Pediatric Cervical Lymphadenopathy

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Practice Gaps

Pediatric cervical lymphadenopathy is a common disease entity, with multiple processes ranging from benign and self-resolving to malignant. The changing use of imaging modalities, including ultrasonography, computed tomography, and magnetic resonance imaging, continues to alter the recommended diagnostic evaluation. This review provides a general outline of the differential diagnosis for cervical lymphadenopathy, with updates on the current data regarding imaging and biopsy modalities to guide practitioners on when lymphadenopathy is concerning enough to warrant further evaluation, and what that evaluation should entail.

Objectives After completing this article, readers should be able to:

1. Understand basic anatomical considerations when evaluating the pediatric population for cervical lymphadenopathy.
2. Develop a broad differential diagnosis, including the most common and most life-threatening causes of cervical lymphadenopathy.
3. Determine a reasonable diagnostic pathway for patients who present with acute, subacute, and chronic lymphadenopathy.
4. Initiate treatment for certain conditions when appropriate.

Abstract

Cervical lymphadenopathy affects as many as 90% of children aged 4 to 8 years. With so many children presenting to doctors' offices and emergency departments, a systematic approach to diagnosis and evaluation must be considered. In the following review, we aim to provide the pediatric clinician with a general framework for an appropriate history and physical examination, while giving guidance on initial diagnostic laboratory testing, imaging, and potential need for biopsy. The most common cause of cervical lymphadenopathy in the pediatric population is reactivity to known and unknown viral agents. The second most common cause includes bacterial infections ranging from aerobic to anaerobic to mycobacterial infections. Malignancies are the most concerning cause of cervical lymphadenopathy.

AUTHOR DISCLOSURE Drs Weinstock, Patel, and Smith have disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

ABBREVIATIONS

CMV	cytomegalovirus
CT	computed tomography
EBV	Epstein-Barr virus
FNA	fine-needle aspiration
HIV	human immunodeficiency virus
MRI	magnetic resonance imaging

The explosion in the use of ultrasonography as a nonradiating imaging modality in the pediatric population has changed the diagnostic algorithm for many clinicians. We aim to provide some clarity on the utility and shortcomings of the imaging modalities available, including ultrasonography, computed tomography, and magnetic resonance imaging.

INTRODUCTION

Cervical lymphadenopathy is a strikingly common occurrence; estimates vary, but the incidence of lymphadenopathy in the pediatric population ranges from 62% in patients aged 3 weeks to 6 months to 41% in those 2 to 5 years old (1) to upwards of 90% of all children 4 to 8 years old. (2) A study by Larsson et al (3) estimated that approximately 40% of healthy children have palpable lymphadenopathy. Nearly every pediatric physician will encounter scores of patients with lymphadenopathy—in this article, we aim to provide practitioners with a review of the diagnostic and treatment modalities available.

HISTORY AND PHYSICAL EXAMINATION

The most powerful, most cost-effective, and least invasive diagnostic tool available is the history and physical examination. Several questions will direct the differential diagnosis: 1) What is the duration of the lymphadenopathy? 2) Does the size fluctuate? 3) Are there any concerning associated symptoms, including fever, weight loss, night sweats, easy bruisability, fatigue? 4) Has the patient attempted a treatment of any type yet? If so, which antibiotics, etc? 5) Does the patient have any recent animal (eg, cats) or travel exposures?

The physical examination should focus on the lymph chains of the head and neck. In general, they are divided into submental, submandibular, parotid, anterior cervical, posterior cervical, and supraclavicular chains. The size and location of the lymph node and whether located unilaterally or bilaterally will direct the differential diagnosis, as well as the quality of the lymph node. Is it firm or matted, rubbery or soft, fluctuant/ballotable, mobile or immobile, tender to palpation, warm, and/or erythematous? Are there overlying skin changes? The range of motion of the neck should also be noted. In terms of location, palpable supraclavicular nodes are the most likely to be malignant and should always be investigated. Posterior cervical lymph nodes drain the scalp and raise the differential diagnosis for mononucleosis. Submandibular lymphadenopathy is more likely to suggest mononucleosis or atypical mycobacterium. (4)

DIFFERENTIAL DIAGNOSIS

Several key components exist in making the diagnosis of a patient who presents with cervical lymphadenopathy. It may be helpful to couch the discussion in terms of 1) what is most likely/most common, 2) what is most dangerous, and 3) what further diagnostic steps, if any, one should take to make a diagnosis. For a more complete list of the differential diagnosis of cervical lymphadenopathy, refer to the Table.

REACTIVE CERVICAL LYMPHADENOPATHY SECONDARY TO VIRAL INFECTION

The most common cause of cervical lymphadenopathy in the pediatric population is lymphadenopathy secondary to a viral infection. Because of lymphadenopathy's inflammatory nature, it could also be termed *lymphadenitis*. Typically, patients will have a history of a viral prodrome. The reactive lymph node(s) may be tender to palpation and have a unilateral or bilateral location. Most importantly, the lymphadenopathy typically resolves with resolution of the viral illness. Common viruses, including rhinovirus, adenovirus, influenza, parainfluenza, and respiratory syncytial virus, may induce a self-resolving and uncomplicated cervical lymphadenopathy.

Some other viral causes of cervical lymphadenopathy may present in an acute (<3 weeks), subacute (3–6 weeks), or chronic (>6 weeks) manner. These causes include Epstein-Barr virus (EBV), causing mononucleosis, and cytomegalovirus (CMV), as well as human immunodeficiency virus (HIV). Often, EBV and CMV present in a similar manner, with both producing acute to subacute periods of fatigue, fever, and tender, bilateral, often posterior cervical lymphadenopathy. Often, EBV produces pharyngitis and a sore throat, whereas CMV rarely does. When patients have several of these symptoms, a monospot test, with or without EBV antibody titers and CMV serologic assay, may be warranted to help with the diagnostic evaluation.

TABLE. **Causes of Pediatric Cervical Lymphadenopathy**

o Infectious
■ Reactive to viral antigens
• Acute: Rhinovirus, adenovirus, influenza, parainfluenza, respiratory syncytial virus, others
■ Subacute or chronic: Epstein-Barr virus, cytomegalovirus, human immunodeficiency virus bacterial
• Acute: *Staphylococcus aureus*, group A streptococcus
• Neonates: Group B streptococcus
• Rarely: Anaerobes
• Subacute or chronic: *Bartonella*
■ Atypical mycobacterial and *Mycobacterium tuberculosis*
■ Fungal
■ Parasites
o Congenital neck mass
■ Thyroglossal duct cyst, dermoid, branchial cleft, lymphovascular malformation, hemangioma, ectopic thymus
o Malignancies
■ Lymphoma
■ Rhabdosarcoma
■ Neuroblastoma
o Metastasis (especially from nasopharyngeal and thyroid cancer)
o Miscellaneous
■ Kikuchi-Fujimoto disease
■ Rosai-Dorfman disease
■ Langerhans cell histiocytosis
■ Kawasaki disease
■ Castleman disease

HIV may also cause subacute/chronic reactive lymphadenopathy in the pediatric population. This will often be accompanied by a constellation of symptoms, including fever and fatigue, as well as a potential source for the infection.

Viral lymphadenopathy, in general, will require supportive care only. However, viral lymphadenopathy may develop into suppurative or bacterial lymphadenopathy over time.

ACUTE BACTERIAL LYMPHADENITIS/SUPPURATIVE LYMPHADENITIS

The second most common cause of lymphadenopathy in the pediatric population is secondary to a bacterial infection and could be termed *lymphadenitis*. The pathogens most commonly isolated include *Staphylococcus aureus* and group B streptococcus (in neonates), group A streptococcus, and anaerobic infections. (5)(6) The history and physical examination findings may point the clinician toward a diagnosis of acute bacterial lymphadenitis. In general, the timing of onset will be days to perhaps a week of fever with an enlarging neck swelling. On physical examination, the neck range of motion may be limited. Neck swelling may be firm and/or tender, with or without overlying erythema.

Approximately 25% of patients with an abscess will be noted to have fluctuance on physical examination. (7) Induration and immobility of the neck mass may also be present; if these findings are present over a longer time course, the clinician should also be concerned about possible malignancy. When differentiating between viral and bacterial lymphadenitis, it is important to remember that viral

lymphadenitis self-resolves. If the patient does not begin to show resolution of infection within 4 to 7 days, the clinician should become concerned about the presence of either a primary bacterial lymphadenitis or a viral lymphadenitis that has become infected with bacteria.

The treatment for suspected bacterial cervical lymphadenitis starts with appropriate antibiotic coverage. Patients may begin oral treatment with agents that cover for the most common pathogens (*S aureus*, *Streptococcus pyogenes*, anaerobic pathogens). This may include clindamycin, amoxicillin/clavulanate, or macrolides. If patients require intravenous antibiotics, the typical regimen starts with clindamycin or ampicillin/sulbactam. A combination of vancomycin and ceftriaxone can be used if the initial empirical regimen is insufficient. A recent analysis of incision and drainage of acute suppurative bacterial cervical lymphadenitis revealed that more than 54% of pathogens isolated were *S aureus* or *S pyogenes* (35.7% and 18.8%, respectively). Only 1% of isolates revealed anaerobes, and 2% revealed acid-fast bacilli. (8)

Antibiotics alone may be able to treat many bacterial infections that result in cervical lymphadenitis. Large fluctuant or persistent cervical lymphadenitis that does not respond within 48 to 72 hours with systemic signs of infection should alert the clinician to the possibility of abscess formation. Clinicians may first consider ultrasonography to evaluate for abscess formation. The specificity and sensitivity of ultrasonography for detecting abscess formation is user dependent and variable. However, the downside of a brief noninvasive examination with no radiation exposure is minimal. If equivocal, or if the lymphadenitis is highly suspicious for abscess formation or present in an anatomical area requiring more detailed information (eg, deep to the sternocleidomastoid muscle), a computed tomographic (CT) scan or magnetic resonance image (MRI) with intravenous contrast will give more detailed information. This is especially valuable if the differential diagnosis includes an infected branchial cleft anomaly or lymphatic malformation (Figs 1 and 2).

An abscess smaller than 1 × 1 × 1 cm may not require surgical drainage. Some children with abscesses approximating 1.5 cm may also resolve on their own with a trial of antibiotics. Clinicians may consider a trial of 24 to 48 hours of intravenous antibiotics before incision and drainage for abscesses less than 1.5 to 2 cm if the child is clinically stable. If the location of the abscess is anatomically difficult, or if the abscess is small but persistent, image-guided needle aspiration with or without drain placement may be appropriate, although recurrence rates are likely higher for needle drainage versus incision and drainage. Cultures should be taken to help direct the antibiotic regimen.

SUBACUTE OR CHRONIC LYMPHADENOPATHY

When patients have an infectious process causing cervical lymphadenopathy occurring for 2 to 6 weeks it is considered a subacute infection; when that process occurs for more than 6 weeks it is considered chronic. Possible causes of these infections include a *Bartonella* infection causing cat-scratch disease, toxoplasmosis, viral infections (eg, CMV, HIV), and mycobacterial infections. Of course, with prolonged lymphadenopathy, the possibility of a malignancy needs to be considered. Clinicians should never assume that all enlarged cervical lymph nodes are infectious in etiology.

Figure 1. A 20-month-old girl presents with fever and tender lymphadenopathy. Ultrasonography shows a large complex collection measuring 4.0 × 2.6 × 3.0 cm, consistent with a suppurative lymph node.

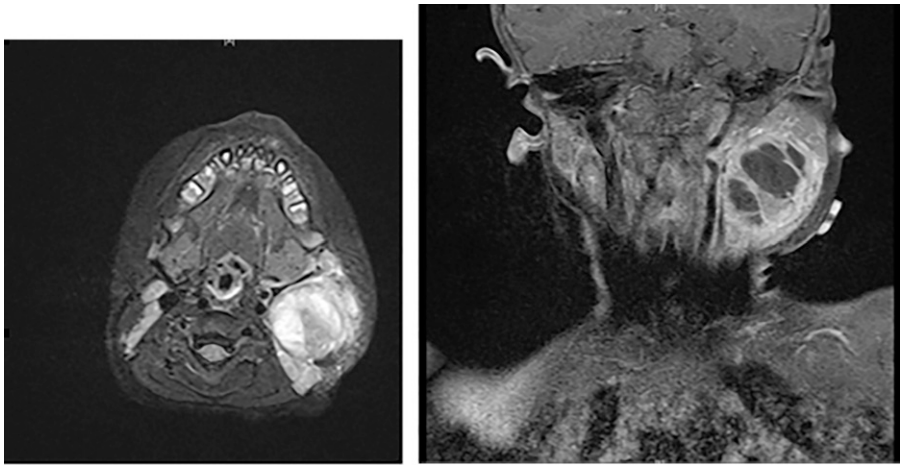

Figure 2. A 20-month-old girl presents with a large lateral neck collection. T2-weighted axial and coronal magnetic resonance images show a 3.9 × 2.7 × 3.0-cm multiloculated neck abscess.

Bartonella henselae causes a granulomatous infection, usually transmitted by the scratch or bite of a cat. It results in lymphadenopathy that may occur either immediately or several weeks after the injury. Many patients will have spontaneous resolution of symptoms without any antibiotics. The first line of antibiotic treatment is azithromycin; however, clarithromycin, ciprofloxacin, or sulfamethoxazole/trimethoprim may be considered. If the patient does not improve with antibiotic therapy, surgical excision of the infected material can be undertaken. (9)

Atypical mycobacterial infections cause indolent, chronic cervical lymphadenopathy, usually present in the submandibular region of the neck. Children are often afebrile, and nodes are classically enlarged, nontender, indurated, and possibly fluctuant. Often there is an overlying violaceous discoloration of the skin (Fig 3). Purified protein derivative skin testing may be weakly positive but will be negative in many cases of atypical mycobacterial infections. If an atypical mycobacterial infection is suspected, diagnosis may be confirmed with fine-needle aspiration (FNA). Treatment options are variable and controversial and range from medical therapy or surgical therapy alone to a combination of the two. Surgical treatment would usually involve complete excision of the involved lymph node. Incision and drainage should be avoided because this may result in a chronically draining fistula. Complete surgical excision results in a cure rate of more than 95% compared with medical therapy with a cure rate of only 66%. (10) If the involved lymph node cannot be safely excised (for instance due to the proximity of the facial nerve), surgeons can consider curettage of the affected tissue with observation and medical management (often with dual therapy of clarithromycin and rifampin).

Scrofula, or *Mycobacterium tuberculosis*, may also be a cause of chronic cervical lymphadenopathy. Purified protein derivative skin testing and QuantiFERON-TB Gold® (Qiagen, Valencia, CA) testing can be used make the diagnosis; FNA of the lymph node may also be attempted to confirm the diagnosis. When in doubt, excisional biopsy of the node in question may be required. If positive, treatment will typically involve medical management. Although they may occur anywhere, these lesions are classically supraclavicular in location. Again, an incision and drainage procedure may result in a chronically draining fistula. Fine-needle aspirate may also be helpful for diagnosis.

Chronic infectious lymphadenopathy may also be caused by parasitic infections, the most common of which is toxoplasmosis. A common protozoan in cat feces and raw pork, *Toxoplasma gondii* may present with nontender, nonsuppurative lymphadenopathy. If toxoplasma infection is

Figure 3. A 4-year-old girl with an atypical mycobacterial infection. The overlying skin is violaceous and indurated.

suspected, polymerase chain reaction may be used to analyze blood samples for diagnostic purposes. It is treated with a combination of pyrimethamine, sulfadiazine, and leucovorin initially. The infection typically resolves in 4 to 6 weeks. (11)

NONINFECTIOUS CAUSES OF CERVICAL LYMPHADENOPATHY IN CHILDREN

Although most cases of cervical lymphadenopathy in the pediatric population are caused by infectious processes, cervical lymphadenopathy may be caused by other processes that can be confused with infectious cervical lymphadenopathy and are worth mentioning in this review.

MALIGNANCY

Patients with persistent cervical lymphadenopathy may present with either primary or metastatic malignancy. Before age 6 years, the most common malignancies are rhabdomyosarcoma and non-Hodgkin's lymphoma. After age 6 years, the most common malignancy is Hodgkin lymphoma. (12) A history of night sweats, fatigue, fever, easy bleeding or bruising, and/or weight loss may point the clinician toward a possible malignant diagnosis. More common (although still very rare) metastatic disease to the neck in the pediatric population includes papillary thyroid cancer and nasopharyngeal cancer. Physical examination characteristics concerning for malignancy include firm, indurated masses that are matted down and often nontender to palpation. Bilateral nodes are less concerning than unilateral lymph nodes; in a recent study, none of the patients with bilateral nodes had concerning pathology, whereas up to 20% of patients with unilateral lymphadenopathy had concerning pathology. (13) However, unilaterality cannot necessarily be used as a reliable predictor of pathology. Niedzielska et al (14) found that up to 70% of patients with reactive nodal changes only had unilateral disease (Fig 4).

CONGENITAL NECK MASSES

Congenital neck mass may be confused for lymphadenopathy. Midline neck masses are often not lymph nodes. These lesions are usually either thyroglossal duct cysts or dermoid cysts. Ultrasonography can be helpful to characterize these lesions and differentiate them from lymphadenopathy. Most dermoid and thyroglossal duct cysts should be treated with surgical excision. Preoperative ultrasonography to confirm the presence of a normal orthotopic thyroid gland should be performed before excision of a thyroglossal duct cyst to ensure that the thyroglossal duct cyst does not represent an ectopic thyroid gland.

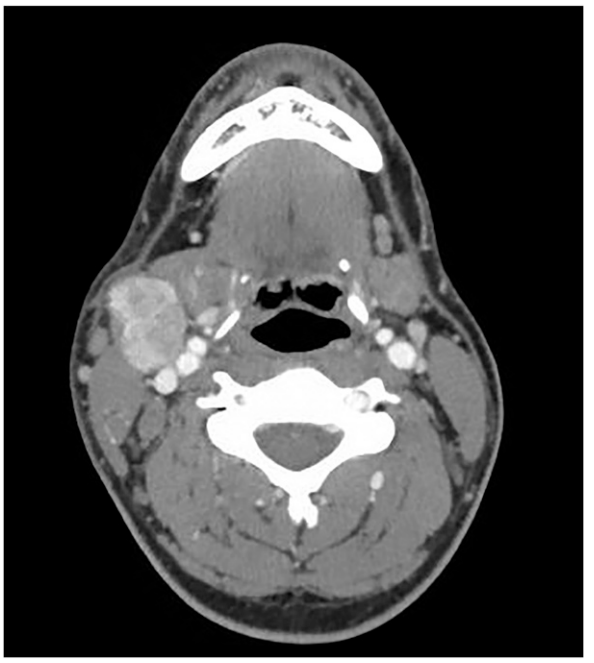

Figure 4. Axial cut of a computed tomographic scan with contrast of an 8-year-old girl with papillary thyroid carcinoma. The 3 × 4-cm lymph node superficial to the great vessels in the right neck represents a regional metastasis of the disease.

In the lateral neck, second branchial cleft cysts may present as a swelling deep to the sternocleidomastoid muscle that can be confused for lymphadenopathy. Screening ultrasonography may be performed. Computed tomography or MRI is usually diagnostic. If there is uncertainty, FNA may be performed. Most second branchial cleft cysts are treated with complete surgical excision.

Third branchial anomalies (or pyriform sinus anomalies) will usually present just off midline in the region of the thyroid gland, most often posterior to the left lobe of the thyroid gland. Computed tomography or MRI is usually diagnostic in these cases, and treatment usually requires surgery, during which time the surgeon may use an endoscopic technique to cauterize the pyriform sinus outflow tract. (15)

An ectopic thymus can also present as a lateral neck mass. Ultrasonography is usually diagnostic and avoids unnecessary surgery. An FNA can be performed if the diagnosis is still in question.

NONINFECTIOUS CAUSES

Several disease processes that are not congenital, infectious, or malignant may cause cervical lymphadenopathy. Kikuchi-Fujimoto disease (or histiocytic necrotizing lymphadenitis) is a benign, self-limited disease characterized by tender cervical lymphadenopathy with night sweats as well as general malaise and sore throat, nausea, and vomiting. The diagnosis is usually made by incisional or excisional biopsy. It is a self-resolving disease, with complete resolution of symptoms in 1 to 3 months. (16) The onset of symptoms is typically in the subacute range, with approximately 2 to 4 weeks of cervical tenderness, and the disease is most frequently found in young Japanese women.

Rosai-Dorfman disease, also known as non–Langerhans cell histiocytosis, and Langerhans cell histiocytosis are lymphoproliferative disorders that can also affect children. Patients with Rosai-Dorfman disease classically present with bilateral painless lymphadenopathy, fever, and abnormal laboratory findings including an elevated erythrocyte sedimentation rate. (17) These lesions require biopsy to confirm the diagnosis. Langerhans cell histiocytosis is characterized by an accumulation of Langerhans cells in the lymph nodes, with a diagnosis made on biopsy. (18)

Kawasaki disease may also present with tender cervical lymphadenopathy, as this is 1 of the 5 major findings required to diagnose Kawasaki disease, the other criteria including edema and peeling of the extremities, polymorphous exanthem, conjunctival injection, lip cracking, and strawberry tongue, in addition to fever for more than 5 days. (19)

Castleman disease is another rare lymphoproliferative disorder that can present with tender cervical lymphadenopathy. Patients often experience fever, night sweats, fatigue, and cachexia with 2 to 4 weeks of subacute cervical lymphadenopathy. The disease is characterized by excessive growth of B lymphocytes and plasma cells. It typically resolves on its own, although new immunotherapies have also helped in refractory cases. (20)

PAROTID, SUBMANDIBULAR, AND SUBLINGUAL GLAND PATHOLOGY

Salivary gland pathology may also be confused with cervical lymphadenopathy. The tail of the parotid gland dips posterior and sometimes inferior to the angle of the mandible, which may confuse the location with cervical lymph nodes located in the upper jugular area of the neck. The submandibular and sublingual glands can also be confused with superior lymph nodes of the neck. The most likely salivary pathology in children is sialadenitis, the most common organism being *S aureus*. Treatment includes massage of the area with warm compress, antibiotic coverage for *S aureus*, sialagogues, and aggressive oral and possible intravenous hydration.

IMAGING

If the diagnosis is in question or the practitioner is considering a malignancy as a possibility, or if the infectious/inflammatory process in question may potentially require surgical intervention, such as abscess drainage, then imaging is usually required.

Ultrasonography may be conducted to further delineate the nature of the lymph node. Concerning features for malignancy on ultrasonography may include heterogeneity of the node, round shape (as opposed to oval shape), narrow or absent hilum, irregular borders, cystic necrosis, or irregular blood flow patterns to the capsule. (21) An abscess may also be diagnosed using ultrasonography; inflammatory or reactive nodes may have increased vascularity, with or without central necrosis, and soft tissue inflammation adjacent to the node. (22) On ultrasonography, abscess collections typically have a characteristic "swirling debris pattern" when the probe is pressed against the collection. This diagnostic modality may be all that is required before incision and drainage of a superficial abscess.

A CT scan may provide additional diagnostic information. Furthermore, if surgical intervention is required for deeper lymph nodes, then a CT scan with contrast is helpful in surgical planning and diagnosis. Although the risk of radiation exposure from a CT scan is low, physicians should be judicious in use of CT. An MRI provides similar information as a CT scan without the radiation exposure; however, MRI is more time-consuming and more likely to require sedation for young children. Furthermore, it may be a challenge to obtain MRI in a timely manner at many centers. For these reasons, we would advocate for judicious use of both CT and MRI. In general, these studies should be obtained when surgical management is being explored. In many uncomplicated cases of bacterial cervical lymphadenitis, physical examination with or without ultrasonography may be all that is required before initiation of a course of antibiotics. If the child does not respond after 24 to 72 hours of antibiotic treatment, then it may be appropriate to obtain a CT scan or an MRI in preparation for possible surgical intervention (Fig 5).

Figure 5. An 8-year-old girl with 6 days of right neck pain, fever, nausea, and vomiting was found to have a suppurative bacterial lymphadenopathy that extended into her mediastinum, requiring surgical drainage. Coronal computed tomographic scan with intravenous contrast shows the multiloculated abscess extending from the right neck and into the mediastinum.

An MRI may be preferred over a CT scan to further evaluate the lymphadenopathy if a malignancy is suspected. An MRI generally provides better resolution of soft tissue and nerve involvement, so if the practitioner suspects possible rhabdomyosarcoma or neuroblastoma then an MRI may be more useful than a CT scan. Mediastinal lymphadenopathy, diagnosed on chest radiography, has been observed in 56% of malignant cases but only 2.6% of benign cases. (23)

BIOPSY VERSUS FNA?

Patients who continue to have persistent symptoms for more than 4 to 6 weeks despite appropriate therapies may require tissue diagnosis. Patients with history, physical examination, or imaging findings consistent with malignancy should obtain a timely tissue diagnosis.

The gold standard for tissue diagnosis has been excisional biopsy. Biopsy should be considered for the following reasons: 1) suspicion of malignancy, 2) if the patient does not have resolution of lymphadenopathy over 4 to 6 weeks, 3) lymphadenopathy that steadily increases in size over 2 to 3 weeks, 4) lymphadenopathy greater than 2.0 cm, or 5) multiple lymph nodes that have concerning features on ultrasonography or CT. (24)(25) An FNA biopsy has been shown to have sensitivity of 86% and specificity of 96%. (26) Unfortunately, FNA has several limitations. Up to 20% of FNA biopsy results are nondiagnostic, requiring further interventions to ascertain a diagnosis, (27) and up to 39% of patients who undergo FNA biopsy still require further surgery for diagnosis. More importantly, FNA in young children typically requires sedation. (28) Although the complication rate of FNA is minimal, the ability to obtain a quality biopsy may be limited in the pediatric population. However, physicians should not hesitate to perform FNA biopsy in older children who are cooperative because this may often be performed without sedation and with minimal risk.

Although open excisional biopsy remains the gold standard in diagnosing persistent, worrisome lymphadenopathy, the procedure should not be undertaken lightly. Connolly and MacKenzie (29) reported complication rates of 11% in 360 patients who underwent open biopsy and excision of neck masses.

Summary

- The most common etiology for acute cervical lymphadenopathy in the pediatric population is reactivity to viral antigens. Subacute or chronic lymphadenopathy with accompanying symptoms such as malaise, sore throat, and fatigue should be evaluated for possible Epstein-Barr virus, cytomegalovirus, or even human immunodeficiency virus.
- Based on clinical evidence, ultrasonography may be a useful initial diagnostic modality. (20)(21) Sensitivity and specificity are user and institution dependent. If there is a concern for an abscess formation in an anatomically sensitive area, computed tomography or magnetic resonance imaging with intravenous contrast should be used to better delineate the anatomy.
- Based on expert and consensus opinion, a trial of 24 to 48 hours of intravenous antibiotics may be initiated for patients with small abscess formation (<1–1.5 cm in the largest dimension) because many of these patients will respond without incision and drainage.
- Abscess formation in the subacute/chronic presentation of cervical lymphadenopathy raises the concern for mycobacterial infection, *Bartonella*, or protozoan infection such as toxoplasmosis.
- Based on clinical evidence, cervical lymphadenopathy may also be caused by malignancy, although this is rare in the pediatric population. (11)(12)(13)
- Congenital neck masses, such as branchial arch abnormalities, and dermoid and thyroglossal duct cysts may masquerade as cervical lymphadenopathy. Imaging, coupled with history and physical examination, often helps to differentiate these from infectious or malignant causes.

- Salivary gland pathology may also present as a cervical neck mass or possible lymphadenopathy.
- Noninfectious causes of lymphadenopathy should also be considered in the case of subacute or chronic lymphadenopathy.
- Based on strong clinical evidence and expert opinion, biopsy of lymphadenopathy should be undertaken if there is a suspicion for malignancy, subacute/chronic lymphadenopathy, worsening lymphadenopathy despite appropriate treatment, persistent lymph nodes larger than 2 cm, or multiple lymph nodes with concerning features on computed tomography, ultrasonography, or magnetic resonance imaging. (23)(24)
- Based on clinical evidence and expert opinion, fine-needle aspiration should be considered as a diagnostic tool in patients requiring biopsy as long as they are able to tolerate the procedure under local anesthesia. (26)(27)

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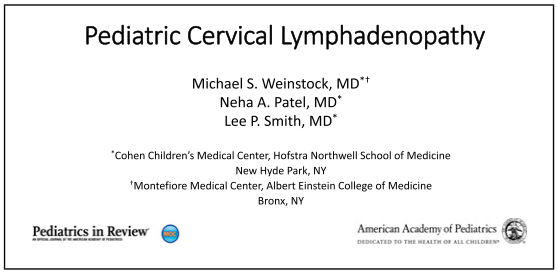

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1. A 2-year-old boy is brought to the office with swelling on the right side of the neck. He was noted to have a runny nose, fever, and a cough 7 days earlier, which are improving. The mother noted swelling on the right side of the neck 3 days earlier and states that the child is complaining of discomfort in the area of the swelling. On physical examination his temperature is 100.4°F (38°C), heart rate is 100 beats/min, and respiratory rate is 24 breaths/min. There is a 1 × 1.5-cm palpable lymph node in the right anterior cervical chain that is mildly tender but movable and with no overlying tenderness, erythema, or warmth. Nasal congestion is seen. The remainder of the physical examination findings are normal. Which of the following is the most appropriate next step in management of this patient?
   A. Chest radiograph.
   B. Fine-needle aspiration of the lymph node.
   C. Monospot test.
   D. Reassurance.
   E. Ultrasonography of the neck.
2. A 15-year-old girl is brought to the office with a sore throat, difficulty swallowing, fatigue, and persistent fever for the past 5 days. In the past 2 days she has noted increased fatigue and swollen lymph nodes in the neck. On physical examination the patient appears ill and tired. Her temperature is 101.3°F (38.5°C), respiratory rate is 18 breaths/min, and heart rate is 80 beats/min. Her oropharynx is injected with enlarged tonsils and a white exudate. Her breath is foul. Her neck shows multiple lymph nodes in the posterior cervical chain ranging in size from 0.5 to 1.5 cm in diameter. There is mild overlying tenderness. The scalp has no lesions. Examination of the heart and lungs is normal. The spleen is palpable 2 cm below the left costal margin, and the liver is not palpable. Laboratory data are as follows: white blood cell count, 15,000/μL (15 × 10^9/L); hemoglobin, 13 g/dL (130 g/L); hematocrit, 42%; platelet count, 300 × 10^3/μL (300 × 10^9/L); mean corpuscular volume, 84 μm^3 (84 fL); neutrophils, 25%; bands, 2%; monocytes, 5%; lymphocytes, 50%; atypical lymphocytes, 18%; alanine aminotransferase, 100 U/L (1.67 μkat/L) (reference range, 7–56 U/L [0.12–0.94 μkat/L]); aspartate aminotransferase, 80 U/L (1.34 μkat/L) (reference range, 10–40 U/L [0.17–0.67 μkat/L]); total bilirubin, 1.5 mg/dL (25.66 μmol/L); and rapid streptococcal antigen negative. Which of the following is the most likely diagnosis in this patient?
   A. Acute lymphocytic leukemia.
   B. Atypical mycobacterium.
   C. Cat-scratch disease.
   D. Epstein-Barr virus infection.
   E. Streptococcal pharyngitis.
3. A 3-year-old boy is brought to the emergency department with a red swollen area on the left side of the neck. The child had an upper respiratory tract infection 1 week earlier with fever and a cough. At that time the mother noted a small "swollen" area on the left side of the neck. The initial fever resolved, but over the past 2 days the fever recurred, and the swelling has gotten larger, more red, and painful. On physical examination his temperature is 101.1°F (38.4°C), respiratory rate is 18 breaths/min, and heart rate is 110 beats/min. A 2 × 2-cm red, warm, and tender lymph node is noted in the left anterior cervical chain. The node is rubbery, movable, and nonfluctuant. The oropharynx shows mild erythema with no exudates and with normal-sized tonsils. The remainder of the physical examination findings are normal. Which of the following is the most appropriate next step in the management of this patient?

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A. Computed tomography of the chest.
B. Excisional biopsy.
C. Incision and drainage of the node.
D. Oral antibiotics.
E. Ultrasonography of the neck.

4. A 12-year-old girl is brought to the office with increasing swelling above the left collar bone. She was well until 8 weeks ago when she developed a small swelling in the left lower cervical area. She was seen at an urgent care center and was treated with oral amoxicillin. The swelling did not resolve, and 4 weeks ago she was seen for follow-up in the office of her primary care provider and received a course of clindamycin. The swelling continued and is now extending above the left clavicle. The area is nontender with mild redness. She has been more tired than usual but has had no night sweats. She does not think she has lost weight. She has not had a fever since the initial presentation 8 weeks ago, when she was warm to the touch. She has no history of foreign travel and no exposure to pets or populations at risk for tuberculosis. On physical examination her weight is at the 40th percentile (was the 45th percentile at the time of her last health supervision visit 6 months ago). Her height is at the 50th percentile. Her temperature is 100.0°F (37.8°C), respiratory rate is 16 breaths/min, and heart rate is 80 beats/min. The oral cavity is normal. The neck shows a 2.5 $\times$ 3-cm firm, nontender, fixed, and nonerythematous node in the left supraclavicular area. Several smaller nodes 1.5 $\times$ 1 cm and 1 $\times$ 1 cm are noted in the left cervical chain. There are no thyroid nodules detected. The axilla and inguinal areas have no palpable lymph nodes. The remainder of the physical examination findings are normal. Results of laboratory studies (including complete blood cell count), metabolic profile, and chest radiography are normal. Which of the following is the most likely diagnosis in this patient?

A. Hodgkin lymphoma.
B. Nasopharyngeal carcinoma.
C. Neuroblastoma.
D. Rhabdomyosarcoma.
E. Thyroid carcinoma.

5. A 5-year-old boy is brought to the office by his parents due to a swelling on his neck. The mother noted this several months ago. The swelling got bigger initially but has remained the same size for the past 8 weeks. The swelling is located in the middle of his neck and moves when he sticks his tongue out. The area has occasionally been red. On physical examination a 2-cm-diameter soft mass is noted on the middle of the neck just superior to the larynx. There are no lymph nodes palpable in the cervical, supraclavicular, or axillary areas. The remainder of the physical examination findings are normal. Ultrasonography of the neck shows a normal-appearing thyroid gland with a cystic structure in the midline just superior to the larynx. A thyroid uptake scan shows a normal-appearing thyroid gland. Which of the following is the most appropriate management plan of this lesion in this patient?

A. Fine-needle aspiration.
B. I_{131} radioablation.
C. Levothyroxine.
D. Propylthiouracil.
E. Surgical excision.