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ABSTRACT

Cervical lymphadenopathy is a common problem in children. The condition most commonly represents a transient response to a benign local or generalized infection, but occasionally it might herald the presence of a more serious disorder. Acute bilateral cervical lymphadenopathy usually is caused by a viral upper respiratory tract infection or streptococcal pharyngitis. Acute unilateral cervical lymphadenitis is caused by streptococcal or staphylococcal infection in 40% to 80% of cases. The most common causes of subacute or chronic lymphadenitis are cat scratch disease, mycobacterial infection, and toxoplasmosis. Supraclavicular or posterior cervical lymphadenopathy carries a much higher risk for malignancies than does anterior cervical lymphadenopathy. Generalized lymphadenopathy is often caused by a viral infection, and less frequently by malignancies, collagen vascular diseases, and medications. Laboratory tests are not necessary in the majority of children with cervical lymphadenopathy. Most cases of lymphadenopathy are self-limited and require no treatment. The treatment of acute bacterial cervical lymphadenitis without a known primary source should provide adequate coverage for both *Staphylococcus aureus* and group A beta hemolytic streptococci. *J Pediatr Health Care.* (2004). 18, 3-7.

Childhood Cervical Lymphadenopathy



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Enlarged cervical lymph nodes are common in children (Leung & Robson, 1991). About 38% to 45% of otherwise normal children have palpable cervical lymph nodes (Larsson et al., 1994). Cervical lymphadenopathy is usually defined as cervical lymph nodal tissue measuring more than 1 cm in diameter (Darville & Jacobs, 2002; Margileth, 1995; Schreiber & Berman, 1996). Cervical lymphadenopathy most commonly represents a transient response to a benign local or generalized infection, but occasionally it might herald the presence of a more serious disorder such as malignancy. This article reviews the pathophysiology, etiology, differential diagnosis, clinical evaluation, and management of children with cervical lymphadenopathy.

PATHOPHYSIOLOGY

The superficial cervical lymph nodes lie on top of the sternomastoid muscle and include the anterior group, which lies along the anterior jugular vein, and the posterior group, which lies along the external jugular vein (Darville & Jacobs, 2002). The deep cervical lymph nodes lie deep to the sternomastoid along the internal jugular vein and are divided into superior and inferior groups. The superior deep nodes lie below the angle of the mandible, whereas the inferior deep nodes lie at the base of the neck (Malley, 2000).

The superficial cervical lymph nodes receive afferents from the mastoid, tissues of the neck, and the parotid (preauricular) and submaxillary nodes (Darville & Jacobs, 2002). The efferent drainage terminates in the upper deep cervical lymph nodes (Darville & Jacobs). The superior deep cervical nodes drain the palatine tonsils and the submental nodes. The lower deep cervical nodes drain the larynx, trachea, thyroid, and esophagus.

Lymphadenopathy might be caused by proliferation of cells intrinsic to the node, such as lymphocytes, plasma cells, monocytes, and histiocytes, or by infiltration of cells extrinsic to the node, as with neutrophils and malignant cells (Chesney, 1994).

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BOX 1 Causes of cervical lymphadenopathy

- A. Infection
 - 1. Viral
 - a. Viral upper respiratory infection
 - b. Epstein-Barr virus
 - c. Cytomegalovirus
 - d. Rubella
 - e. Rubeola
 - f. Varicella-zoster virus
 - g. Herpes simplex
 - h. Coxsackievirus
 - i. Human immunodeficiency virus
 - 2. Bacterial
 - a. Staphylococcus aureus
 - b. Group A β -hemolytic streptococci
 - c. Anaerobes
 - d. Diphtheria
 - e. Cat-scratch disease
 - f. Tuberculosis
 - 3. Protozoal
 - a. Toxoplasmosis
- B. Malignancies
 - 1. Neuroblastoma
 - 2. Leukemia
 - 3. Lymphoma
 - 4. Rhabdomyosarcoma
- C. Miscellaneous
 - 1. Kawasaki disease
 - 2. Collagen vascular diseases
 - 3. Serum sickness
 - 4. Drugs
 - 5. Postvaccination
 - 6. Rosai-Dorfman disease
 - 7. Kikuchi-Fujimoto disease

Data from Leung & Robson (1991).

BOX 2 Differential diagnosis of cervical lymphadenopathy

- Mumps
- Thyroglossal cyst
- Branchial cleft cyst
- Sternomastoid tumor
- Cervical rib
- Cystic hygroma
- Hemangioma
- Laryngocele
- Dermoid cyst

Data from Leung & Robson (1991).

(HIV). Bacterial cervical lymphadenitis is usually caused by group A β -hemolytic streptococci or Staphylococcus aureus. Anaerobic bacteria can cause cervical lymphadenitis, usually in association with dental caries and periodontal disease. Group B streptococci and Haemophilus influenzae type b are less frequent causal organisms. Diphtheria is a rare cause. Bartonella henselae (cat scratch disease), atypical mycobacteria, and mycobacteria are important causes of subacute or chronic cervical

Cervical masses are common in children and might be mistaken for enlarged cervical lymph nodes.

lymphadenopathy (Spyridis, Maltezou, & Hantzakos, 2001). Chronic posterior cervical lymphadenitis is the most common form of acquired toxoplasmosis and is the sole presenting symptom in 50% of cases (Leung & Robson, 1991).

More than 25% of malignant tumors in children occur in the head and neck, and the cervical lymph nodes are the most common site (Leung & Robson, 1991). During the first 6 years of life, neuroblastoma and leukemia are the most common tumors associated with

cervical lymphadenopathy, followed by rhabdomyosarcoma and non-Hodgkin's lymphoma (Leung & Robson, 1991). After 6 years, Hodgkin's lymphoma is the most common tumor associated with cervical lymphadenopathy, followed by non-Hodgkin's lymphoma and rhabdomyosarcoma.

The presence of cervical lymphadenopathy is one of five diagnostic criteria for Kawasaki disease; the other four are bilateral bulbar conjunctival injection, changes in the mucosa of the oropharynx, erythema or edema of the peripheral extremities, and polymorphous rash. Generalized lymphadenopathy might be a feature of systemic onset juvenile rheumatoid arthritis, systemic lupus erythematosus, or serum sickness. Certain drugs, notably phenytoin and isoniazid, might cause generalized lymphadenopathy (Malley, 2000). Cervical lymphadenopathy has been reported following immunization with diphtheria-pertussis-tetanus, poliomyelitis, or typhoid fever vaccine (Leung & Robson, 1991). Rosai-Dorfman disease is a benign form of histiocytosis characterized by generalized proliferation of sinusoidal histiocytes. The disease usually manifests in the first decade of life with massive and painless cervical lymphadenopathy and is often accompanied by fever, neutrophilic leukocytosis, and polyclonal hypergammaglobulinemia (Swartz, 2000). Kikuchi-Fujimoto disease (necrotizing lymphadenitis) is a benign cause of lymphadenopathy that primarily affects young Japanese females. Fever, nausea, weight loss, night sweats, arthralgia, or hepatosplenomegaly might be present.

DIFFERENTIAL DIAGNOSIS

Cervical masses are common in children and might be mistaken for enlarged cervical lymph nodes. The differential diagnosis of cervical lymphadenopathy is listed in Box 2. In general, congenital lesions are painless and are present at birth or identified soon thereafter (Twist & Link, 2002). Clinical features that may help distinguish the various conditions from cervical lymphadenopathy are discussed next in this article.

Mumps. The swelling of mumps parotitis crosses the angle of the jaw. On the other hand, cervical lymph nodes are usually below the mandible (Leung & Robson, 1991).

ETIOLOGY

Common or important causes of cervical lymphadenopathy are listed in Box 1. The most common cause is reactive hyperplasia resulting from an infectious process, most commonly a viral upper respiratory tract infection (Peters & Edwards, 2000). Upper respiratory tract infection might be caused by rhinovirus, parainfluenza virus, influenza virus, respiratory syncytial virus, coronavirus, adenovirus, or reovirus. Other viruses associated with cervical lymphadenopathy include Epstein-Barr virus (EBV), cytomegalovirus, rubella, rubeola, varicella-zoster virus, herpes simplex virus (HSV), coxsackievirus, and human immunodeficiency virus

Thyroglossal cyst. A thyroglossal cyst is a mass that can be distinguished by the midline location between the thyroid bone and suprasternal notch and the upward movement of the cyst when the child swallows or sticks out his or her tongue.

Branchial cleft cyst. A branchial cleft cyst is a smooth and fluctuant mass located along the lower anterior border of the sternomastoid muscle.

Sternomastoid tumor. A sternomastoid tumor is a hard, spindle-shaped mass in the sternomastoid muscle resulting from perinatal hemorrhage into the muscle with subsequent healing by fibrosis (Leung & Robson, 1991). The tumor can be moved from side to side but not upward or downward. Torticollis is usually present.

Cervical ribs. Cervical ribs are orthopedic anomalies that are usually bilateral, hard, and immovable. Diagnosis is established with a radiograph of the neck.

Cystic hygroma. Cystic hygroma is a multiloculated, endothelial-lined cyst that is diffuse, soft, and compressible, contains lymphatic fluid, and typically transilluminates brilliantly.

Hemangioma. Hemangioma is a congenital vascular anomaly that often is present at birth or appears shortly thereafter. The mass is usually red or bluish.

Laryngocele. A laryngocele is a soft, cystic, compressible mass that extends out of the larynx and through the thyroid membrane and becomes larger with the Valsalva maneuver. There might be associated stridor or hoarseness, and a radiograph of the neck might show an air fluid level in the mass.

Dermoid cyst. A dermoid cyst is a midline cyst that contains solid and cystic components; it seldom transilluminates as brilliantly as a cystic hygroma, and a radiograph might show that it contains calcifications.

CLINICAL EVALUATION

History

Age of the child. Some organisms have a predilection for a specific age

group (Box 3). The prevalence of various childhood neoplasms changes with age.

Laterality and chronicity. Acute bilateral cervical lymphadenitis is usually caused by a viral upper respiratory tract infection or streptococcal pharyngitis (Malley, 2000). The cervical lymphadenopathy in Kawasaki disease is usually unilateral. Acute unilateral cervical lymphadenitis is caused by streptococcal or staphylococcal infection in 40% to 80% of cases (Chesney, 1994; Peters & Edwards, 2000). The most common causes of subacute or chronic cervical lymphadenitis are cat scratch disease, mycobacterial infection, and toxoplasmosis; less frequent causes include EBV and cytomegalovirus infection (Malley, 2000; Margileth, 1995).

Fever, night sweats, and weight loss suggest lymphoma or tuberculosis. Unexplained fever, fatigue, and arthralgia raise the possibility of a collagen vascular disease or serum sickness.

Associated symptoms. Fever, sore throat, and cough suggest an upper respiratory tract infection. Fever, night sweats, and weight loss suggest lymphoma or tuberculosis. Unexplained fever, fatigue, and arthralgia raise the possibility of a collagen vascular disease or serum sickness.

Concurrent illness and past health. Preceding tonsillitis suggests streptococcal infection; recent facial or neck abrasion or infection suggests staphylococcal infection; and periodontal infection might indicate an anaerobic

BOX 3 Organisms with predilection for specific age groups

- A. Neonates
 1. Staphylococcus aureus
 2. Group B streptococci
- B. Infancy
 1. Staphylococcus aureus
 2. Group B streptococci
 3. Kawasaki disease
- C. 1 to 4 years
 1. Staphylococcus aureus
 2. Group A β -hemolytic streptococci
 3. Atypical mycobacteria
- D. 5 to 15 years
 1. Anaerobic bacteria
 2. Toxoplasmosis
 3. Cat-scratch disease
 4. Tuberculosis

Data from Chesney (1994).

organism. A history of cat scratch raises the possibility of *B henselae*. Lymphadenopathy resulting from cytomegalovirus, EBV, or HIV might follow a blood transfusion. Immunization-related lymphadenopathy might follow diphtheria-pertussis-tetanus, poliomyelitis, or typhoid fever vaccination.

Drug use. The response of cervical lymphadenopathy to specific antimicrobial therapies might help to confirm or exclude a diagnosis. Lymphadenopathy might follow the use of medications such as phenytoin and isoniazid.

Exposure to infection. Exposure to a person with an upper respiratory tract infection, streptococcal pharyngitis, or tuberculosis suggests the corresponding disease.

Physical Examination

General. Malnutrition or poor growth suggests chronic disease such as tuberculosis, malignancy, or immunodeficiency.

Characteristics of the lymph tissue.

All accessible node-bearing areas should be examined to determine whether the lymphadenopathy is generalized. The nodes should be measured for future comparison (Leung & Robson, 1991). Tenderness, erythema,

TABLE Differentiation of atypical mycobacterial and *Mycobacterium tuberculosis* cervical lymphadenitis

Clinical characteristics	Atypical mycobacteria	<i>Mycobacterium tuberculosis</i>
Age	1-4 y	All ages (most >5 y)
Race	Predominantly White	Predominantly Black or Hispanic
Exposure to tuberculosis	Absent	Present
Bilateral involvement	Rare	Not uncommon
Chest radiograph	Normal (97%)	Abnormal (20% to 70%)
Residence	Rural	Urban
PPD >15 mm of induration*	Uncommon	Usual
Response to antimycobacterial drugs	No	Yes

Data from Darville & Jacobs (2002).

*PPD refers to 5 tuberculin units (5 TU) intracutaneous skin test.

warmth, mobility, fluctuance, and consistency should be assessed.

Acute posterior cervical lymphadenitis is classically seen in persons with rubella and infectious mononucleosis (Leung & Pinto-Rojas, 2000). Supraclavicular or posterior cervical lymphadenopathy carries a much higher risk for malignancy than does anterior cervical lymphadenopathy. Cervical lymphadenopathy associated with generalized lymphadenopathy is often caused by a viral infection. Malignancies such as leukemia or lymphoma and collagen vascular diseases such as juvenile rheumatoid arthritis or systemic lupus erythematosus, along with medications, are usually associated with generalized lymphadenopathy.

In lymphadenopathy resulting from a viral infection, the nodes are usually bilateral and soft and are not fixed to the underlying structure. When a bacterial pathogen is present, the nodes are usually tender, either unilateral or bilateral, might be fluctuant, and are not fixed. The presence of erythema and warmth suggests an acute pyogenic process and fluctuance suggests abscess formation. In patients with tuberculosis, the nodes might be matted or fluctuant, and the overlying skin might be erythematous but is not warm (Spyridis, Maltezou, & Hantzakos, 2001). Clinical features that help differentiate atypical mycobacterial from *Mycobacterium tuberculosis* are summarized in the Table. In lymphadenopathy resulting from malignancy, signs of acute inflammation are absent, and the lymph

nodes are hard and often fixed to the underlying tissue.

Associated signs. A beefy red throat, exudate on the tonsils, petechiae on the hard palate, and a strawberry tongue suggest group A streptococcal infection. Diphtheria is associated with edema of the soft tissues of the neck,

Supraclavicular or posterior cervical lymphadenopathy carries a much higher risk for malignancy than does anterior cervical lymphadenopathy.

often described as a “bull neck” appearance. Sinus tract formation is commonly seen in tuberculosis. The presence of gingivostomatitis suggests infection with HSV, whereas herpangina suggests coxsackievirus. The presence of pharyngitis, maculopapular rash, and splenomegaly suggest EBV infection (Leung & Pinto-Rojas, 2000). Conjunctivitis and Koplik spots are

characteristic of rubeola. The presence of pallor, petechiae, bruises, sternal tenderness, and hepatosplenomegaly suggests a diagnosis of leukemia. Prolonged fever, conjunctival injection, oropharyngeal mucous membrane inflammation, peripheral edema or erythema, and a polymorphous rash are consistent with Kawasaki disease.

LABORATORY EVALUATION

Laboratory tests are not necessary in the majority of children with cervical lymphadenopathy. A complete blood cell count might help to diagnose a bacterial lymphadenitis, which is often accompanied by a leukocytosis with a shift to the left, and toxic granulations. Atypical lymphocytosis is prominent in infectious mononucleosis (Leung & Pinto-Rojas, 2000). Pancytopenia or the presence of blast cells suggests leukemia. The erythrocyte sedimentation rate is usually significantly elevated in persons with bacterial lymphadenitis. A rapid streptococcal antigen test or a throat culture might be useful to confirm a streptococcal infection. Skin tests for tuberculosis should be performed if these infections are suspected. Additional studies that might be helpful include chest radiography and serologic tests for *B henselae*, EBV, cytomegalovirus, and toxoplasmosis. An electrocardiogram and echocardiogram are indicated if Kawasaki disease is suspected. Ultrasonography and computed tomography might help to differentiate a solid from cystic mass and to establish the presence and extent of suppuration or infiltration.

Fine-needle aspiration and culture of a lymph node is a safe and reliable procedure to isolate the causative organism and to determine the appropriate antibiotic when bacterial infection is the cause (Buchino & Jones, 1994). All aspirated material should be sent for both gram and acid-fast stain and cultures for aerobic and anaerobic bacteria, mycobacteria, and fungi (Umapathy, De, & Donaldson, 2003). If the gram stain is positive, only bacterial cultures are mandatory.

An excisional biopsy with microscopic examination of the lymph node might be necessary to establish the diagnosis if there are symptoms or signs of malignancy or if the lymphadenopathy persists or enlarges in spite of appropriate antibiotic therapy and the

diagnosis remains in doubt (Leung & Robson, 1991). The biopsy should be performed on the largest and firmest node that is palpable, and the node should be removed intact with the capsule (Leung & Robson, 1991; Twist & Link, 2002).

MANAGEMENT

Treatment of cervical lymphadenopathy depends on the underlying cause. Most cases of lymphadenopathy are self-limited and require no treatment other than observation. Failure of regression after 4 to 6 weeks might be an indication for a diagnostic biopsy (Chesney, 1994).

The treatment of acute bacterial cervical lymphadenitis without a known primary infectious source should provide adequate coverage for both *S aureus* and group A β -hemolytic streptococci. Appropriate oral antibiotics include cloxacillin, cephalixin, or clindamycin (Peters & Edwards, 2000). When a primary source of infection is identified, therapy should be directed empirically against the microorganism most frequently associated with that source, pending the results of the culture and sensitivity tests (Leung & Robson, 1991). Children with cervical lymphadenopathy and periodontal or dental disease should be treated with penicillin V or clindamycin (Peters & Edwards, 2000).

Toxic or immunocompromised children and those who do not tolerate, will not take, or fail to respond to an oral medication should be treated with intravenous nafcillin, cefazolin, or clindamycin (Peters & Edwards, 2000). Oral analgesia with medications such as acetaminophen might be helpful to relieve associated pain. If the lymph

nodes become fluctuant, incision and drainage should be performed. The current recommendation for treatment of isolated cervical tuberculosis lymphadenitis is isoniazid, rifampin, pyrazinamide, and ethambutol, streptomycin, or another aminoglycoside or ethionamide for the first 1 or 2 months, followed by isoniazid and rifampin for a total of 9 to 12 months (American Academy of Pediatrics, 2003). Atypical mycobacterial lymphadenitis is unresponsive to conventional medical therapy and requires surgical excision of all visibly infected nodes. When surgery is not feasible, a macrolide-containing antimycobacterial regimen should be considered (Harza, Robson, Perez-Atayde, & Husson, 1999; Peters & Edwards, 2000).

CONCLUSION

Cervical lymphadenopathy is a common and usually benign finding. A good history and thorough physical examination is usually all that is necessary to establish a diagnosis. The problem is usually self-limited, and most children with cervical lymphadenopathy do not require specific treatment.

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