Generalized Lymphadenopathy

Overview

- The body has approximately 600 lymph nodes, but only those in the submandibular, axillary or inguinal regions may normally be palpable in healthy people.
- Simple and clinically useful system is to classify lymphadenopathy as “generalized” if lymph nodes are enlarged in two or more noncontiguous areas or “localized” if only one area is involved.

Evaluation of lymphadenopathy

1. Age of the patient
2. Location of lymphadenopathy
3. Associated symptoms
4. Presence or absence of splenomegaly

Evaluation of lymphadenopathy

- Age is the most important consideration because it helps predict the likelihood of a benign versus malignant process.
- In patients younger than 30 years, lymphadenopathy is due to a benign underlying process approximately 80% of the time.
- In individuals older than 50 years, it is due to a malignant process ,approximately 60% of the time.

Evaluation of lymphadenopathy

- In localized lymphadenopathy, the lymphatic drainage areas should be investigated for infection or malignancy.
- Presence of splenomegaly makes malignancy of hematological origin more likely

Diagnostic Approach to Lymphadenopathy

- History
  - Are there localizing symptoms or signs to suggest infection or neoplasm in a specific site?
  - Are there constitutional symptoms such as fever, weight loss, fatigue or night sweats to suggest disorders such as tuberculosis, lymphoma, collagen vascular diseases, unrecognized infection or malignancy?
  - Are there epidemiologic clues such as occupational exposures, recent travel or high-risk behaviors that suggest specific disorders?
  - Is the patient taking a medication that may cause lymphadenopathy? (e.g., phenytoin while others, such as cephalosporins, penicillins or sulfonamides, are more likely to cause a serum sickness-like syndrome with fever, arthralgia and rash in addition to lymphadenopathy

Diagnostic Approach to Lymphadenopathy

Epidemiologic Clues to the Diagnosis of Lymphadenopathy

1) Cat - Cat-scratch disease, toxoplasmosis
2) Undercooked meat – Toxoplasmosis
3) Tick bite - Lyme disease
4) Recent blood transfusion or transplant - Cytomegalovirus, HIV
5) High-risk sexual behavior - HIV, syphilis, Herpes simplex virus, cytomegalovirus, hepatitis B infection
6) Intravenous drug use - HIV, endocarditis, hepatitis B infection

Diagnostic Approach to Lymphadenopathy

- Medications That May Cause Lymphadenopathy
  - Phenytoin
  - Sulphonamide
  - Carbamazepine
  - Captopril
  - Atenolol
  - Allopurinol

Diagnostic Approach to Lymphadenopathy

- PHYSICAL EXAMINATION
  - **Size** - Nodes are generally considered to be normal if they are up to 1 cm in diameter; however, some authors suggest that epitrochlear nodes larger than 0.5 cm or inguinal nodes larger than 1.5 cm should be considered abnormal.
  - **Pain/Tenderness** - When a lymph node rapidly increases in size, its capsule stretches and causes pain. Pain is usually the result of an inflammatory process or suppuration, but pain may also result from hemorrhage into the necrotic center of a malignant node. The presence or absence of tenderness does not reliably differentiate benign from malignant nodes.

Diagnostic Approach to Lymphadenopathy

- PHYSICAL EXAMINATION

  - **Consistency** - Stony-hard nodes are typically a sign of cancer, usually metastatic. Very firm, rubbery nodes suggest lymphoma. Softer nodes are the result of infections or inflammatory conditions. Suppurant nodes may be fluctuant. The term "shotty" refers to small nodes that feel like buckshot under the skin, as found in the cervical nodes of children with viral illnesses.

  - **Matting** - A group of nodes that feels connected and seems to move as a unit is said to be "matted." Nodes that are matted can be either benign (e.g., tuberculosis, sarcoidosis or lymphogranuloma venereum) or malignant (e.g., metastatic carcinoma or lymphomas).

Diagnostic Approach to Lymphadenopathy

- PHYSICAL EXAMINATION

- **Location** - The anatomic location of localized adenopathy will sometimes be helpful in narrowing the differential diagnosis.

- cat-scratch disease – cervical and axillary

- Infectious mononucleosis –cervical

- STDs - Inguinal

- Supraclavicular - Highest risk of malignancy estimated as 90 percent in patients older than 40 years

  R/S - mediastinum, lungs or esophagus

  L/S - testes, ovaries, kidneys, pancreas, prostate, stomach or gallbladder.

- Paraumbilical (Sister Joseph's) node - abdominal or pelvic neoplasm

Diagnostic Approach to Lymphadenopathy

- In most cases, a careful history and physical examination will identify a readily diagnosable cause of the lymphadenopathy, such as upper respiratory tract infection, pharyngitis, periodontal disease,conjunctivitis, lymphadenitis, tinea, insect bites, recent immunization, cat-scratch disease or Dermatitis, and no further assessment is necessary
- In other cases, a definitive diagnosis cannot be made on the basis of the history and physical examination alone; however, the clinical evaluation may strongly suggest a particular cause, confirmatory testing should be performed in order to correctly identify the patient's illness

  Eg: HIV, Syphilis, Lymphoma, IMN

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Diagnostic Approach to Lymphadenopathy

- In patients with unexplained localized lymphadenopathy and a reassuring clinical picture, a three- to four-week period of observation is appropriate before biopsy.
- Patients with localized lymphadenopathy and a worrisome clinical picture or patients with generalized lymphadenopathy will need further diagnostic evaluation that often includes biopsy
- Fine-needle aspiration is occasionally considered an alternative to excisional biopsy but often yields a high number of non-diagnostic results because of the small amount of tissue obtained and the inability to examine the architecture of the gland

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Diagnostic Approach to Lymphadenopathy

- Mediastinal lymphadenopathy
  - Usually a sign of serious underlying disease
  - Unlike most other adenopathies, mediastinal lymphadenopathy is less frequently a result of infection
  - More than 95% of mediastinal masses are caused by tumors or cysts and lymphomas and acute lymphoblastic leukemia are the most common etiologies
  - Nonneoplastic conditions may also be confused with mediastinal adenopathy. These include the typically large thymus of a child, substernal thyroid glands, bronchogenic cysts, and abnormalities of the great vessels.

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Diagnostic Approach to Lymphadenopathy

- Abdominal lymphadenopathy
  - Mesenteric adenitis is thought to be viral in etiology and is characterized by right lower quadrant abdominal pain caused by nodal enlargement near the ileocecal valve.
  - Mesenteric adenopathy may be caused by non-Hodgkin lymphoma or Hodgkin disease.
  - Typhoid fever and ulcerative colitis are other etiologies of mesenteric adenopathy.

Causes for generalized lymphadenopathy

1. Infections

- **Viruses** - EBV, CMV, Varicella ,Roseola infantum, Varicella, Adenovirus, HIV, Rubella Measles
- **Bacteria** -Typhoid, TB, Syphilis, Plague, Infective endocarditis
- **Parasites** -Toxoplasma
- **Fungal** - Coccidiomycosis

2. Malignancies

- ALL - 2/3 of all
- AML – 1/3 of all
- Hodgkin disease - 1/3 of all
- NHL – 10%

Causes for generalized lymphadenopathy

3. Storage diseases

- Niemann-Pick disease
- Gaucher disease

4. Drug reactions

5. Autoimmune and inflammatory disorders

- Langerhans cell histiocytosis
- SLE
- Still's disease
- Sarcoidosis
- Serum sickness

Kikuchi disease [Histiocytic necrotizing lymphadenitis]

- Most frequently manifests as a relatively acute onset of cervical adenopathy associated with fever and a flulike prodrome.
- Cervical nodes are affected in about 80% of cases
- Lymphadenopathy is isolated to a single location in 83% of cases, but multiple chains maybe involved
- Cases of generalized adenopathy involving axillary, inguinal, and mesenteric nodes are unusual