Approach to Lymphadenopathy

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Lymphadenopathy (LAP)

• Best estimates of palpable adenopathy in childhood varies from 38-45%¹
• LAP is one of the most common clinical problems encountered in paediatrics
• As many as two thirds of patients examined for other reasons may be found to have LAP²

Epidemiology

• Findings from a Dutch study revealed a 0.6% annual incidence of unexplained lymphadenopathy in the general population.

• Of 2,556 patients in the study who presented with unexplained lymphadenopathy to their family physicians, 256 (10%) were referred to a subspecialist and 82 (3.2%) required a biopsy, but only 29 (1.1%) had a malignancy.³

Objectives

• Approach to Adenopathy
  o Who to investigate
  o When to investigate
  o How to define risk for underlying malignancy

Case 1

• 12 year old female referred with a large (6cm) lymph node in the right neck area (4 week duration and growing in size)
• NO TB CONTACT
• Loss of appetite, intermittent fever and occasional night sweats
• FBC and CXR essentially normal
• Significant lymphadenopathy on the left (2cm)
• HIV negative
• No rashes or arthralgia
• No previous significant medical or family history

Diagnosis

TB!!
**Lymphatic circulation**

- **Anatomy**
  - Collection of lymphoid cells attached to both vascular and lymphatic systems
  - Over 600 lymph nodes in the body

- **Function**
  - To provide optimal sites for the concentration of free or cell-associated antigens and re-circulating lymphocytes – “sensitization of the immune response”
  - To allow contact between B-cells, T-cells and macrophages

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**Lymph node**

- Waves stop lymph flowing in wrong direction
- Lymph flows out of node through narrow vessels
- Lymph flows out of node through wider vessels
- Density packed B- and T-cells, macrophages and plasma cells

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**Lymphadenopathy**

- Enlargement of the lymph nodes beyond this normal state
- Practically this is any node >1.0 cm in greatest diameter
- Lymphadenopathy also refers to nodes that are abnormal in either size, consistency or number
- Certain nodes should be considered enlarged at different sizes (i.e. Epitrochlear nodes > 0.5 cm, inguinal nodes > 1.5 cm, submandibular nodes > 1.5 cm)

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**Lymphadenopathy**

- Ultrasound / CT scan report
  - “Two para-aortic lymph nodes measuring 1.2 cm in diameter, most likely reactive nodes but lymphoma cannot be excluded”

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[Image of lymph nodes and lymphatic circulation diagram]
Approach

- **Generalized** - if lymph nodes are enlarged in three or more non-contiguous areas. It almost always indicates the presence of a significant systemic disease.
- **Localized** - if only one group / area is involved.
- **Limited** - 2-3 groups involved
- Palpable lymph nodes are normal in anterior cervical, axillary and inguinal regions in healthy children.

Why do lymph nodes enlarge?

- Increase in the number of benign lymphocytes and macrophages in response to antigens
- Infiltration of inflammatory cells in infection (lymphadenitis)
- In situ proliferation of malignant lymphocytes or macrophages
- Infiltration by metastatic malignant cells
- Infiltration of lymph nodes by metabolite laden macrophages (lipid storage diseases)

When to worry?

- Age
- Characteristics of the node
- Location of the node
- Clinical setting associated with lymphadenopathy

Age

- Children/young adults – more likely to respond to minor stimuli with lymphoid hyperplasia
  - Lymph nodes in patients less than the age of 30 are clinically benign in 80% of cases whereas in patients over the age of 50 only 40% are benign
  - Biopsies done in patients less than 25 yrs have a incidence of malignancy of <20% vs the over-50 age group has an incidence of malignancy of 55-80%
Characteristics of the node

- Nodes lasting less than 2 weeks or greater than one year with no progression of size have a low likelihood of being neoplastic – excludes low grade lymphoma
- Cervical nodes – up to 90% of children (aged 4-8 yrs) have adenopathy on clinical exam
- Inguinal adenopathy is common – up to 1-2 cm in size and often benign reactive nodes

Consistency
- Mobile vs Fixed/Matted
- Tender vs Painless
- Clearly demarcated
- Size
  - When to worry – 1.5-2cm in size
  - Epitroclear nodes over 0.5cm; Inguinal over 1.5cm
- Duration and Rate of Growth

Location of the node

- Supraclavicular lymphadenopathy
  - Highest risk of malignancy – estimated as 90% in patients older than 40 years vs 25% in those younger than 40 yrs
  - Right sided node – cancer in mediastinum, lungs, esophagus
  - Left sided node (Virchow’s) – testes, ovaries, kidneys, pancreas, stomach, gallbladder or prostate
- Paraumbilical node (Sister Joseph’s)
  - Abdominal or pelvic neoplasm

- Epitroclear nodes
  - Unlikely to be reactive
- Isolated inguinal adenopathy
  - Less likely to be associated with malignancy

Clinical Setting

- B symptoms – fever, night sweats, weight loss
- Fatigue
- Bone pain
- Petechia
- Evidence of other medical conditions – connective tissue disease
- Young patient – mononucleosis type of syndrome

Approach

- History
- Physical exam
- Confirmatory testing
- Indication for biopsy
History

• Age:
  o Normally, lymphoid tissue enlarges until puberty and then undergoes gradual atrophy throughout the rest of life. Normal lymph nodes are most prominent in children ages 4 to 8 years old.

• Symptoms of infection
• Symptoms of primary/metastatic malignancy
• Constitutional / B symptoms

History

• Arthralgia, rash and myalgia
• Epidemiological clues:
  o Exposure to pets
  o Travel history
  o TB contact
• Duration:
  o >4 weeks: chronic infection, collagen vascular disease, malignancy

Drugs

• Allopurinol
• Atenolol
• Captopril
• Carbamazepine
• Gold
• Hydralazine
• Penicillins
• Phenytoin
• Primidone
• Pyrimethamine
• Quinidine
• Trimethoprim/Sulfa methozole
• Suldinac

Physical examination

• Vital signs
• Fever
• Pallor
• Petechiae
• Ecchymosis
• Gum bleeds
• Epistaxis
• Examination of lymph nodes

Physical examination

• Site of lymph node: generalised/localised
• Size of lymph node
• Consistency and Texture
  o Soft nodes - usually benign
  o Hard nodes - infiltration by cancers.
  o Rubbery nodes - lymphomas.
  o Matted - TB
• Fixity:
  o Fixed, immobile lymph nodes - Malignant infiltration
  o Lymph nodes in lymphoma - Freely mobile, unattached to overlying skin or underlying structures
  o Tubercular lymph nodes may be tethered to overlying skin
Systemic examination

- Respiratory Examination: Evaluate for evidence of:
  - Tuberculosis
  - Pleural effusion
  - Mass lesion
- Abdominal examination:
  - Hepatomegaly
  - Splenomegaly
  - Intra-abdominal lymph nodes
  - Ascites
- Head and neck examination

Investigations

- FBC including peripheral smear examination
- ESR
- CXR
- Lactate dehydrogenase
- Uric acid
- Liver function tests
- Purified Protein Derivative skin test (PPD)
- Viral titres

Differentiation between benign and malignant lymphadenopathy

<table>
<thead>
<tr>
<th>Feature</th>
<th>Malignant</th>
<th>Benign</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>&gt; 2 cm</td>
<td>&lt; 2 cm (&lt; 1 cm)</td>
</tr>
<tr>
<td>Consistency</td>
<td>Hard, firm or rubbery</td>
<td>Soft</td>
</tr>
<tr>
<td>Duration</td>
<td>&gt; 2 weeks</td>
<td>&lt; 2 weeks</td>
</tr>
<tr>
<td>Mobility</td>
<td>Fixed</td>
<td>Mobile</td>
</tr>
<tr>
<td>Surroundings</td>
<td>Attached/Invasion</td>
<td>Not attached</td>
</tr>
<tr>
<td>Location</td>
<td>Supraclavicular,</td>
<td>Inguinal, Submandibular</td>
</tr>
<tr>
<td></td>
<td>Epitrochlear or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Generalized</td>
<td></td>
</tr>
<tr>
<td>Tenderness</td>
<td>Usually non-tender</td>
<td>Usually tender</td>
</tr>
</tbody>
</table>

Investigations

- Auto-immune screen
- HIV Elisa / PCR
- Ultrasound / CT
- Bone marrow aspiration

Localized lymphadenopathy

1. Local infection in draining area
2. Metastasis from cancers
3. Lymphoma—Hodgkin’s disease
4. Scrofuloderma

Generalised lymphadenopathy

**Infections**

- **Viral illnesses**
  - Ebstein Barr virus infection
  - Cytomegalovirus infection
  - Infectious mononucleosis
  - HIV
- **Bacterial**
  - Tuberculosis
  - Brucellosis
  - Chancreoid (usually localized)
- **Parasitic**
  - Toxoplasmosis
  - Leishmaniasis
  - Trypanosomiasis
- **Fungal**
  - Histoplasmosis
  - Coccidioidomycosis
- **Chlamydia**
  - Lymphogranuloma venereum (usually localised)
## Indications for biopsy

- Increase in size over baseline in 2 weeks
- No decrease in size in 4-6 weeks
- No regression to normal in 8-12 weeks
- Development of new signs and symptoms
- Preferred nodes: supraclavicular, cervical, axillary

## References