode
  - Effective in 80-95% of patients
  - Does not prevent further attacks
PFAPA Surgical treatment

- Tonsillectomy with or without adenoidectomy
- Curative in >90% of patients
Rosai-Dorfman Disease

- AKA Sinus Histiocytosis with Massive Lymphadenopathy (SHML) or non-Langerhans cell histiocytosis
- Rare
  - <1000 cases reported since 1969
- Benign
- Painless often bilateral cervical lymphadenopathy
- Fever
- Overproduction/accumulation of histiocytes
  - Usually in lymph nodes
  - May affect other organs
    - Extranodal localization in 40% of cases
      - Skin, orbit, CNS, digestive system, salivary glands
Rosai-Dorfman Disease

- Peak incidence is second or third decade
- Male predominance
- Common in African descent
- Etiology unknown
  - Infection or Immunological disorder?

Aleksandra Miękus et al.
Rosai-Dorfman Disease Labs

- Leukocytosis with neutrophilia
- Elevated erythrocyte sedimentation rate
  - 90% of cases
- Mild normochromic normocytic anemia
  - Ferritin usually normal or slightly elevated
- Frequent hypergammaglobulinemia
- May have elevated RF and positive ANA
Rosai-Dorfman Disease Pathology

- Matted lymph node
- Thickened capsule
- Sinus expansion with histiocyte-like cells
- **Hallmark:** Lymphophagocytosis or phagocytosed intact RBCs, neutrophils or plasma cells
- Extensive fibrosis in late lesions
- CD163, CD68 and S100, alpha 1-antitrypsin, alpha 1-antichymotripsin positive
- **Differentiate from Langherhans Cell Histiocytosis**
  - No BRAF V600E or Birbeck granules in RDD
Rosai-Dorfman Disease Course

- Average duration 3-9 months but may last years
- Relapsing remitting RDD may occur in 70% of cases
- 20% spontaneously regress
- 10% progress
- Poor prognosis if
  - Multiorgan involvement
  - Immune dysfunction
- No definite treatment
  - “watch and wait” if no severe symptoms
  - Surgery for compressive symptoms
  - Steroids are an option
    - No guidelines about therapy duration
  - Rarely radiation or chemotherapy
Fun Facts 😊
Beethoven discovered that if he bit into a metal pole while playing, he could still hear.
Castleman Disease

- Slow growing neck mass
  - Often painless
  - May have compressive symptoms
- Most often in young or middle aged adults (3\textsuperscript{rd} or 4\textsuperscript{th} decade)
  - Rare in peds
    - Multiple reports
- Excessive growth of B lymphocytes and plasma cells
- Can occur anywhere along lymphatic system
  - Mediastinum (60\%), neck (14\%), abdomen (11\%), and axilla (4\%)
Types of Castleman Disease

- **multicentric**
  - Systemic disease
  - Widespread lymphadenopathy
  - Higher morbidity and mortality
  - More commonly plasma cell variant

- **unicentric**
  - Localized disease
  - Rarely have systemic features
  - Good prognosis
  - All reported pediatric cases
Castleman Pathogenesis

- Overactivation of normal immune response triggers abnormal lymph node changes
- Possible role of IL-6
- Multicentric
  - Immunosuppression
  - HIV
  - Herpesvirus 8
- **No specific laboratory abnormalities noted in pediatric patients**
Castleman Histology

- Hyperplastic lymphoid follicles
- Capillary proliferation
- Hyalinization of capillary walls
- Plasma cell infiltration

- 2 types
  - hyaline vascular (90%)
  - plasma-cell types (10%)
    - More common in multicentric

-Prominent blood vessels
-Plump endothelium
-Vessels projecting radially with into abnormal follicles “Lollipop appearance”
-Concentrically arranged lymphocytes give “Onion skin” appearance
Castleman Disease Treatment

- Unicentric
  - Excision
  - Rare recurrence rates
- Multicentric
  - Controversial
  - steroids, chemoradiation, or immunotherapy
The hole in pen caps is to make them less of a choking hazard.
Kawasaki disease

- Acute systemic vasculitis
- Unknown origin
- Primarily affects children 6 months to 5 years
- Fever > 5 days plus
- 4/5 major criteria to diagnose Kawasaki
  - Erythema, edema and peeling of the extremities
  - Polymorphous exanthem
  - Non exudative conjunctival injection. Usually bilateral with perilimbal sparing.
  - Lip cracking or strawberry tongue (no tonsil exudates)
  - Tender cervical adenopathy, often unilateral and large
- Associated with coronary artery complications
Black patients- 36.8%
- White patients - 16.4%
- Asian cohorts – 13.6 %
MIS-C

- Fever - 82.4%
- Polymorphous maculopapular exanthema - 63.7%
- Mucosal changes of lips and oral cavity - 58.1%
- Bilateral non-purulent conjunctival congestion - 56.0%
- Peripheral extremity changes - 40.7%
- Non-purulent cervical lymphadenopathy - 28.5%
Case

- 5-year-old Hispanic female with no PMH
- LAD for 2 months
- Had 10-day course of antibiotic- no improvement
- Worsening neck pain over the past couple days
- occasional sore throat, and recent decreased PO intake
- No fevers/night sweats
- Clothes fitting looser but no known weight loss
- Has dog but no cats/kittens
- Normal vital signs. Afebrile
- Large tender area of swelling mid SCM extending postauricular and over scalp
- Labs showed a microcytic anemia and an elevated LDH, with moderate hemolysis.
  - CMV IgG positive
  - EBV IgG and Anti-Nuclear Antigen positive
**US:** Within the left retroauricular area in the cervical region, there are a cluster of enlarged, hypoechoic, somewhat confluent rounded lymph nodes, measuring up to 1.6 cm. There is decreased internal vascularity, and many of these lymph nodes lack a normal fatty hilum, and contain areas of linear reticulation. There is adjacent subcutaneous edema.

More superiorly and posteriorly, within the cervical region, there is a large, rounded, hypoechoic lymph node, which lacks normal internal vascularity and a normal fatty hilum. There areas of linear reticulation within the lymph node. Likely related to underlying inflammatory/infectious etiology. Neoplasm can not be excluded.

- **CXR showed rounded densities in the bilateral axillary regions, might be related to lymph nodes., otherwise, a Normal chest radiograph.**
- Biopsy- reactive adenopathy 1.6 cm node
- Still very tender in clinic at follow up visit
- B Lymphoblastic lymphoma/leukemia
Figure 1. Algorithm for the management of cervical lymphadenopathy in children. LA: lymphadenopathy, CRP: C reactive protein, LDH: lactate dehydrogenase, EBV: Epstein-Barr virus, TST: tuberculin skin test, IGRA: interferon-gamma release assay.
- Small fluctuating size- discharge
- Greater than 2 cm- Biopsy
- Supraclavicular- Biopsy
- Chest x-ray abnormal- Biopsy
- Blood work: CBC, toxoplasmosis, bartonella, EBV- treat
- Allow 4 weeks to improve
- Nodes smaller- discharge
- Nodes larger, unchanged- Biopsy
- Blood work suspicious- Biopsy
- Ultrasound suspicious- Biopsy
Pediatric Health Disparity in ENT
Nonwhite children have delayed surgical management for:

- Recurrent acute otitis media
  - 10.8% of white children had received tympanostomy tube placement, compared with the 5.4% of black children (Simons et al. 2014)
- Severe to profound sensorineural hearing loss
- Obstructive sleep apnea
- Sinus disease

**Trach placement and airway stenosis is more common in nonwhite children**
Patients on Medicaid (adjusted hazard ratio = 1.61, 95% confidence interval 1.22-2.12) or uninsured (aHR = 1.51, 95% CI 1.03-2.21) increased hazard of death from head and neck cancer, compared with those with private insurance.
Telephone survey to missed appointment patients using a modified Barriers to Care Survey

- Compared to a random sample of 321 pts who kept their appointment

No-show patients more likely:
- Hispanic than not (OR 2.3, 95% CI: 1.3, 3.9, P=.002)
- live in a zip code that had a median income less than 200% of the federal poverty level (OR 1.7, 95% CI: 1.2, 2.4, P=.004)

Respondents with a high school degree tended to report more barriers to care compared to those with less education. (Baseline expectations?)
Ways to research/reduce inequities in ENT

- Telehealth
- Social worker for trach team
  - Does this decrease the time to decannulation?
- In person interpreter
  - Does this reduce postoperative complications or ER visits?
References


Questions???
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