Otolaryngology–Head and Neck Surgery

AMERICAN ACADEMY OF OTOLARYNGOLOGY-HEAD AND NECK SURGERY FOUNDATION®

Original Research

# Management of Pediatric Persistent Asymptomatic Cervical Lymphadenopathy

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# Introduction

- Cervical lymphadenopathy is common in the pediatric population ( prevalence ranging from 28% to 55%)
- Lymphoma: one of the most common malignancies presenting in children with high cure rates when identified early
- Workup and initial management usually includes:
  - Hematologic labs to rule out infectious etiologies
  - Empiric antibiotic therapy
  - A period of observation
- Presence of B symptoms or supraclavicular lymphadenopathy

  → Pursue further investigation

- Does not reveal an etiology
  → Referred to a pediatric surgical specialist
  → Invasive sampling to rule out malignancy

- Persistent asymptomatic lymphadenopathy
  - Individual practice patterns vary among specialists
  - No evidence-based guidelines for safe and appropriate follow-up
- A recent prospective study showed:
  - The majority of lymphadenopathy resolved within 8 weeks
  - Malignancies were associated with B symptoms or abnormal hilar findings on ultrasound

  → watchful waiting is a rational approach for asymptomatic cervical lymphadenopathy

- Historically, excision lymph node biopsy served as the gold standard for diagnostic workup of PACL.
  → lead to a large number of unnecessary invasive procedures.
  → See if a **less invasive monitoring protocol** would be safe for our patients without missing malignancy diagnoses

- Ultrasound
  - Growing availability
  - Refinement in its technique

  → Affords a noninvasive option for lymph node surveillance
- Surgical biopsy
  - Risks of general anesthesia
  - Risks of  bleeding ,infection and potential injury to neurovascular structures
- Aim to characterize the natural history, radiologic and pathologic findings to be able to **potentially provide guidance for noninvasive surveillance for this common pediatric referral diagnosis**

# Method

# Methods

- A retrospective electronic chart review of 276 patients, age $<$ 18 years at a single, tertiary care children's hospital
- Inclusion criteria
  - Were referred to the Otolaryngology–Head and Neck Surgery clinic at UCSF for persistent asymptomatic cervical lymphadenopathy (PACL)
  - Had undergone at least 1 soft tissue neck ultrasound from January 1, 2007 to June 30, 2021
- Exclusion criteria
  - Patients with infectious adenopathy identified by laboratory or imaging studies, congenital neck masses, or known rheumatologic, immunologic, or malignant conditions

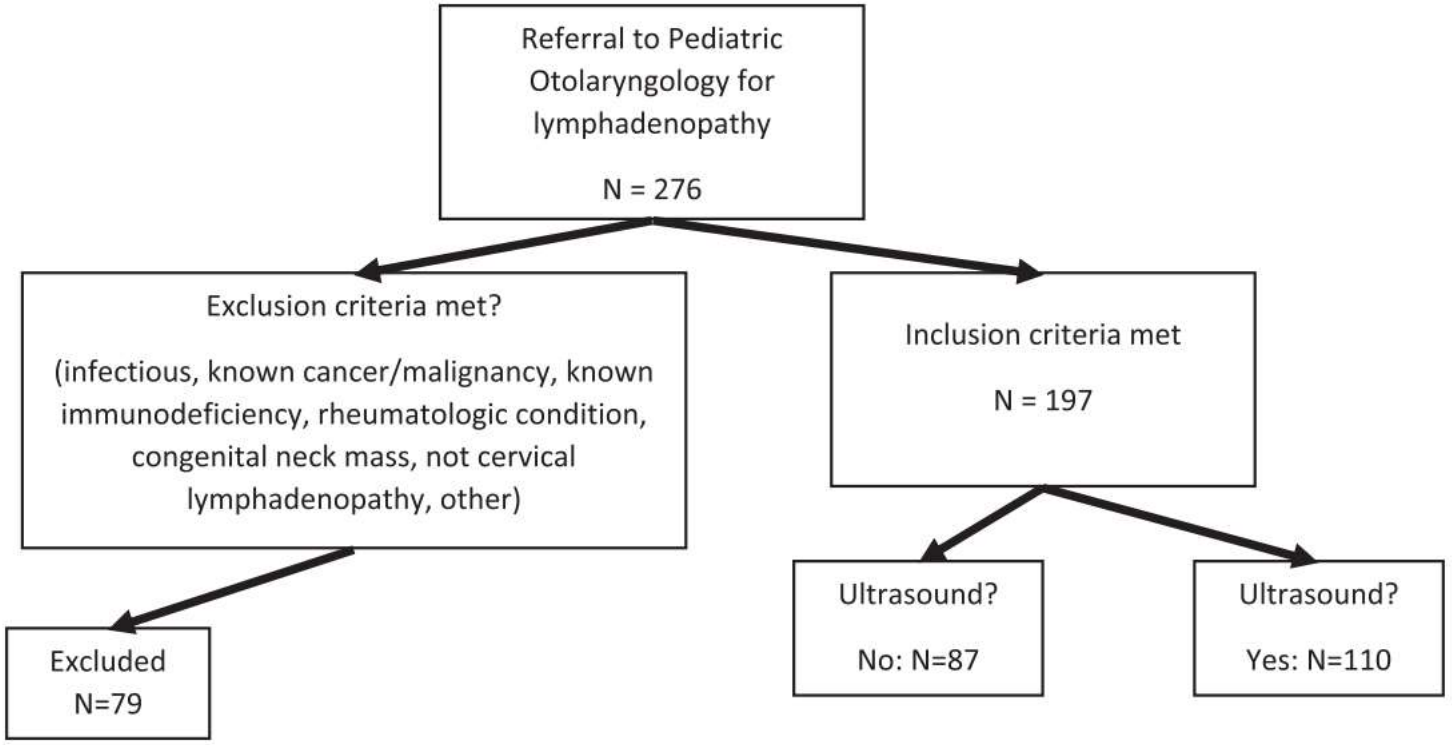
# Methods

- Demographics:
  Sex, age, ethnicity, clinical and physical exam features: presence of pain, node firmness, neck location
- Ultrasound Findings: Extracted from radiologists' imaging reports
- Statistical Methods Used:
  Both univariate and multivariate logistic regression models were applied
- Study Objectives:
  - To identify patient and lymph node factors linked to the decision for surgical intervention
  - To offer guidance for clinical management and follow-up

# Result

# Results - Patient Characteristics

- Patient Characteristics



# Results - Patient Characteristics

**Table 1.** Patient Characteristics

| Characteristic | Mean (±SD) or N (%) |
|---|---|
| Age, y | 6.4 (±4.7) |
| Male | 106 (54%) |
| Persistence of mass, mo | 8.79 (±10.2) |
| Painful on exam | 15 (8.9%) |
| Firm on exam | 17 (11.4%) |
| Location on neck | |
| Anterior | 82 (42%) |
| Posterior | 69 (35%) |
| Submental | 9 (4.6%) |
| Submandibular | 32 (16.3%) |
| Postauricular | 10 (5.1%) |
| Supraclavicular | 7 (3.6%) |

# Results - Patient Characteristics

| | |
|---|---|
| Size on physical exam, cm | 1.6 (±1.04) |
| Size on ultrasound, cm | 1.51 (±1.3) |
| Subsequent ultrasound ordered | 44 (26%) |
| Subsequent ultrasound interval, mo | 6.6 (±5.7) |
| Change in size on ultrasound, cm | −0.35 (±1.64) |
| Fine needle aspiration biopsy | 15 (7.7%) |
| Surgical biopsy | 30 (15.2%) |

- Of the 30 who had an excisional biopsy, 7 (3.6%) had a prior FNA.
- Seven (46.7%) of the 15 patients who had an FNA ultimately underwent excisional biopsy because the results were nondiagnostic.
- In general, our group of pediatric otolaryngology faculty **did NOT** recommend FNA due to the high false negative and sampling error rates.

# Results - Patient Characteristics

- In addition, at the initial clinical encounter, **66 patients (33.5%) were prescribed antibiotics prior to subspecialty evaluation**.
- Approximately **a third of the study cohort (31.9%)** had undergone laboratory studies prior to referral to the pediatric otolaryngology practice
  → more than half having a positive test suggestive of an infectious etiology for the cervical lymphadenopathy.

**Table 2.** Surgical Biopsy Versus No-Surgical Biopsy Cohort Characteristics

| Characteristic | Surgical biopsy status: No surgical biopsy (n = 80) | Surgical biopsy status: Surgical biopsy (n = 30) | *p* Value |
|---|---|---|---|
| Age | 6.2 (±4.7) | 7.4 (±5.3) | .281 |
| Male | 45 (56%) | 11 (37%) | .075 |
| Persistence of mass, mo | 8.94 (±10.3) | 4.21 (±3.3) | <.001 |
| Painful on exam | 2 (2.7%) | 8 (27%) | <.001 |
| Firm on exam | 3 (3.75%) | 10 (33%) | <.001 |
| Location on neck | | | |
| Anterior | 31 (38%) | 12 (40%) | .85 |
| Posterior | 29 (36%) | 10 (33%) | .77 |
| Submental | 6 (7.5%) | 1 (3%) | .38 |
| Submandibular | 14 (17.5%) | 5 (16%) | .85 |
| Postauricular | 4 (5%) | 3 (10%) | .34 |
| Supraclavicular | 1 (1.25%) | 5 (16%) | .002 |
| Size on physical exam, cm | 1.33 (±0.68) | 2.42 (±1.36) | <.001 |
| Size on ultrasound, cm | 1.37 (±1.15) | 1.6 (±1.41) | .428 |

**Table 2.** Surgical Biopsy Versus No-Surgical Biopsy Cohort Characteristics

| Characteristic | Surgical biopsy status: No surgical biopsy (n = 80) | Surgical biopsy status: Surgical biopsy (n = 30) | *p* Value |
|---|---|---|---|
| Lack of fatty hilum | 25 (3.13%) | 1 (3.33%) | .96 |
| Subsequent ultrasound ordered | 20 (25%) | 3 (10%) | .085 |
| Subsequent ultrasound interval, mo | 6 (±5) | 9.3 (±10.7) | .114 |
| Change in size on ultrasound | −0.14 (±1.11) | 0.53 (±1.12) | .007 |
| Fine needle aspiration biopsy | 7 (8.8%) | 7 (23%) | .046 |

- **Pain** (p = .03) and the **presence of a normal fatty hilum** on ultrasound (p = .02) statistically significantly correlated with **ultrasound monitoring** as an appropriate option

**Table 3.** Odd Ratios of Surgical Biopsy

| Predictor variable | Odds ratio (95% CI) | *p* Value |
|---|---|---|
| Age | 0.96 (0.86-1.06) | .44 |
| Persistence of mass, mo | 0.89 (0.80-0.98) | .02 |
| Painful on exam | 6.65 (1.16-38.0) | .03 |
| Firm on exam | 2.86 (0.72-11.8) | .13 |
| Size on ultrasound | 1.02 (0.74-1.42) | .90 |
| Absence of fatty hilum | 0.08 (0.01-0.60) | .02 |

Abbreviation: CI, confidence interval.

# Result - Analysis of Surgical Pathology

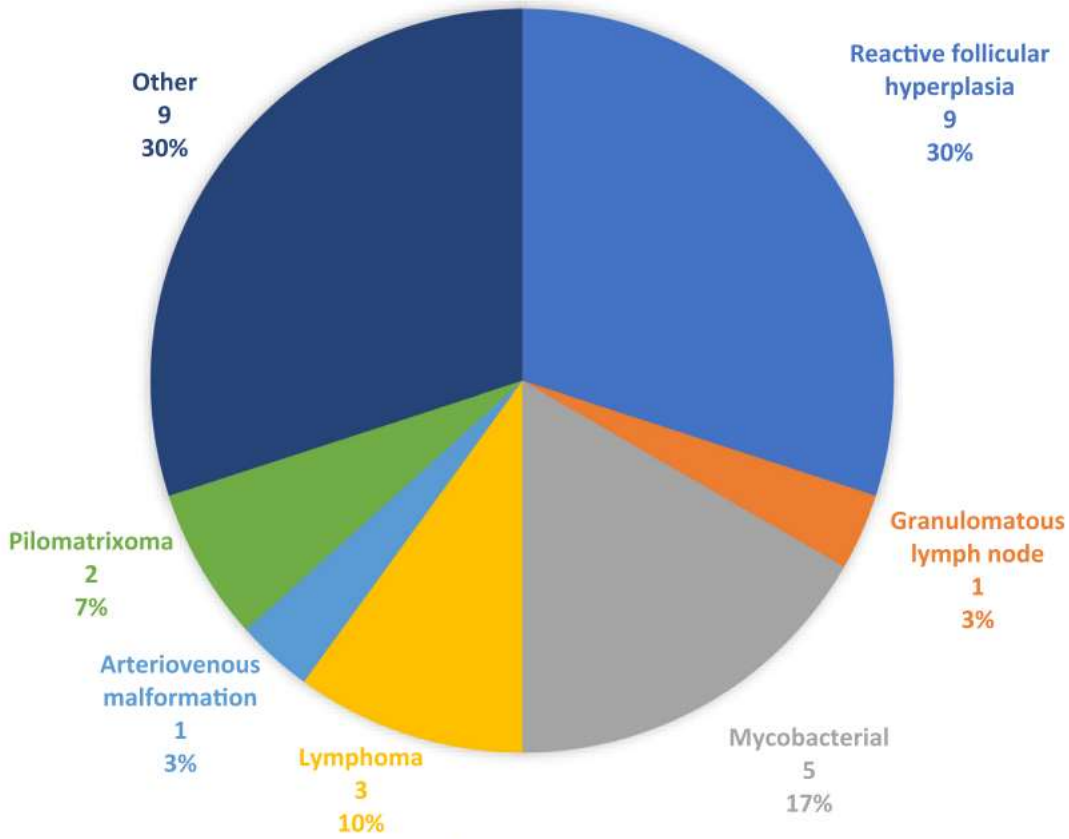



**Figure 2.** Breakdown of neck mass diagnoses after surgical biopsy. Among patients who underwent biopsy (N = 30), 3 patients had a malignant final pathology. The other category includes pilomatrixoma, neurofibroma, epidermoid cyst, calcifying fibrous tumor, and additional diagnoses.

# Discussion

# Discussion

- Those with **larger lymph nodes** identified on clinical exams for a **shorter time period** were more likely to undergo surgical excision
- Among that surgical cohort, some of whom chose to have an excisional biopsy due to anxiety with the watchful waiting approach
- Among surgical cases, only **10% were diagnosed with lymphoma**
- None of the patients who have been followed with minimally invasive surveillance, have developed lymphoma

- PACL **is extremely rarely** the presenting sign of lymphoma
- **Can be followed clinically and by serial ultrasound** as long as the characteristics of firmness, supraclavicular location, or loss of fatty hilum on ultrasound are not identified

# Factors Supporting Conservative Surveillance

- Prospective Cohort Study from Bozlak et al.
  - In a study of 218 children who met inclusion criteria:
    **70 underwent biopsy, malignancy rate was 2.7%**
  - Most malignant cases presented with **high clinical suspicion before** imaging or biopsy.

  → Suggests that in asymptomatic clinical presentations, a surgical biopsy may be deferred
- Serial ultrasounds were performed every ~6 months, with small change in size between the 2 time points (decrease of 0.35 cm)

  → Suggests benign adenopathy can shrink over time, and thus can be followed with minimally invasive surveillance

# Ultrasound Characteristics and Utilization

- Prior studies :
  - the size of the node increases the suspicion of malignancy with greater than 3 cm as raising concern
- Our study:
  - **size alone should not be a determinant** for surgical intervention without other associated concerning features
  - even larger, otherwise asymptomatic **nodes can be monitored, and are likely to shrink with time**

- High-resolution ultrasound imaging
  - More detailed nodal architecture assessment, such as the detection of a fatty hilum
  - Can be utilized as a safe surveillance modality

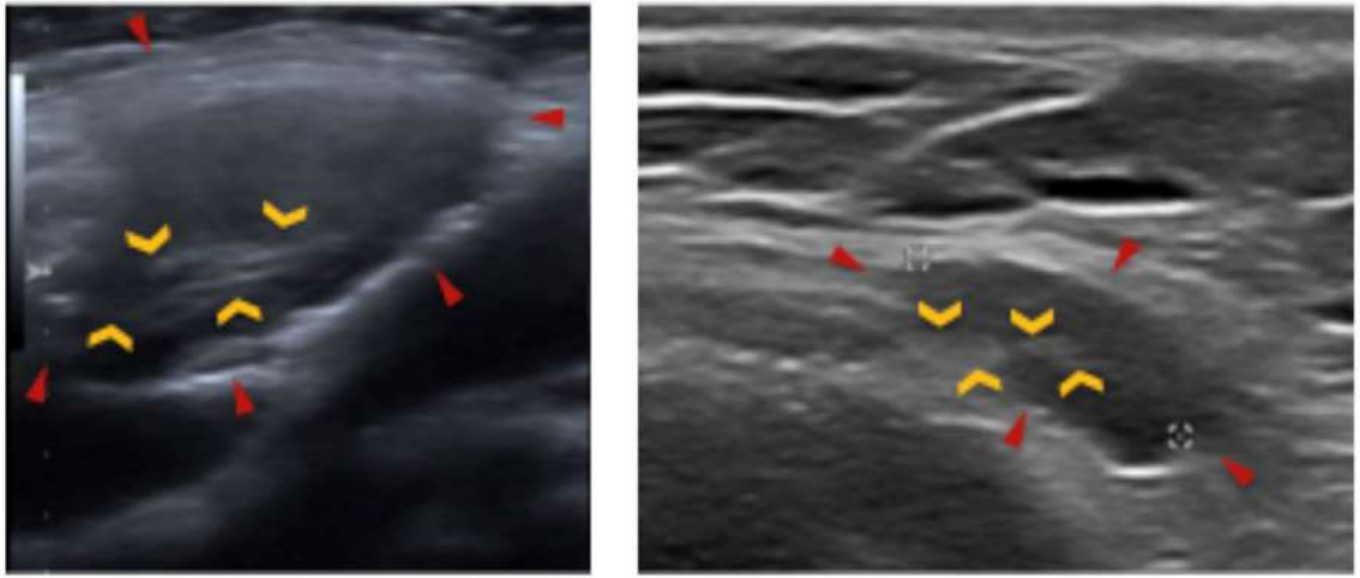


**Figure 3.** Representative fatty hilum on long-axis view. Examples of normal lymph node architecture. Red arrows demonstrate smooth, regular borders. The lymph node substance is homogenous. Yellow arrows mark the presence of normal vascular, fatty hilum on the long-axis view.

- A retrospective cohort study:
  - 50 hospitalized pediatric patients with cervical lymphadenopathy
  - Abnormal ultrasound characteristics (the long to short axis, heterogenous echogenicity, and chaotic vascularity)  may help guide the decision for surgical excision
- Our study
  - High-resolution ultrasonography is a safe and minimally invasive approach for the surveillance of patients with PACL

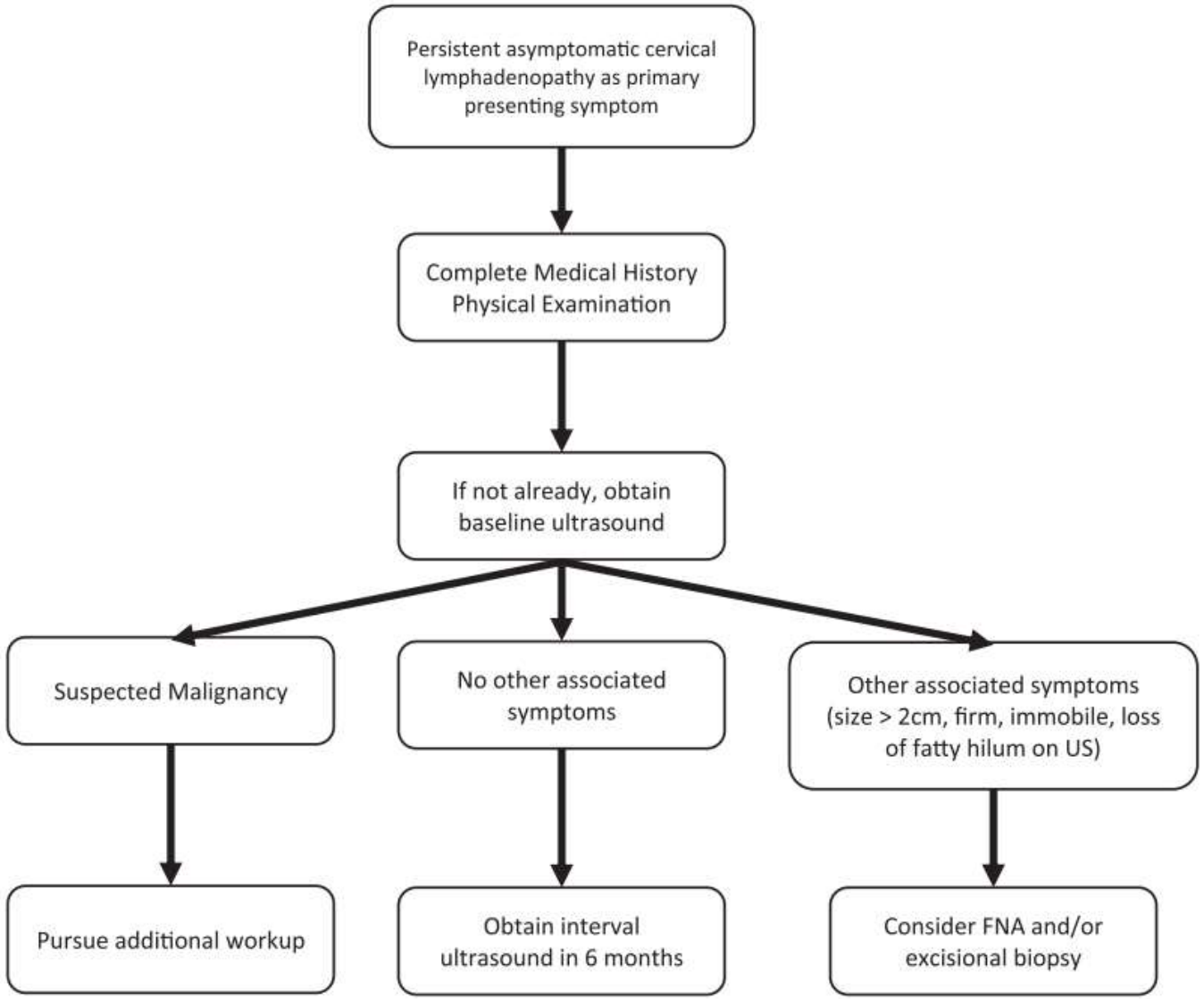



**Figure 4.** Proposed management algorithm for PACL. Flowchart describing our institution's approach to PACL, specifically when to pursue observation versus more invasive intervention. It does not describe an approach to infectious cervical lymphadenopathy or suspected malignancy. FNA, fine needle aspiration; PACL, persistent asymptomatic cervical lymphadenopathy; US, ultrasound.

# Surgical Biopsy

- Prior literature: FNA biopsy as an alternative to open surgical biopsy for pediatric patients
  → A retrospective study: 73% still required sedation or general anesthesia.
  → False negative or inconclusive results can occur, up to 28%
  → Agreement with our study: among the who underwent an FNA, 50% still underwent surgical excision due to nondiagnostic results of the FNA

# Surgical Biopsy

- The most common pathology was **reactive follicular hyperplasia**
- Followed by atypical mycobacterial infection
  →challenging to diagnose with the gold standard being culture obtained during surgical excision
- More patients with **supraclavicular** nodes underwent excisional biopsy
  - The supraclavicular location has been found to have a higher association with **malignancy** than other locations
  - Thus lymph nodes identified in this area are treated with a higher index of suspicion

# Limitations

- Based on retrospective data collection, and thus subject to missing information
- Ultrasound data were collected from the imaging reports, rather than a review of the raw images
- Details of nodal architecture and size were not uniformly reported in earlier patients
- Our study analyzed children referred to a tertiary care institution → Our results may not be generalizable to broader populations
- Sample size still limited → Some clinical or imaging differences may not have been detected

# Conclusion

- For pediatric patients with PACL referred to our institution, the diagnosis of malignancy remains quite rare
- Even for patients with long- standing, palpable cervical lymphadenopathy, minimally invasive surveillance with serial ultrasounds is a safe and reasonable approach
- Only a very small proportion of our patients ultimately underwent excisional biopsy, and this was in large part due to parental preference
- Benefits of This Approach:
  - Reduces risks associated with general anesthesia and surgery.
  - Potentially lowers overall healthcare costs for managing this common pediatric condition.

# Thanks for listening