

# Cervical Lymphadenopathy in Children-A Clinical Approach

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## ABSTRACT

Lymphadenopathy is a disorder of lymph nodes which are abnormal in consistency and size. Cervical lymphadenopathy is a common problem encountered in pediatric clinic and is mostly due to infectious etiology. Since the diagnosis varies from a simple infection to malignancy, this can be a matter of anxiety for both the family as well as the treating doctor. A systemic clinical approach is required to avoid unnecessary investigations. The current article addresses a stepwise approach to diagnosis and management of cervical lymphadenopathy.

**Keyword:** Cervical Lymphadenopathy, pediatric clinic

## INTRODUCTION

Lymph nodes are organs found in the neck, chest, underarm, abdomen, and groin. They play the role of filters for the lymph fluid as it circulates throughout the body. The lymph nodes contain T and B cells along with antigen presenting macrophages which are also called dendritic cells. They form part of the immune system and function to fight disease and infections. Lymphadenopathy is a disease process which involves lymph nodes that are abnormal in consistency and size. Lymphadenitis refers specifically to lymphadenopathies which are caused due to inflammatory processes.<sup>1</sup> Cervical lymphadenopathy is a common problem encountered in pediatric patients and is mostly attributable to infectious etiologies.

In India, a large number of patients with enlarged cervical, axillary or inguinal lymph nodes are seen in the outpatient clinic.<sup>2</sup> Cervical lymphadenopathy is a very common but challenging medical condition for the family as well as the treating physician.<sup>3</sup> Around 90% of children aged 4-8 years old have cervical lymphadenopathy.<sup>4</sup>

### Epidemiology

The exact incidence of lymphadenopathy is unknown, but the number varies from 38-45%.<sup>5</sup> These are usually found by parents and caregivers. Tuberculosis still remains one of the challenging and leading health problems in developing countries, with vast social and massive economic implications.<sup>6</sup> Additionally, high incidence of HIV has led to the resurgence of cervical lymphadenopathy in developed countries.

In India about 1.5% of the population is affected with tuberculosis.<sup>7</sup>

Tuberculous lymphadenitis is a common form of extrapulmonary tuberculosis, approximately 30-40% in reported series.<sup>8</sup>

### Definition<sup>3</sup>

Pathologic Lymph Node	> 2 cm in pediatric patients is considered abnormal <sup>9</sup>
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Acute Lymphadenopathy	< 2 weeks' in duration
Sub -acute Lymphadenopathy	2-6 weeks' in duration
Chronic Lymphadenopathy	> 6 weeks' in duration

### Pathophysiology of Cervical Lymphadenopathy

The pathophysiology differs according to the etiology which maybe infectious or noninfectious.

After an initial insult with infections of upper respiratory tract, teeth or soft tissue of the face or scalp, microorganisms are carried to the draining lymph nodes via afferent lymphatics.<sup>3</sup> The cervical lymphatic system plays a role of defence against the infections that occur in the head and neck region. Once the organisms enter into the lymph nodes, the macrophages and dendritic cells trap, phagocytose, and present the organisms as antigens to T cells. B cells with the help of T cells are activated and release immunoglobulins which help in the immune response. The signs and symptoms are a result of this immune response. Nodal enlargement occurs due to cellular hyperplasia and lymphocyte infiltration. Swelling and erythema occur as a result of dilation of blood vessels. When lymphadenopathy occurs as part of malignant process, the lymph node enlargement is due to malignant or metastatic cells.

### Classification of Cervical Lymphadenopathy Based on Clinical Presentation<sup>10</sup>

1. Acute Unilateral: This is the most common type of cervical lymphadenopathy. This is usually reactive and secondary to upper respiratory tract infection (URTI), skin infection, or dental infection. Other rare causes are Kawasaki, cat scratch disease (Bartonella) and Kikuchi-Fujimoto disease (histolytic necrotising lymphadenitis).
2. Acute Bilateral: This type of lymphadenitis occurs secondary to viral URTI, Epstein-Barr virus (EBV), and cytomegalovirus (CMV).
3. Sub-acute: The common cause for this is *Mycobacterium tuberculosis*.
4. Chronic: This can be reactive in process secondary to neoplasia, lymphoma, leukemia, or soft tissue tumours.

### Infectious Etiologies

#### Acute Viral Lymphadenitis

This is the most common form of reactive lymphadenopathy and typically develops following URTI. The common viruses involved are adenovirus, rhinovirus, Coxsackie virus A

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**How to cite this article:** Sachin Darne, Trusha Rajda. Cervical lymphadenopathy in children-a clinical approach. International Journal of Contemporary Medical Research 2016;3(4):1207-1210.

and B, Epstein-Barr virus, parainfluenza, influenza and cytomegalovirus. Less frequent etiologies are mumps, measles, rubella, varicella, and herpes simplex viruses.<sup>11</sup>

This type of lymphadenopathy is often bilateral, diffuse, and nontender, without warmth or erythema of the overlying skin and often has other signs and symptoms that are consistent with URTI. Viral lymphadenitis resolves spontaneously within a short period of time or may require symptomatic treatment. Specific antiviral therapy is rarely recommended except in immunocompromised patients.

Mononucleosis is commonly caused by Epstein-Barr virus. The clinical features comprise of generalized fever along with lymphadenopathy, pharyngitis and splenomegaly. The blood test is suggestive of lymphocytosis, however, monospot test and serum heterophile antibody are more definitive tests for the diagnosis.<sup>3</sup> The treatment encompasses symptoms' management.

In cases of CMV infection, rashes and hepatosplenomegaly are often seen along with other symptoms.

#### Acute Bacterial Lymphadenitis

*Streptococcus pyogenes* or *Staphylococcus aureus* are the main reasons of acute cervical lymphadenitis in age group of 1-4 years in around 40% to 80% of cases.<sup>11</sup> Cervical adenitis may also occur due to Group B streptococcal infection. Anaerobic bacteria may be the causative agent in older children with dental disease.<sup>12</sup>

The presentation includes fever, sore throat, cough, cold, or earache. Physical examination elucidates pharyngitis, tonsillitis, or otitis media while in case of anaerobic infection, there may be evidence of periodontal disease. Treatment involves initial management with oral or intravenous antibiotics depending on severity of infection. If this does not get resolved then an ultrasound and further fine needle aspiration cytology (FNAC) is advised. Surgical incision and drainage may be required in case an abscess is identified.

#### Subacute Lymphadenitis

This is the type of lymphadenitis which is mostly attributable to infectious etiology and persists for 2-6 weeks' duration. The most common causative agents are *Mycobacterium tuberculosis*, *Atypical mycobacterium*, cat scratch disease, and toxoplasmosis. Sometimes EBV and CMV are also responsible for this type of lymphadenitis. These are explained in detail in subsequent sections.

#### Mycobacterium Tuberculosis

Chronic cervical lymphadenitis may be caused by *Mycobacterium tuberculosis* (scrofula). The patients present with cervical lymph node enlargement mostly the paratracheal or the supraclavicular lymph nodes. Tuberculin test may help in the diagnosis. Tuberculin test may turn out to be positive even in nontuberculous causes but generally are less reactive (<15 mm induration). A history of contact can also be found. Chest radiograph reveals abnormal findings in most cases. The treatment of choice would be multi-agent antituberculous therapy for 12 -18 months. Regression of the enlarged nodes occurs within 2-3 months of starting the therapy.

#### Atypical Mycobacterium

In *Atypical mycobacterium* the species involved are *Mycobacterium avium-intracellulare* and *Mycobacterium scrofulaceum*.

This lymphadenitis may develop over weeks to months. The lymph nodes are tender and rubbery with discoloured skin over the node. The diagnostic test is acid fast stain and culture of material from lymph node. This condition if left untreated may lead to sinus tract and cutaneous drainage for up to 12 months.<sup>3</sup> The treatment of choice is surgical excision of involved lymph nodes and not incision and drainage to avoid sinus formation. This lymphadenitis is different from tuberculous variety where it is more of a disseminated disease.<sup>3</sup> This does not respond to the treatment with antituberculous drugs. Appropriate antibiotic treatment should be started after sensitivity testing.

#### Cat Scratch Disease

This is a lymphocutaneous syndrome caused by bacterial infection with species *Bartonella henselae*, a gram negative rickettsial organism. A small papule may develop at the site of inoculation which may or may not be evident on examination. In 90% of cases who have had exposure to cat bite or scratch, lymphadenitis can take up to 2 weeks to develop. The papule may resolve till the lymphadenitis develops. It presents commonly in younger age group patients with tender lymph nodes associated with fever and malaise. It is diagnosed by serology for antibodies or polymerase chain reaction (PCR). This is usually a self-limiting disease with symptomatic treatment. Antibiotics may be recommended in some cases.<sup>13,14</sup>

#### Toxoplasmosis

Lymphadenitis is the most common clinical form of toxoplasmosis where the causative organism is *Toxoplasma gondii*. The mechanism of illness is usually after consumption of undercooked meat, leading to ingestion of oocytes from cat faeces. The symptoms are malaise, fever, sore throat, and myalgias. Lymphadenitis usually occurs in the head and the neck region and 90% have cervical lymphadenitis. The diagnosis is done by serologic testing. The complications include myocarditis and pneumonitis. The treatment is with pyrimethamine or sulphonamides.

#### Noninfectious Etiologies

##### Kikuchi-Fujimoto Disease

This seemingly benign and rare condition which is also called necrotizing lymphadenitis, is seen to be associated with signs and symptoms of fever, nausea, weight loss, night sweats, arthralgia, and hepatosplenomegaly. The cause is thought to be likely viral or autoimmune etiology. It does spontaneously regress within 6 months and is unresponsive to antibiotics. Some patients are known to have recurrences.

##### Kawasaki Disease

This is a mucocutaneous lymph node syndrome which usually affects children less than 5 years of age. The disease is manifested by vasculitis throughout the body. There are 5 characteristic features associated with this disease:

1. Fever for  $\geq 5$  days
2. Cervical lymphadenopathy
3. Edema, erythema and desquamation of the skin of the palms/soles
4. Bilateral conjunctivitis
5. Inflammation of the lips, mouth and/or tongue

The diagnosis is established if 4/5 features are present. One

of the earliest symptoms is lymphadenopathy which is unilateral, within anterior triangle of the neck, and nonfluctuant. Resolution of cervical lymphadenitis occurs on its own.

### Sarcoidosis

Sarcoidosis is a chronic granulomatous disease of unknown etiology which involves multiple organs. Cervical lymphadenitis is most common manifestation of head and neck involvement. The confirmatory test for diagnosis would be biopsy for histologic examination. Supportive therapy with corticosteroids is currently the treatment of choice.

### Langerhans Cell Histiocytosis

This condition is also called eosinophilic granuloma. It presents as solitary bone, skin, lung, or stomach lesion. The severe form of this condition is associated with life threatening multisystem disorder. The histopathology shows normal lymph node but increased sinusoidal Langerhans cells, macrophages, and eosinophils.<sup>3</sup> The treatment involves systemic steroids. Chemoradiation therapy is also sometimes administered.

### Malignancies

Lymphadenopathy which is persistent for more than 6 six weeks' increases the risk factor of malignancy. Out of the total incidence, around 25% of malignant tumors occur in the head and neck. In these cases, cervical lymphadenopathy is a common finding.<sup>15</sup> Neuroblastoma and leukemia associated with cervical lymphadenopathy are the commonest tumors until 6 years of age, followed by rhabdomyosarcoma and non-Hodgkin's lymphoma.<sup>15</sup> Hodgkin's lymphoma associated with cervical lymphadenopathy is one of the common tumor after 6 years of age, followed by non-Hodgkin's lymphoma and then rhabdomyosarcoma.<sup>15</sup>

A biopsy is done to establish the diagnosis. Depending on the diagnosis, the patient may be referred to oncologist for further management.

### Clinical Approach to Case of Cervical Lymphadenopathy

Currently there is no defined pathway for investigating pediatric patients with lymphadenopathy.<sup>16</sup>

### Proforma for Clinical Examination<sup>3</sup>

#### History

- Fever, anorexia, myalgias, night sweats
- Node is tender or nontender
- Toothache, earache, bone pain
- Bruising, pallor
- Sore throat, URTI symptoms
- Preceding tonsillitis
- Contact with tuberculosis patients
- Medications/Immunizations
- Exposure to animals/cats
- Use of medications like phenytoin or isoniazid
- Recent immunization history with diphtheria-pertussis-tetanus (DPT), poliomyelitis, or typhoid vaccination

#### Examination Findings

- General Appearance: Malnutrition, poor health, febrile, toxic
- Rash, pallor, erythema, edema
- Poor dental hygiene, otitis, pharyngitis
- Lymph node examination for size, mobility, consistency, tenderness

cy, tenderness

- Location of lymphadenitis: Unilateral versus bilateral
- Associated findings of lungs consolidations/hilar lymphadenopathy/TB/hepatosplenomegaly
- Associated inguinal and axillary adenopathy

### Investigations

#### Laboratory

- Complete blood count (CBC)/Urea and Electrolytes/C-reactive protein
- Throat swab/antistreptolysin O titre (ASOT)
- Serology EBV/CMV/Toxoplasmosis/Bartonella based on clinical findings. It is important to rule out immunocompromised state of the patient by doing serology for HIV
- The polymerase chain reaction (PCR) is useful for pathogen identification in pediatric cervical lymphadenitis, although it is less sensitive in identification of mycobacteria.<sup>17</sup>

#### Imaging

- Chest x-ray
- Ultrasonography is an extremely helpful diagnostic tool which helps in differentiation and following the treatment of childhood lymphadenopathy. Failure of regression after 4-6 weeks might be an indication for a diagnostic biopsy
- CT Scan imaging study for retropharyngeal or deep neck abscess, or suspected malignancy
- ECG/ECHO based on clinical findings if Kawasaki is suspected to rule out any complications

#### Invasive

- FNAC should be performed if the enlarged node has not responded to antibiotics and has been present for 2-6 weeks' duration
- Excisional biopsy to be performed if the FNAC results are negative however the clinical findings are strongly suggestive of malignancy

Guidelines for early referral for biopsy especially to rule out malignancy

- a. Lymph nodes are non-tender, firm or hard
- b. Lymph nodes are greater than 2 cm in size
- c. Lymph nodes are progressively enlarging
- d. Other associated features of general ill-health, fever or weight loss
- e. Axillary nodes are involved (in the absence of local infection or dermatitis)
- f. Supraclavicular nodes are involved.
- g. Generalised lymphadenitis
- h. Hepatosplenomegaly

### CONCLUSION

Cervical lymphadenopathy is a common but challenging clinical problem especially in pediatric age group. A thorough history and physical exam are very helpful in determining the cause of lymphadenitis. Cervical lymphadenopathy occurs mostly as part of reactive process from viral and bacterial pathogens. In India, tuberculosis is a prevalent cause of cervical lymphadenopathy which needs antitubercular therapy. Most cases of acute lymphadenopathy are treated

with antibiotics for 1-2 weeks' duration. Further laboratory and radiologic investigations can help identify other important risk factors and conditions associated with cervical lymphadenopathy. In some cases of cervical lymphadenopathy when one suspects abscess formation or if the patient is toxic, the investigation of choice is ultrasound scan. Ultrasound scan is a good option to differentiate reactive from malignant nodes. The lymph nodes can be subjected to FNAC however it has false negative rate of around 45%. Excisional biopsy is gold standard for diagnosis. A stepwise approach along with close followup can lead to right and timely management of this condition.

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**Source of Support:** Nil; **Conflict of Interest:** None

**Submitted:** 08-03-2016; **Published online:** 04-04-2016