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.¹ 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.² Cervical lymphadenopathy is a very common outpatient medical condition for the family as well as the treating physician.³ Around 90% of children aged 4-8 years old have cervical lymphadenopathy.³

Epidemiology
The exact incidence of lymphadenopathy is unknown, but the number varies from 38-45%.⁵ 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.⁶ 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.⁷ Tuberculous lymphadenitis is a common form of extrapulmonary tuberculosis, approximately 30-40% in reported series.⁸

Definition³
Pathologic Lymph Node > 2 cm in pediatric patients is considered abnormal⁹

<table>
<thead>
<tr>
<th>Type of Lymphadenopathy</th>
<th>Duration</th>
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</thead>
<tbody>
<tr>
<td>Acute Lymphadenopathy</td>
<td>&lt; 2 weeks¹⁰ in duration</td>
</tr>
<tr>
<td>Sub-acute Lymphadenopathy</td>
<td>2-6 weeks¹⁰ in duration</td>
</tr>
<tr>
<td>Chronic Lymphadenopathy</td>
<td>&gt; 6 weeks¹⁰ in duration</td>
</tr>
</tbody>
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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.³ 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. 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 Presentation¹⁰
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 Kawasaki-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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The treatment encompasses scrofula. The patients present with cervical adenitis. The treatment of choice is multi-agent 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.

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 ≥ 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. The treatment involves systemic steroids. Chemoradiation therapy is also sometimes administered.

**Malignancies**

Lymphadenopathy which is persistent for more than 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. Neuroblastoma and leukemia associated with cervical lymphadenopathy are the commonest tumors until 6 years of age, followed by rhabdomyosarcoma and non-Hodgkin's lymphoma. 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.

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. Proforma for Clinical Examination

**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, consisten-
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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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