



Managing Cervical Lymphadenitis—A Total Pain in the Neck!

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Abstract

Patients presenting with cervical lymphadenitis are a complex and common occurrence in a general pediatric practice. Although *Staphylococcus aureus* (often methicillin-resistant *S. aureus* [MRSA]) and *Streptococcus pyogenes* predominate as causative pathogens, the next most common pathogens, *Bartonella*, atypical mycobacterium, and mononucleosis, also must be considered early on. The best way to diagnose and manage these cases initially is to proceed methodically, with detailed history and physical examination, initial streptococcal mono rapid tests, serial office visits, and complete blood counts. In non-viral cases, an empiric oral antibiotic trial is usually prescribed as early as possible to cover for MRSA or *Bartonella*. Very tender or reddened lymph nodes larger than 5 cm that are unresponsive and worsening may likely require inpatient parenteral antibiotics and sometimes surgical removal. The practitioner must also realize that submandibular and supraclavicular node

locations are highly suggestive of atypical mycobacterium and cancer, respectively. [*Pediatr Ann.* 2014;43(10):390-396.]

In your private general pediatric practice, almost daily you are on a “nodes-to-know-basis” with the multitude cases of cervical lymphadenitis you assess and manage. Even as you were collecting your thoughts today for this teaching article, the child in Figure 13 appeared in your office with another “whopper” of an anterior cervical node. Worried (about cancers), stymied (about the huge differential diagnosis), and perplexed (by the complexity of etiologies), you still plodded onwards with your assessment.

Over the years, you have found, however, that proceeding methodically along certain levels of complexity in pursuit of an accurate diagnosis may often lead to your improved successful management of this common enigmatic problem (Table 1). Etiologic diagnosis often times requires astute history taking and physical examination skills, along with selective and appropriate laboratory testing in stages. Often, this must be combined with reasonable empiric antibiotic therapy for specific targets to determine whether the clinical response corroborates your suspicions.

Nonetheless, you will be dealing with some clear cut exceptions to this approach in Table 1. While you

are pursuing the diagnosis, here are some general rules and some exceptions to remember during the evaluation that are helpful, but by no means pathognomonic:

HISTORY

Obtaining a history of each of the following may be helpful: level of fever, sore throat, oropharyngeal blisters, nearby impetigo lesions, and tuberculosis exposure. Furthermore, you should inquire about exposure to the following zoonoses (Just remember cats, farms, rabbits, ticks):

- Above the shoulders scratch by a cat (or dog) within the last approximately 2 months (*Bartonella henselae*)
- Aquarium or farm animal or unpasteurized milk exposure (atypical mycobacterium, brucellosis)
- Nearby tick bite, with or without an ulceration (*S. aureus* or rarely tularemia)
- Rabbit exposure via hunting or skinning (tularemia)

PHYSICAL FINDINGS

The cervical gland should be carefully assessed for size, pain, redness, discoloration, induration, fluctuance, mobility, and probably for any additional satellite nodes in the cervical, axillary, and inguinal areas (hunting for the stealth lymphoma or leukemia).

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The following ancillary findings on physical examination may often point you in certain diagnostic directions:

- High fever: *S. aureus* and *S. pyogenes* top the list
- Exudative pharyngitis: *S. pyogenes* and mononucleosis
- Scarletini or morbilliform rash: *S. pyogenes* and mononucleosis
- Hepato- or spleno-megaly: mononucleosis and lymphoid cancers
- Scalp and facial lesions, such as insect or tick bites
- Dental or periodontal disease or salivary duct inflammation (sialadenitis)
- Puffy upper eyelids in the morning: present in half of cases of Epstein-Barr (EB) virus
- Scalp kerion: epidermophyton

ETIOLOGY OF CERVICAL LYMPHADENITIS

S. aureus and *S. pyogenes* are by far the most common pathogens identified, accounting for 65% to 89% of the pathogens.¹ The next most commonly identified group of pathogens are EB virus, *Bartonella*, and atypical mycobacteria. But, also note that both *S. pyogenes* and EB virus uncommonly present with unilateral lymphadenitis (except in your private practice, of course, as you will see).

A more esoteric and quite rare etiologic group includes *Brucella*, leptospirosis, tuberculosis, Kawasaki disease, thyroid nodules, branchial cleft cysts, cystic hygromas, and finally, the most dreaded of all—lymphomas and leukemia types.

CASES

Solitary Nonlymphoid Neck Masses

Figure 1. This 3-month-old child had an ultrasound performed on the neck that revealed a cystic hygroma or lymphangioma of the neck. Often quite disfiguring, it is usually observed before

age 2, and can be associated with either Turner's or Noonan's syndromes.² Therapy usually involves surgical removal or sclerosing agents.

Figure 2. This 6-year-old male had developed a thyroglossal duct cyst. Note the supra-hyoid location here, in comparison with the child in Figure 3. Abrupt onset is surprisingly common, and most children are euthyroid. Unlike branchial cleft cysts, thyroglossal duct cysts often appear acutely after a recent upper respiratory infection.² Diagnosis is nearly confirmed by the midline location and the mobility of the mass with

TABLE 1.

Laboratory Evaluation for Cervical Lymphadenitis

Level 1. Rapid antigen detection test (ADT) for strep; complete blood count and monospot (by simple easy finger stick); without a significant pharyngitis. Be wary that a positive ADT may actually be strep carrier state.
Level 2. If high leukocyte count (>15,000 white blood cells/mm ³) or increased erythrocyte sedimentation rate and negative strep ADT, strongly consider oral therapy for methicillin-resistant <i>Staphylococcus aureus</i> (MRSA), particularly prescribing oral clindamycin or trimethoprim-sulfamethoxazole and amoxicillin; earlier treatment is better. <ul style="list-style-type: none"> • If no response, highly febrile, or marked worsening, consider hospitalization for intravenous therapy of MRSA and surgical consultation.
Level 3. If normal leukocyte count/ESR or history suggestive, consider: <ul style="list-style-type: none"> • Serum testing for <i>Bartonella henselae</i>, <i>Francisella tularensis</i>, and Epstein-Barr virus (EBV) titers. • Intradermal tuberculosis (TB) skin test (uncommonly positive in patients from private practice with atypical mycobacterium). • A trial of targeted empiric antibiotic therapy almost as a diagnostic test: <ul style="list-style-type: none"> Oral azithromycin (10-12 mg/kg/day for 5 days) should be considered with any history of recent local cat (or even dog) scratches; a trial of oral clindamycin if any recent regional tick bites⁶ to cover for MRSA first.
Level 4A. If fluctuant or markedly enlarging, consider ultrasound to determine abscess vs solid node. Consider fine-needle aspiration or "incision and drainage" as a starting point, along with empiric intravenous clindamycin or even vancomycin or linezolid.
Level 4B. Consider surgical extirpation if ill, unresponsive, or markedly enlarging (>5 cm), or if atypical TB is most likely, especially for <i>submandibular</i> nodes. Your experience suggests that nodes that are initially >5 cm will most likely need surgical extirpation. Most nontender <i>supraclavicular</i> nodes >2 cm will require biopsy.

Be very cautious if there is a history of a tick bite, with a nearby skin ulceration—tularemia is considered a Centers for Disease Control and Prevention level 3 biohazard for the surgical team and laboratory personnel. They should be warned appropriately.

any tongue extrusion. An ultrasound is confirmatory, and many surgeons prefer a thyroid scan before total surgical excision to ensure that it is not an ectopic thyroid gland.

Figure 3. Because the location of this solitary neck mass is infra-hyoid, your most likely diagnosis is a branchial cleft cyst or rarely a thymoma. Computed tomography (CT) scan or magnetic resonance imaging (MRI) is often needed to confirm the diagnosis and to evaluate whether the cleft is contiguous with any underlying structures. Antibiotics are indicated when

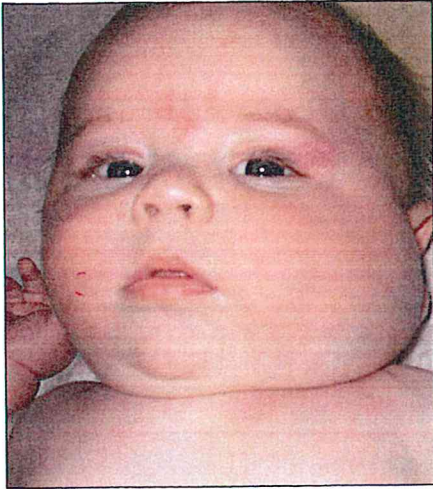


Figure 1. Asymptomatic, afebrile 3-month-old infant presenting with a large left anterior cervical/facial mass. Note the location.



Figure 2. Asymptomatic, afebrile 6-year-old male with an enlarging midline neck lump present for over 4 months. Note the location.

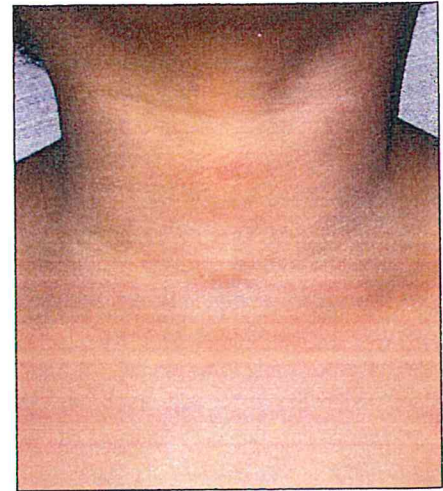


Figure 3. Asymptomatic, afebrile 5-year-old African-American male with a small mass present "for years." The mother became worried when the boy's aunt told her that she needed to have it checked out. Note the location.



Figure 4. A 2-year-old white female who had been very fussy for the previous 2 weeks and was thought to be teething. The mother noted a small purplish knot under her right mandible that was evaluated with a normal CBC and physical examination. On the earlier assumption that this lesion was related to *Staphylococcus*, it was treated with oral cephalexin for a week. This photo is what you see after initial treatment. It is now redder, fluctuant, and tender. She also has developed a low-grade fever. Note the location. The family raises a multitude of rabbits.

infection is present. Surgical removal is curative.

Lymphadenitis

Figure 4. This 2-year-old female has now developed some generalized low-grade signs and symptoms from her apparent submandibular lymphad-



Figure 5. A 7-year-old African-American male with a slowly enlarging mass in the left submandibular region for over 2 weeks. He is afebrile, but now does complain of localized pain. Is this a salivary duct problem? Note the location.

enitis. Her tuberculosis (TB) skin test was negative. Note the purplish hue of the skin. A repeat complete blood count (CBC) was normal and her titers for *Bartonella* were negative, whereas her immunoglobulin G (IgG) titers for tularemia were elevated. Is this acute infection or a convalescent titer from long-term rabbit exposure? With her tremendous exposure to rabbits, you send her to the surgeon for a fine-needle aspiration to explore the likelihood of tularemia, along with a culture for *Bartonella* and mycobacterium. You opt for

empiric therapy with oral doxycycline liquid for 10 days while awaiting her results. Her small amount of purulent aspirated fluid did not grow a pathogen over the week.

Her infected node briefly responded to the doxycycline, but seemed to worsen during the last few days of her 10-day oral therapy. Considering the location of the node, you send her back to the surgeon for total extirpation. You now must consider that atypical mycobacterium has a quite distinct predilection for the submandibular region,¹ and that it will usually require total excision to cure it. The week after the node has been removed, the surgeon continued the doxycycline for another 10 days on the assumption that the tularemia titers were most likely real. About 10 days later the skin still appears slightly reddened so you initiate azithromycin therapy (10 mg/kg/day) for 5 days, which has some reasonable atypical mycobacterium coverage and is more palatable and convenient than clarithromycin.³

Two days later the culture now reveals an atypical mycobacterium strain. Another 5-day course of azithromycin

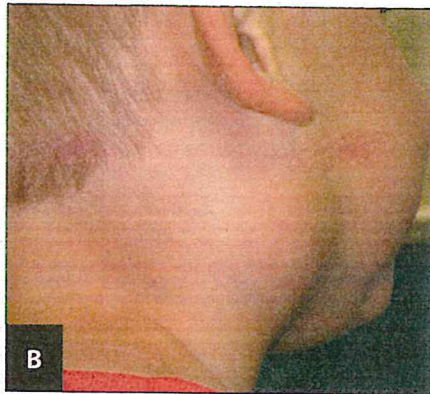
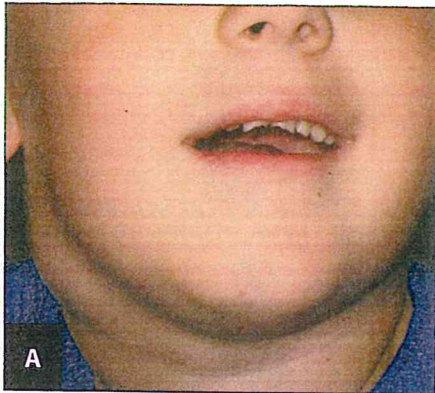


Figure 6. (A) A previously healthy 4-year-old male who developed an abrupt onset of this painful moderately swollen right anterior cervical node. He has not had a sore throat, but did have fever today of 100.7°F. Should you start standard oral antibiotic therapy? (B) After 7 days of two different appropriate oral antibiotics, his node continues to be more swollen, tender, and reddened. How should you proceed?

was prescribed the next week, and the child has fully recovered.

Figure 5. This afebrile 7-year-old boy had a solitary tender submandibular node that continued to enlarge over 2 weeks despite oral clindamycin and azithromycin therapy. You do not think that the node is dental related—nor is it sialadenitis with his normal CBC, normal amylase, and normal looking salivary gland ducts.

Location, location! You send him to the surgeon who removes the node, carefully avoiding the parotid gland and the facial nerve. His culture grows atypical

mycobacterium about 10 days later, and no further therapy was prescribed due to his rapid good response.

Figures 6A and 6B. This 4-year-old boy had a positive rapid antigen detection test for *S. pyogenes*; it was positive despite the lack of a red pharynx and only a unilateral tender lymph node (**Figure 6A**). However, even after 10 days of oral amoxicillin, his node continued to enlarge with more redness and tenderness (**Figure 6B**). His leukocyte count was 16,700 with a left shift. Even during your additional course of oral clindamycin over the



Figure 7. This previously healthy 15-year-old female has had low-grade fevers (101.5°F), malaise, fatigue, and sore throat. She also has a mildly tender large right unilateral anterior cervical node. Her rapid Streptococcal testing was negative. Which pathognomonic sign in this photo gives you the probable diagnosis even before you proceed to further testing? Is unilateral lymphadenitis unusual here?

next few days, the enlarging node and fevers continued to worsen, and he was subsequently hospitalized for parenteral higher dose clindamycin therapy. Three days into the hospitalization, surgical excision was performed due to the lack of any substantial progress. You surmise, as outlined in the **Table 1** algorithm, that many of the nodes >5 cm, despite parenteral antibiotics, will require surgical excision—even with an

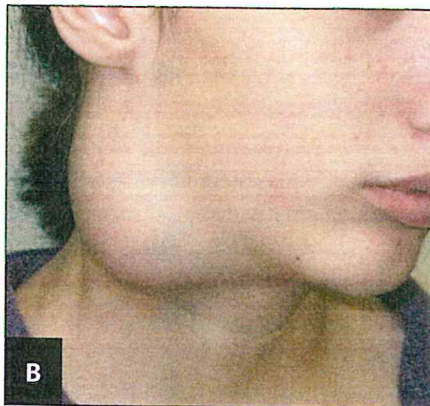
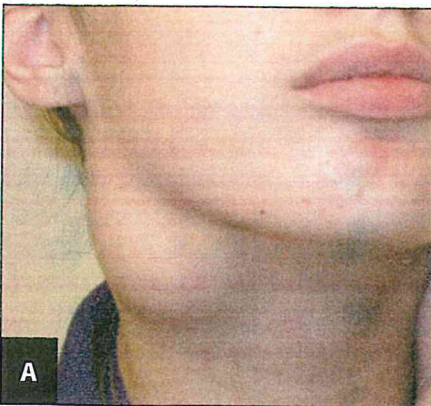


Figure 8. (A) A previously healthy 11-year-old female who presents with a markedly swollen, mildly tender anterior cervical node. She has had some malaise, fatigue, and “low-grade fevers.” She has no cats, tick bites, or tuberculosis exposure. (B, C) After 2 weeks of multiple oral antibiotics, including azithromycin (10 mg/kg/day) and clindamycin, her node has continued to enlarge notably. She has been seen by two different surgeons this week; neither wants to pursue a surgical evaluation. What further tests and diagnoses are you considering now that she is back in your office? In an “Oh by the way” moment as you review her history again, you just learned that her dog had scratched her on her right shoulder a month ago.



Figure 9. This previously healthy 4-year-old male has developed some “swelling” behind his left ear. He denies any sore throat, but he did complain of some “fever to touch” per the mother. His ear and throat examinations are normal. Note the location.

antibiotic-susceptible bacteria such as *S. pyogenes*!

Figure 7. Upon re-examination of this young lady 5 days into her illness, you can clearly see the upper eyelid periorbital edema, which has been worse in the mornings. Although the most common cause of this edema may be allergic conjunctivitis and infectious mononucleosis (~50% of infected patients⁵), one should also be suspicious for possible renal and cardiac causes, particularly if both upper and lower eyelids are swollen. A careful auscultation of the heart, examination of liver and the feet (pretibial edema), and a urinalysis for proteinuria are prudent here. When found in conjunction with any pharyngitis and/or lymphadenopathy, this periorbital edema is usually pathognomonic for mononucleosis. However, the unilateral lymphadenitis in mononucleosis is quite unusual here.

Figure 8. During the first week of this 11-year-old female’s illness she had a normal CBC, erythrocyte sedimentation rate (ESR), monospot, and EB virus titers, and later a nonreactive TB skin test. Her huge lymph node was mildly tender and not reddened, but it still continued to massively enlarge (**Figure 8A**). You could only think the

worst, so within a week you had sent her to two different surgeons (pediatric and otolaryngologist) while you initiated treatment with clindamycin and azithromycin to cover for methicillin-resistant *S. aureus* (MRSA) and *Bartonella*, respectively. Both surgeons declined to perform any procedures—thinking the futility of treating cat scratch lymphadenitis, perhaps? But, you were still so concerned that you obtained a chest radiograph (normal), neck ultrasound (solid mass), and *Bartonella* IgG titers (positive at 1:256). Although she had no history of cats, on your third visit with you she divulged that her dog had recently scratched her clavicular region while she was holding it. And yes dog-lovers, dog scratches can paradoxically cause cat scratch fever!

After week 2, her ESR was now elevated at 85 mm/hour. Because of the continued enlargement (**Figures 8B and 8C**), you reordered a neck ultrasound that now revealed a large fluid filled abscess.

During week 3, the surgeon was finally ready to operate. During the surgical removal of the massive node, she was discovered to have a branchial cleft cyst with a tract tunneling into her esophagus. However, to cover for the

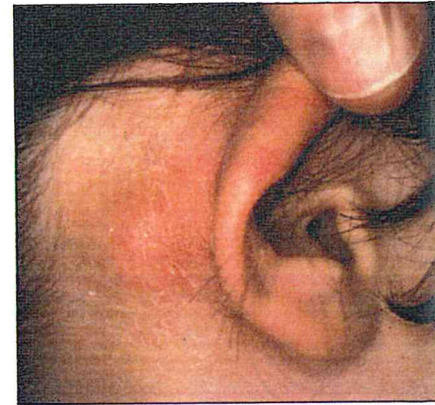


Figure 10. This previously healthy 3-year-old female has had this posterior auricular node for 10 days. This is the node’s appearance after four different oral antibiotics. The lesion is now fluctuant and she has just recently developed a small ulcer in her scalp, near a previous tick bite. How should you proceed? Should you aspirate it?

positive *Bartonella* titers another course of azithromycin was prescribed. She did well postoperatively, with a good cosmetic outcome. And once again, you patients do not read the textbooks: branchial cleft cyst in an 11 year old? And an abrupt onset?

Figure 9. Finding isolated, tender posterior and/or retroauricular lymphadenitis as in **Figure 9**, should always make you consider skin infections and insect bites in the scalp.³ You carefully scour his scalp, and find nothing. So you fortunately stick to your rule of laboratory evaluation as outlined in level 1 of **Table 1**. His CBC is normal, mononucleosis screen is negative, but much to your surprise, his rapid ADT for strep was positive. You have stumbled upon another case of isolated streptococcal unilateral lymphadenitis without pharyngitis. He responded well to 10 days of oral amoxicillin.

Figure 10. This 3-year-old female with a retroauricular smaller lymphadenitis and no external otitis⁵ really baffled you. Her 10 days of persistent constitutional symptoms of malaise, fevers, and anorexia all seemed totally out



Figure 11. A previously healthy 7-year-old male with a swollen, tender, and moderately reddened node in the supraclavicular area. He has a history of a dog tick bite in his scalp. This is the node's appearance after 3 weeks of multiple oral antibiotics, including azithromycin, clindamycin, and even doxycycline. The node is now quite fluctuant. What are you thinking, and how should you proceed? Note the location.

of proportion to a typical staphylococcal lymphadenitis. Her ESR was elevated at 45 mm/hour, but her leukocyte count was normal. But you had warned the mother about the possible etiology of this lymphadenitis, so when your partner saw the patient in your absence she reassured the mother that the new small ulcer in her scalp was merely a herpetic reaction. OOPS!

When you saw the skin ulcers in the next 48 hours, that clinched your earlier suspicions. You very carefully (and perhaps cavalierly) needle aspirated about 5 mL of pus from the node, and submitted the specimen for culture. Along with a large note for the lab to process it as a level 3 biohazard!

Yes, you had your first of 4 cases of *Francisella tularensis* that year! Think tick bite, fluctuant node, and nearby skin ulcer—and you have ulcero-glandular tularemia. You discussed with the parents the antibiotic choices for outpatient treatment: twice daily intramuscular gentamicin for 10 days that would require baseline and 2 more hearing tests, and a series of about three serum chemistries and gentamicin levels by veni-



Figure 12. A previously healthy 4-year-old female who, over the last few days, has developed this marked posterior cervical node that is mildly tender and seems to have two smaller satellite nodes around it. She is afebrile, but has had no appetite for a week. How should you proceed?

puncture as well. Gentamicin = Potential for oto-toxicity and renal toxicity?

Or you could prescribe twice daily oral doxycycline liquid with a slightly lower cure rate than gentamicin, and basically adverse effects of gastrointestinal distress (without concomitant food) along with a slight risk of posterior molar dental staining when using such a short course of this lipophilic antibiotic. The American Academy of Pediatrics RED Book Report Committee has long considered a single course of doxycycline to be safe to use in children with suspected rickettsial infections.⁴

Subsequently, you elected to use oral doxycycline to treat the node at this point, and she had a rapid successful response. Perhaps needle aspiration would have been preferred in the pediatric surgeon's office, too?

Figure 11. The purplish red node seen in this image is highly suspicious for our esoteric pathogen again—tularemia. The history of a nearby tick bite and lack of any response to multiple antibiotics, including doxycycline (see discussion in **Figure 10**) are suggestive. But the patient also lacked any constitu-



Figure 13. This previously healthy 8-year-old male with a history of four episodes of recurrent lymphadenitis infections of the left cervical area presents with a 24-hour onset of tender, very swollen unilateral anterior cervical node at the angle of the jaw. His father says he always gets better with oral antibiotics that were used for the previous four similar infections. How should you proceed?

tional symptoms of fever or malaise as far as you could tell. In addition his CBC and ESR were normal. However, his tularemia IgG titers were 512:1.

Should you aspirate the node? Perhaps too risky for you. Hospitalize? The child is not ill acting. So you do the next best approach—send him to the pediatric surgeon for total node extirpation with cultures. His culture never grew a pathogen—probably due to doxycycline suppression. But he responded well to the node removal.

Figures 12 and 13. Both of these children had an abrupt onset of a markedly enlarged but mildly tender lymph node in the anterior cervical region, with low-grade fevers and decreased appetite. The parent of the child in Figure 13 had you convinced that this was just another episode of his recurrent staphylococcal lymphadenitis infections, and that you just needed to start the clindamycin again. You were also thinking that he was a good candidate for branchial cleft cyst as a cause for his recurrent infection. However, you stuck to your principles as outlined in **Table 1**. His strep test was negative, his leukocyte count

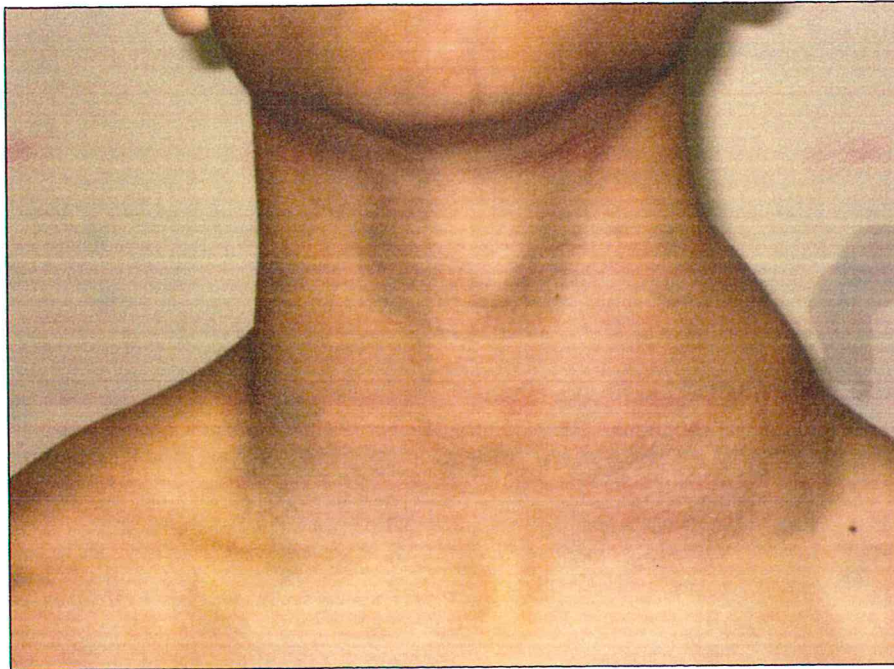


Figure 14. This previously healthy, afebrile 15-year-old African-American male has developed this slightly tender, very large node in his left lower neck. How should you proceed? Note the location.

was 13,500 cells/cm³, and his monospot was...

Positive. Just like it was in the young girl in **Figure 12**. So do not let the lymph node unilaterality, or the lack of a substantial pharyngitis, or the lack of duration of symptoms dissuade you from performing the tests in level 1 of **Table 1**. Even children as young as 12 months old can be infected with either mononucleosis or *S. pyogenes*.

Figure 14. Perhaps, you would like to perform all your tests in **Table 1** right out of the gate. Do not bother! This is a large nontender or minimally tender supraclavicular mass or lymph node.

Just send the patient to the hematology-oncology group directly, as you did here. Not much good will usually arise out of a larger supraclavicular node. The patient needed immediate further evaluation and treatment for his non-Hodgkin's lymphoma.

In the child with "nonsuppurative" cervical lymphadenitis, routinely examine the child's other node regions (ie, inguinal, axillary) and the liver and spleen on each serial visit.³ You may again, just like you did a few years ago, uncover a child who has leukemia or lymphoma despite his presumptive diagnosis of mononucleosis. A life may depend on it.

CONCLUSION

Although *S. aureus* and MRSA and *S. pyogenes* seem to predominate as causative pathogens, symptomatic unilateral cervical lymphadenitis is truly "a pain in the neck" and a physical finding that is messy to evaluate and to manage. I think that the process outlined in **Table 1** to diagnose and treat it will optimize your outcomes. You must be thorough in checking a patient's history (ie, details about scratches and bites from cats, ticks, farm animals, rabbits) and in your physi-

cal examinations. Serial office visits and even CBC's are often required. Empiric antibiotic trials for specific pathogens such as MRSA (high leukocyte count) and *Bartonella*, may be worthwhile for both diagnosis and treatment when findings suggest them.

Certain node locations with specific node characteristics seem to more reliably predict particularly troublesome etiologies, eg, supraclavicular and submandibular. Tender or reddened lymph nodes >5 cm that are obviously nonviral and do not respond rapidly to empiric outpatient anti-staphylococcal antibiotics may require inpatient parenteral antibiotics and sometimes surgical removal. Finally, the practitioner must realize that the unilaterality of the node or the lack of a significant pharyngitis does NOT preclude 2 of the more common pathogens: *S. pyogenes* and EB virus.

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