

Evaluation of lymphadenopathy in children

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Abstract

Lymphadenopathy, the presence of abnormal lymph nodes, is a common finding in paediatric practice. This may be the sole presenting feature or one of a constellation of symptoms and signs. The underlying aetiological causes are numerous and diverse, but can broadly be considered to be reactive, infective or malignant in nature. Investigation of these children ranges from observation to detailed radiological imaging and biopsy and is led by pertinent history taking and examination. Significant anxiety can surround the finding of lymphadenopathy in children in both parents and health professionals due to concern regarding sinister underlying pathology. A structured clinical approach to these children utilizing appropriate background knowledge and the multidisciplinary team facilitates diagnosis and guides management. This review aims to provide a useful clinical guide for paediatric trainees to assist in the assessment and management of such children.

Keywords lymph node; lymphadenitis; lymphadenopathy

Introduction

Palpable lymph nodes are a common finding in childhood. They often represent an appropriate response to regional infection, particularly ear and respiratory tract infections in early childhood. However, whilst enlarged lymph nodes are predominantly benign, lymphadenopathy can represent serious underlying disease. Key features from the history and examination should allow differentiation of benign versus potentially malignant pathology. This allows reassurance to be given when appropriate and facilitates subsequent investigation and management where there is diagnostic uncertainty or concern.

Pathogenesis

The lymphatic system, which arises from the mesoderm, has a central role in immunological defence. It is closely approximated anatomically with the cardiovascular system and together they comprise the circulatory system. Lymphatic vessels connect numerous areas of lymph tissue, otherwise known as lymph nodes, which permits the flow of lymph around the body from the lymphatic plexuses in the intercellular spaces ultimately to

the venous system at the thoracic and right lymphatic ducts. Transport of lymph is facilitated by the action of skeletal muscle, peristalsis and intrathoracic pressure variation. Lymphatic vessels drain lymph to common anatomical nodes, therefore a knowledge of lymphatic anatomy can identify the anatomical site of the underlying pathology (Box 1).

The lymphatic system not only comprises lymphatic vasculature as discussed but also includes the lymphatic organs or mucosal associated lymphoid tissue (MALT), which includes the spleen, components of Waldeyer's ring (tonsils and adenoids), ileal Peyer's patches and the thymus. The lymphatic system serves three main functions: transportation of tissue fluid and lymph, absorption and transportation of fat and immune defence. The lymphocyte rich lymph fluid is directed to macrophage-laden follicles inside lymph nodes. Here lymph is filtered so foreign particles including particulate matter and infectious organisms are removed by means of phagocytosis by macrophages and antibodies produced by B-lymphocytes. It is cellular proliferation within a lymph node that results in nodal enlargement. This may either represent an appropriate immune response to an antigenic stimulus, resulting in nodal inflammation from regional infection (reactive lymphadenopathy), infection of the node itself (lymphadenitis), or malignant infiltration. Lymphadenopathy can describe an abnormality of the size, consistency or number of lymph nodes.

Formulating a differential diagnosis

History

A thorough history is essential in formulating likely differential diagnoses and certain key questions are important (Table 1). Elucidation of concerning features is particularly important (Table 2).

The main factors which assist diagnosis include:

- **Age of the child:** certain infections and diseases affect particular age groups more commonly (Table 3). Between the ages of 3 and 5 palpable cervical lymph nodes are particularly common and it has been reported to be present in more than half of such children at any one time, most likely due to the frequent exposure to upper respiratory and ear infections in this age group. Lymph nodes are usually not palpable in the neonate but certain infections can cause lymphadenopathy (including *Staphylococcus aureus* and late onset group B *streptococcus*). Importantly,

Anatomy of regional lymphatic drainage.

- Cervical lymph nodes drain the head and neck lymphatic vessels. Paediatric cervical lymphadenopathy often arises from ENT pathology, particularly infection, in children.
- Submental and submandibular lymph nodes drain lymph from the buccal mucosa, cheek and nose.
- Supraclavicular lymphadenopathy is a sign of pathology in the thorax (if right sided) or the abdomen (if left sided).
- Axillary nodes drain the ipsilateral arm, breast, neck and thorax.
- Inguinal nodes receive lymphatic vessels from the ipsilateral leg, buttock and lower half of the abdominal wall.

Box 1

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Key aspects of the history

When was the lymph node first noticed?

- Anatomical location of node, size, time course of growth, overlying skin changes, tenderness, other nodes involved.
- Have there been any skin rashes or skin lesions/injuries in the nodal basin, particularly including eczema and cellulitis?

Is the child systemically well?

- Any recent regional infections particularly including upper respiratory tract, ear, gum/tooth and skin infections?
- Any concerning features? Tiredness, weight loss, bleeding, bruising, night sweats, fevers. If so consider tuberculosis and malignancy
- Background: is the child growing and developing normally? Consider immunodeficiency if failing to thrive

Any foreign travel?

Any exposure to cats, especially kittens, or other pets or wild animals?

Any exposure to tuberculosis (TB)?

In adolescents if appropriate and inguinal lymphadenopathy present: are they sexually active?

Has the child had any recent immunizations?

Is the child on any medication(s)?

- Generalized lymphadenopathy can be caused by drugs including carbamazepine, phenytoin and isoniazid

Is the child experiencing recurrent or frequent infections suggestive of immunodeficiency?

Maternal, family and social history: assists in identifying and addressing parental concerns and may aid diagnosis

Table 1

congenital abnormalities may simulate an enlarged lymph node (Table 3) but should not be confused as management and prognosis differ. When considering malignant causes of lymphadenopathy it is helpful to recognize the typical ages of presentation of childhood cancers.

- **Time course of lymphadenopathy:** it is important to elucidate if there has been progressive involvement and enlargement of lymph nodes which would point to sinister pathology. In general, benign enlargement of lymph nodes show regression in 4–6 weeks.
- **Associated symptoms:** it is essential to recognize other potentially associated symptoms which may represent bone marrow failure and underlying malignancy or specific infectious or rheumatological diagnoses. ‘B-symptoms’ raise concern of malignancy, particularly lymphoma, and these include fever, night sweats and weight loss.

Examination

- **General observation of the child:** important features include an assessment of how well the child looks and particularly looking for signs of bone marrow failure, including pallor and bruising.
- **Anatomical location of abnormal node(s):** if lymphadenopathy is localized this implies pathology in the area of regional drainage. Whilst palpable cervical lymph nodes are a common and often benign finding within the context

Important features of enlarged lymph nodes and concerning signs

Key features	Concerning features
Onset	Rapid and progressive growth Onset in the neonatal period Associated ‘B-symptoms’, hepatosplenomegaly
Size: measure accurately	≥3 cm in size with firm consistency ≥3 cm node not responsive to treatment after 6 weeks
Anatomical location	Enlarged supraclavicular/posterior cervical node(s)
Mobility	Skin tethering/ulceration
Fixation	Fixed node(s)
Consistency	Firm and rubbery consistency
Tenderness	
Erythema/warmth	

Table 2

of recent infection, supraclavicular lymphadenopathy is concerning and must be investigated. Generalized lymphadenopathy often indicates underlying systemic disease or infection.

- **Size and character of abnormal lymph node(s):** lymph node size is related to the age of the child. Normal lymph nodes typically measure up to 1 cm in diameter in the cervical and axillary regions and up to 1.5 cm in the inguinal region. Benign lymph nodes are typically soft, compressible and mobile. Characteristics of concerning enlarged lymph nodes are listed in Table 2. Tender lymph nodes are typically infected (lymphadenitis), most often by *staphylococcus* or group A *streptococcus*. Surrounding erythema, warmth or fluctuance supports this diagnosis. Importantly however, enlarged malignant lymph nodes may also be painful secondary to intra-nodal haemorrhage.
- **Full general examination** including abdominal examination. Hepato or splenomegaly in the context of lymphadenopathy suggests oncological or specific infective (e.g. EBV) or haematological aetiologies.

Investigation and management

Thorough history and examination guides investigation, although in most children the diagnosis can be reached without further testing. Where the history and examination suggest benign lymphadenopathy, reassurance is the most appropriate management option, ensuring parents are aware of concerning features that should prompt re-evaluation. If there is uncertainty or concern investigations are needed to facilitate diagnosis (see Table 4).

- **Haematological investigations** include a full blood count which can identify signs of malignancy including pancytopenia or lymphocytosis. LDH is a useful marker of haemolysis and malignancy. Raised inflammatory markers such as ESR and CRP indicate infection, although this is non-specific. Serology for specific infectious organisms aids diagnosis where specific organisms are suspected.

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