Cervical Lymphadenopathy and Adenitis

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OBJECTIVES

After completing this article, readers should be able to:

1. **Describe the management of cervical lymphadenopathy in children.**
2. **Identify the cause of most cases of childhood cervical lymphadenopathy and adenitis.**
3. **Identify the etiology of most cases of acute suppurative cervical lymphadenitis in children between the ages of 1 and 5 years.**
4. **Describe the treatment of suppurative cervical lymphadenitis caused by nontuberculous mycobacteria.**
5. **List the causes of chronic cervical lymphadenitis in children.**

Introduction

Cervical lymphadenopathy may be either an important clue to an underlying disease process or a specific clinical syndrome. Appropriate management of children who have enlarged cervical lymph nodes ranges from observation and reassurance to extensive diagnostic evaluation and aggressive medical and surgical intervention. Decisions regarding diagnostic tests and therapy are based entirely on clinical judgment, informed by a thoughtful patient history and careful physical examination. We review the extensive differential diagnosis of cervical lymphadenopathy and lymphadenitis in the context of information gathered in the patient history and examination and suggest the management of children who have common clinical presentations.

Enlargement of lymph nodes (lymphadenopathy) may be caused by proliferation or invasion of inflammatory cells (lymphadenitis) or by infiltration of neoplastic cells. The complex array of lymph nodes of the head and neck efficiently defend against infection and often are considered in anatomic groupings based on lymph drainage patterns. Cervicofacial lymph nodes may reside in the anterior triangle forward of the sternocleidomastoid muscle, the posterior triangle behind the sternocleidomastoid, the submandibular region below the jaw line, the supraclavicular region in the lower neck, and the preauricular and occipital regions. The distribution of enlarged nodes is important in that almost all healthy children have small, palpable lymph nodes in the anterior cervical triangle, but palpable, nontender lymph nodes in the supraclavicular region can suggest malignancy.

Clinical Presentation and Differential Diagnosis

Before considering the extensive differential diagnosis of cervical lymphadenopathy (Tables 1 and 2), it is important to acknowledge that most children who have enlarged cervical lymph nodes have infections, and the most common causes of acute bilateral cervical lymphadenopathy are self-limited, systemic viral infections. Less frequently, clinicians encounter young children who have acute unilateral cervical lymphadenitis that is variably associated with fever and suppuration and most often is caused by *Staphylococcus aureus* or *Streptococcus pyogenes* (group A strep) infection. Nontuberculous mycobacteria (NTM) also deserve special attention as an important cause of chronic suppurative cervical lymphadenitis. Although nearly all cases of clinically significant cervical lymphadenopathy in children can be attributed to infection, these patients are best served when management is guided by a thorough interview and examination.

HISTORY OF PRESENT ILLNESS

A general impression of the etiology of cervical lymphadenopathy frequently can be made from a description of the course of illness. It is useful to consider cervical lymphadenopathy as an acute versus chronic process, with disseminated lymphadenopathy versus localized lymphadenopathy that may be unilateral or bilateral. The lymph node(s) may be tender and inflamed or nontender. Commonly, a child's presentation will fall into one of three broad categories: 1) acute bilateral cervical lymphadenitis, 2) acute unilateral pyogenic lymphadenitis, and 3) chronic cervical lymphadenopathy.

The most common causes of acute bilateral cervical lymphadenitis are viruses that infect the upper respiratory tract, such as adenovirus, influenza virus, and respiratory syncytial virus. Symptoms of cough, rhinorrhea, and sinus congestion suggest these etiologies. Generally the course is self-limited, although node enlargement may persist for weeks. Viral causes of generalized lymphadenopathy, such as Epstein-Barr virus (EBV) and cytomegalovirus (CMV), may present as acute bilateral cervical lymphadenitis.

Acute unilateral pyogenic lymphadenitis is caused by *S aureus* and group A strep in more than 80% of cases. Most cases of adenitis resulting from these organisms occur in children 1 to 4 years of age, who often have a preceding upper respiratory tract infection. The submandibular nodes are involved in more than 50% of cases, with most others showing upper cervical lymphadenitis. Nodes may be very large (up to

ABBREVIATIONS

CMV:	cytomegalovirus
EBV:	Epstein-Barr virus
HIV:	human immunodeficiency virus
NTM:	nontuberculous mycobacteria
PCR:	polymerase chain reaction
PPD:	purified protein derivative of tuberculin
TB:	tuberculosis

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6 cm), and infected children may suffer overlying cellulitis and high fever. Nodes infected with *S aureus* are more likely to suppurate. Pharyngitis, impetigo of the face, and tender bilateral lymphadenopathy are associated with group A strep cervical lymphadenitis.

The differential diagnosis of chronic cervical lymphadenopathy is extensive, although in children it most frequently is caused by infection. The most common presentation of NTM disease in children is cervical lymphadenitis. *Mycobacterium avium-intracellulare* and *M scrofulaceum* are isolated frequently. Infection usually is insidious, with node enlargement occurring over weeks or months, although onset may be very rapid and the clinical course indistinguishable from acute pyogenic cervical lymphadenitis. Infected lymph nodes progress to fluctuance, and the overlying skin often becomes violaceous and thin. Untreated lymphadenitis caused by NTM may resolve, but often it progresses to spontaneous drainage with sinus tract formation and severe scarring.

Chronic lymphadenopathy is a common presenting manifestation of human immunodeficiency virus (HIV) infection.

TABLE 1. Infectious Causes of Cervical Lymphadenopathy

Bacteria
- Gram-positive cocci
  - —*Staphylococcus aureus*
  - —*Streptococcus pyogenes* (group A)
  - —*Streptococcus agalactiae* (group B)
  - —Anaerobic organisms
    - *Peptococcus* sp
    - *Peptostreptococcus* sp
- Gram-positive rods
  - —*Bacillus anthracis*
  - —*Corynebacterium diphtheriae*
- Gram-negative rods
  - —*Bartonella henselae*
  - —*Calymmatobacterium granulomatis*
  - —*Haemophilus influenzae*
  - —*Serratia marcescens*
  - —Associated with the enteric tract
    - *Acinetobacter* sp
    - *Escherichia coli*
    - *Proteus* sp
    - *Pseudomonas aeruginosa*
    - *Salmonella typhi*
    - *Shigella* sp
  - —Associated with zoonoses
    - *Brucella* sp
    - *Francisella tularensis*
    - *Yersinia pestis*
    - *Yersinia enterocolitica*
    - *Yersinia pseudotuberculosis*
  - —Anaerobic
    - *Bacteroides* sp

Mycobacteria and Actinomycetes
- *Actinomyces israelii*
- *Mycobacterium tuberculosis*
- *Mycobacterium avium-intracellulare*
- *Mycobacterium scrofulaceum*
- *Nocardia asteroides*

Spirochetes
- *Leptospira interrogans*
- *Treponema pallidum*

Rickettsiae
- *Rickettsia tsutsugamushi*

(continued)

PATIENT AGE

Acute unilateral cervical lymphadenitis in the newborn is caused by *S aureus* in most cases. Another important cause of neonatal acute cervical lymphadenitis is late-onset group B streptococcal infection—the "cellulitis-adenitis" syndrome. Affected patients are between 3 and 7 weeks of age; are male in 75% of cases; and have fever, poor feeding, and neck swelling with overlying cellulitis that responds quickly to appropriate antibiotic therapy.

Approximately 80% of cases of acute pyogenic cervical lymphadenitis caused by group A strep and *S aureus* occur in children younger than 5 years of age, as do most cases of NTM lymph node infection.

School-age children and adolescents are more likely to present with chronic cervical lymphadenitis than with acute pyogenic disease, and infection with EBV, CMV, *Toxoplasma gondii*, anaerobic bacteria, *M tuberculosis*, and *Bartonella henselae* is seen more frequently. Acquired *Toxoplasma* infection, when symptomatic, generally presents as cervical lymphadenopathy and fatigue without fever. Adenopathy may be localized or generalized, tender or nontender, and may persist for many months. This disease usually is benign and self-limited and should be considered in patients in whom infectious mononucleosis is suspected but who have negative EBV serology.

DENTITION

A history of periodontal disease or dental abscess in children associated with acute suppurative cervical lymphadenitis suggests infection with anaerobic bacteria.

TABLE 1. Infectious Causes of Cervical Lymphadenopathy—Continued

Viruses
- DNA enveloped viruses
  - —Cytomegalovirus
  - —Epstein-Barr virus
  - —Herpes simplex virus types 1 and 2
  - —Human herpesvirus 6
  - —Varicella-zoster virus
- DNA nonenveloped viruses
  - —Adenovirus
- RNA enveloped viruses
  - —Human immunodeficiency virus
  - —Influenza virus
  - —Measles virus
  - —Mumps virus
  - —Parainfluenza virus
  - —Respiratory syncytial virus
  - —Rubella virus
- RNA nonenveloped viruses
  - —Coxsackieviruses
  - —Rhinoviruses

Fungi
- *Aspergillus fumigatus*
- *Candida* sp
- *Cryptococcus neoformans*
- Dermatophytes
- *Histoplasma capsulatum*
- *Paracoccidioides brasiliensis*
- *Sporothrix schenckii*

Protozoa
- *Leishmania* sp
- *Toxoplasma gondii*
- *Trypanosoma brucei gambiense*
- *Trypanosoma brucei rhodesiense*

EXPOSURE TO ANIMALS AND FEEDING INSECTS

Zoonoses are important causes of cervical lymphadenitis, and a history of animal exposure can allow the early diagnosis of cat-scratch disease, tularemia, brucellosis, anthrax, or plague.

Cat-scratch disease is caused by *Bartonella henselae* and commonly results in chronic, tender cervical lymphadenitis. A history of cat exposure is helpful but not present in all cases. Lymphadenopathy may occur weeks after the initial inoculation; careful physical examination reveals a papule at the primary inoculation site in most cases. Constitutional symptoms, when present, are generally mild, with fever occurring in fewer than 50% of patients. Adenopathy may persist for 12 months and may suppurate. Cat-scratch disease also may manifest as Parinaud oculoglandular syndrome, with conjunctivitis and preauricular or submandibular lymphadenopathy following conjunctival inoculation.

Tularemia results from infection with *Francisella tularensis* following contact with infected animals (more than 100 species have been implicated), the bite of a feeding insect, inhalation of organisms in contaminated environments, or ingestion of contaminated water. Inoculation may occur through broken or intact skin and mucous membranes. The ulceroglandular form of the disease manifests as a primary papular lesion at the inoculation site within 72 hours of infection, with painful ulceration following within days. Regional tender lymphadenitis may progress to suppuration. Glandular tularemia is similar in presentation, but there is no skin lesion. Tularemia also may cause Parinaud oculoglandular syndrome.

Brucellosis is acquired by direct contact with infected animals or ingestion of unpasteurized dairy products. In a minority of cases, it may manifest as chronic cervical lymphadenopathy with enlargement of liver and spleen. Cutaneous anthrax can present as acute tender cervical lymphadenitis following exposure to animals and animal products and implantation of spores through skin defects such as insect bites. A nontender papule develops initially at the inoculation site and progresses rapidly to a characteristic eschar surrounded by a ring of vesicles overlying indurated dermis. *Yersinia pestis* is endemic in rodent

TABLE 2. Additional Causes of Cervical Lymphadenopathy

- Neoplasia
- Histiocytosis
- Collagen vascular diseases
  - —Systemic lupus erythematosis
  - —Juvenile rheumatoid arthritis
- Sarcoidosis
- Kawasaki disease
- Kikuchi disease
- Postvaccination
- Immunologic deficiencies predisposing to recurrent infection
  - —Chronic granulomatous disease
  - —Hyper-IgE syndrome (Job syndrome)
  - —Leukocyte adhesion deficiency

populations of the southwestern United States, and the bite of an infected flea may be followed by the fever and painful acute regional lymphadenitis that characterizes bubonic plague.

LOCAL SKIN LESIONS

Skin lesions associated with cervical lymphadenopathy can suggest cat-scratch disease, tularemia, anthrax, plague, scrub typhus, African trypanosomiasis, and cutaneous leishmaniasis.

CONSTITUTIONAL SYMPTOMS

Noninfectious causes of cervical lymphadenopathy should be considered in each case (Table 2). Weight loss associated with chronic nontender cervical or generalized lymphadenopathy can be seen with common childhood neoplasms. Arthralgias and prolonged fever despite antimicrobial therapies can suggest connective tissue disease.

HISTORY OF RECURRENT INFECTIONS OR LYMPHADENOPATHY

Chronic granulomatous disease is the most common inherited disorder of phagocyte function and generally presents as recurrent cervical lymphadenopathy. Affected patients often require surgical intervention to treat granulomas caused by infection with catalase-producing organisms such as *S aureus* and *Aspergillus* sp. Patients suffering from the inherited leukocyte adhesion deficiency disorders and the hyperimmunoglobulin E syndrome (Job syndrome) suffer recurrent skin abscesses and may present with cervical lymphadenitis.

IMMUNIZATION STATUS

Disease caused by measles virus, rubella virus, varicella-zoster virus, *Haemophilus influenzae*, and *Corynebacterium diphtheriae*, which is preventable by vaccination, may present as cervical lymphadenopathy. Respiratory tract diphtheria can present with exudative pharyngitis and cervical lymphadenitis with soft-tissue edema causing a characteristic "bull neck" appearance.

CONTACT WITH SICK PERSONS

Tuberculosis (TB) remains one of the greatest threats to human health worldwide and is an important cause of cervical lymphadenitis. Contact with persons who have symptoms of TB, who have traveled to endemic areas, or who have been incarcerated should prompt an evaluation for *M tuberculosis* infection.

Lymphadenopathy is a common presenting manifestation of congenital HIV infection. The respiratory viruses or enteroviruses generally cause cervical lymphadenitis and are highly communicable. A history of contact with persons who have symptoms of streptococcal pharyngitis can help guide management.

Experience clearly shows that it is not necessary or possible to identify an organism in all children who have infectious cervical lymphadenitis.

PLACE OF RESIDENCE AND TRAVEL

This information is crucial in identifying patients who have TB.

The most common presenting features of African trypanosomiasis occur 2 to 3 weeks after infection mediated by the tsetse fly, with characteristic fever and enlargement of posterior cervical and supraclavicular lymph nodes in most cases. Cutaneous leishmaniasis begins as an indolent erythematous nodule that ulcerates and can be associated with regional lymphadenopathy. It is seen in patients from Africa, Asia, the Mediterranean basin, and much of Central and South America. Scrub typhus, caused by *Rickettsia tsutsugamushi* and transmitted by mite bite, commonly presents as regional or generalized lymphadenopathy and is endemic to southeast Asia and the southwest Pacific.

PHYSICAL EXAMINATION

A thorough physical examination, with careful assessment of liver, spleen, and lymph nodes in the occipital, cervicofacial, axillary, epitrochlear, inguinal, and popliteal regions, is imperative. Generalized adenopathy with enlargement of liver and spleen is an important sign of neoplasm and other noninfectious illnesses as well as TB, syphilis, HIV infection, EBV infection, and histoplasmosis.

EXAMINATION OF THE NECK

Palpation of the presenting neck mass(es) reveals anatomic location and consistency (solid or fluctuant, smooth or nodular, movable or fixed), number, distribution, and size. Structures that can be mistaken for enlarged lymph nodes include cystic hygromas, branchial cleft cysts, thyroglossal duct cysts, dental abscesses, dermoid cysts, and tumors of thyroid or neural tissue. The appearance of overlying skin can suggest disease transmitted by biting insects or show violaceous discoloration associated with NTM disease.

EXAMINATION OF THE PHARYNX AND DENTITION

Pharyngeal vesicles often occur with enteroviral disease (herpangina) and herpesvirus infection, and pharyngitis can be a clue to diphtheria or group A strep infection. Evidence of periodontal disease is an important clue to infection with anaerobic organisms.

EXAMINATION OF THE CONJUNCTIVA

Conjunctival injection in association with preauricular or submandibular adenopathy (Parinaud oculoglandular syndrome) is seen in cat-scratch disease, tularemia, and adenovirus disease.

The cervical lymphadenitis of Kawasaki disease is classically an enlarged solitary node associated with fever, conjunctivitis, oral mucous membrane inflammation, changes in peripheral extremities, and rash.

EXAMINATION OF THE SKIN

A generalized rash is seen in many viral illnesses that cause lymphadenopathy. Scarlet fever has been associated with cervical lymphadenopathy. The presence of petechiae

or ecchymoses can be a sign of hematologic malignancy.

Diagnosis

Given the number of conditions that can present as cervical lymphadenopathy in children, choice of appropriate diagnostic testing must be based on information from the patient interview and examination.

Experience clearly shows that it is not necessary or possible to identify an organism in all children who have infectious cervical lymphadenitis. Observation with reassurance often is the most appropriate management course for children in whom self-limited infection is presumed. In cases of chronic cervical lymphadenitis that are managed conservatively, it can be especially useful to discuss family concerns about cancer early in the course of illness. Many families who suspect cancer in their children fail to raise these concerns during the patient interview unless prompted. Appropriate reassurance can enhance family satisfaction and confidence in their physician.

It can be useful to consider approaches to diagnostic evaluation separately for acute bilateral cervical lymphadenitis, acute unilateral pyogenic lymphadenitis, and chronic cervical lymphadenopathy. Because these categories are artificial and indistinct, no standardized diagnostic approach can be recommended. However, we support a "low threshold" for purified protein derivative of tuberculin (PPD) skin testing and HIV screening tests in all patients at risk for these treatable and often indolent infections.

Patients who have acute bilateral cervical lymphadenitis usually are managed conservatively because infection with respiratory viruses is so common. Viral cultures of nasopharyngeal washes are expensive and seldom helpful in this clinical setting. Bacterial culture of the pharynx may identify group A strep infection treatable with penicillin. For patients in whom systemic infections are suspected and who are febrile and ill-appearing, cultures of blood, a complete blood count, and measurement of liver transaminase levels may be indicated. Serologic studies for EBV, CMV, HIV, *Treponema pallidum*, *T gondii*, or *Brucella* sp can be helpful in selected cases.

Children who have acute pyogenic cervical lymphadenitis may appear well or may suffer high fever and toxicity that necessitates hospitalization. For well-appearing children in whom *S aureus* or group A strep infection is suspected but who have no evidence of abscess formation, a therapeutic trial with an oral antibiotic may be appropriate, recognizing that about 10% of these patients ultimately require incision and drainage despite aggressive medical therapy. However, attempts should be made to isolate the causative organism in the ill-appearing child who has acute suppurative cervical lymphadenitis. To this end, ultrasonographic examination of cervical lymph nodes can be useful in establishing the presence and extent of suppuration. Infecting organisms can be isolated by culture of material from inflamed lymph nodes. Needle aspiration is a safe and reliable means of obtaining diagnostic material. Rarely, an excisional lymph node biopsy may be needed. We routinely send this material for Gram stain, bacterial culture (aerobic and anaerobic), stain for acid-fast organisms, and mycobacterial culture. In selected cases, Gomori-methenamine-silver stain and fungal culture of the material are appropriate, although these studies generally are more helpful in cases of chronic lymphadenitis.

Because lymphadenitis caused by NTM evolves to draining skin fistulas associated with scarring, the safety of needle aspiration when this infection is suspected has been questioned. We feel that needle aspiration does not lead to increased risk for this complication because the treatment of a node found to be infected with NTM is surgical excision—a cure for skin fistulas.

Children who have chronic cervical lymphadenopathy often undergo extensive diagnostic evaluation before an etiology is determined. Special attention should be given to the possibility of TB and HIV disease; the hematologic and serologic

TABLE 3. Antibiotic Therapy of Acute Cervical Lymphadenitis

Suspected *Staphylococcus aureus* or Group A Beta-hemolytic *Streptococcus* Infection • For children who do not appear toxic and have no apparent abscess or cellulitis, oral empiric therapy with cephalexin, oxacillin, or clindamycin • For ill-appearing children who have abscess formation or cellulitis, node aspiration and intravenous therapy with cefazolin, nafcillin or oxacillin, or clindamycin
Suspected Infection With Anaerobic Bacteria • For children who have cervical lymphadenitis associated with periodontal disease, node aspiration and therapy with penicillin or clindamycin
Suspected Nontuberculous Mycobacteria Infection • Surgical excision of the infected lymph node without antibiotic therapy • For patients in whom surgery is not feasible, a macrolide-containing multidrug antimycobacterial regimen
Cat-scratch Disease • Following needle aspiration and PCR diagnosis of *Bartonella* infection, no antimicrobial therapy in patients who have uncomplicated lymphadenopathy. Surgical removal of nodes infected with *Bartonella* frequently results in persistent drainage and poor wound healing. Repeated node aspiration for management of suppurative lymphadenopathy caused by *Bartonella* infection

testing noted previously can be helpful. Urine antigen tests for *Histoplasma capsulatum* occasionally can be helpful.

Among the most common causes of chronic cervical lymphadenopathy in children are NTM infection and cat-scratch disease. Patients who have NTM lymphadenopathy may have a positive PPD skin test, but we have not found this test to be very helpful in establishing the diagnosis of NTM infection. NTM and *Bartonella* infection are diagnosed best using material obtained from a suppurative lymph node, which can be stained and cultured for acid-fast organisms and sent for polymerase chain reaction (PCR) examination to detect *B henselae* infection. Importantly, PCR analysis for *Bartonella* can be performed on material that was obtained recently and preserved by freezing. It is sensible to freeze extra material obtained by needle aspiration so PCR studies can be performed if bacterial studies are unexpectedly negative.

If tularemia is suspected in a patient from whom material has been obtained for culture, it is imperative to inform laboratory personnel so special precautions can be taken. Because *Francisella tularensis* is a serious laboratory hazard, the provisional diagnosis of tularemia should be confirmed by serologic testing.

Treatment

Treatment of children who have cervical lymphadenopathy of known etiology should be initiated following a review of current literature or consultation with a specialist in pediatric oncology, rheumatology, or infectious diseases. Table 3 summarizes our approach to the treatment of patients who have suppurative cervical lymphadenitis. A total antibiotic course of 10 to 14 days is generally sufficient to treat uncomplicated suppurative lymphadenitis caused by *S aureus* or group A strep. Patients who have suppurative cervical lymphadenitis caused by these organisms usually respond positively to therapy within 72 hours. Failure to improve should prompt reconsideration of diagnosis and treatment. Surgery may be necessary if an abscess has formed, and ultrasonographic evaluation can help to direct the management of these patients.

SUGGESTED READING

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PIR QUIZ

Quiz also available online at www.pedsinreview.org.

1. You are seeing a 3-year-old patient who has a neck mass that has been present for 4 days. She had a fever to 40°C (104°F). Physical examination reveals a unilateral, tender, 2×2 cm anterior cervical lymph node with overlying erythema. There is no fluctuance. The girl is eating well and appears nontoxic. Your *best* management plan is to:
   A. Admit her to the hospital and begin therapy with intravenous oxacillin.
   B. Consult surgery for an excisional biopsy.
   C. Perform a needle aspiration for culture and Gram stain.
   D. Prescribe a 10-day course of oral cephalexin and have her return if there is no improvement.
   E. Reassure her mother that this most likely is infectious mononucleosis and will resolve without therapy.

2. You are evaluating a 3-month-old baby who has cervical lymphadenopathy. The history is remarkable for recent fever and poor feeding. Physical examination reveals a smooth, mobile, fluctuant lymph node in the right anterior triangle. Findings on the remainder of the physical examination are normal. Of the following, the *most* likely etiologic agent is:
   A. Adenovirus.
   B. Epstein-Barr virus.
   C. Human immunodeficiency virus.
   D. *Staphylococcus aureus*.
   E. *Streptococcus agalactiae*.

3. An 8-year-old boy presents with a left-sided neck mass that has enlarged over the past 4 weeks. He denies weight loss or fatigue, but does report occasional fever. His grandmother has a kitten, but he denies any scratches. Physical examination reveals a unilateral, slightly tender, 3×3 cm anterior cervical lymph node with no overlying erythema. He has mild bilateral conjunctival injection, but other findings on the examination are unremarkable. Of the following, the *most* likely cause of his lympadenopathy is:
   A. Cat-scratch disease.
   B. Chronic human immunodeficiency virus infection.
   C. Kawasaki disease.
   D. Malignancy.
   E. *Staphylococcus aureus*.

4. You are seeing a 10-year-old girl who has a 2-month history of unilateral lymph node enlargement. There is no history of weight loss, fever, or animal exposure. Physical examination reveals bilateral 2×2 cm nontender lymph nodes with overlying violaceous discoloration. There is no other lymphadenopathy. Of the following, the *most appropriate* next step is to:
   A. Begin therapy with oral erythromycin.
   B. Consult surgery for an immediate surgical excision.
   C. Obtain Epstein-Barr virus titers.
   D. Perform a needle aspiration.
   E. Place a purified protein derivative for tuberculin and begin antimycobacterial therapy if results are positive.

5. The presence of lymphadenopathy in which of the following areas *most* likely suggests malignancy as the etiology?
   A. Anterior cervical triangle.
   B. Posterior cervical triangle.
   C. Preauricular region.
   D. Submandibular region.
   E. Supraclavicular region.