Lymphadenopathy

Definition / Supporting Information

Lymphadenopathy is defined as any lymph node enlargement. Any palpable lymph node may be described as being enlarged; however, this may not be clinically significant. Enlargement of one or more lymph nodes < 1 cm in diameter, particularly in cervical, occipital, and inguinal regions, is a common finding in healthy children.

Fluctuance and signs of inflammation surrounding a group of enlarged lymph nodes strongly suggest an infectious cause of lymphadenopathy.

Keywords / also known as: enlarged lymph nodes, lymph node enlargement, swollen lymph nodes

Essential History

Ask about:

- Infectious exposures
  - Foreign travel
  - Animals
- Medications
- Weight loss
- Fever
  - If persistent, high fever and without otherwise obvious cause, consider Kawasaki Disease and look for other Kawasaki Disease symptoms (eg, rash (multiform), changes of lips or oral mucosa, conjunctivitis without exudate, erythema and oedema of palms and soles) noting these can appear in series and may not be present at the same time
  - Kawasaki Disease lymphadenopathy is commonly cervical, often just one side
- Night sweats
- Pruritus
- Bone pain
- Symptoms of localised infection
  - Dental abscess
  - Mastoiditis
  - Scalp infection
  - Insect bite
  - Cat scratch
- Pharyngitis

- Symptoms of systemic diseases
- Infectious mononucleosis
  - Fever, sore throat, rash, etc.
- Juvenile idiopathic arthritis
  - Joint pains, joint swellings, fever, rash

'Red Flag' Symptoms and Signs

See recommendations 1.10.9 to 1.10.11 in Referral guidelines for suspected cancer [NICE guideline NG12]

Ask about:

- Weight loss
- Bone pain
- Drenching night sweats

Look for:

- Indications of possible cancer
  - Firm, non-mobile nodes with no obvious inflammation
  - Non-tender nodes
  - Lymph nodes that are greater than 2 cm in size
  - Lymph nodes that are progressively enlarging
  - Involvement of axillary nodes in the absence of local infection or dermatitis
  - Involvement of supraclavicular nodes
  - Hepatomegaly / splenomegaly

Differential Diagnosis / Conditions

- Infection
- Post-immunisation
- Neoplasia
- Histiocytoses
- Systemic inflammatory conditions
- Storage disorders
- Immunology deficiency syndromes
- Medications
  - Phenytoin, carbamazepine

Table 1: Entities Associated with Lymphadenopathy

Infections	Generalised	Cervical	Other Regional
VIRAL			
Respiratory viruses (adenoviruses, picornaviruses, respiratory syncytial virus, parainfluenza, influenza, coronaviruses)		1–3+	
Epstein-Barr virus	2–3+	3+	+
Cytomegalovirus	2+	2+	
Primary human herpes virus type 6		+	2–3+ (postoccipital)
Parvovirus B19	1–2+		2+
Human immunodeficiency virus	2–3+	+	+
Rubella	2+	3+	+
Rubeola	1–2+	3+	
Varicella-zoster	1–2+	+	+
Herpes simplex virus		3+	1–2+ (genital infection)
Human herpesvirus type 8	2–3+	2–3+	+
Hepatitis A	+	2+	
BACTERIAL			
Staphylococcus aureus		3+	2–3+
Streptococcal pyogenes	+	3+	2–3+
Bartonella henselae (cat-scratch disease)	+		2–3+
Bartonella bacilliformis (Oroya fever, verruga peruana)	3+	3+	3+
Yersinia enterocolitica	+		3+
Salmonella typhi	2–3+		2+
Tularemia	+	3+	2+
Brucellosis	2–3+	+	+
Anaerobic infections			
Dental, gingival infections		2–3+	2–3+
Postanginal sepsis		2–3+	
Mycobacteria			
Mycobacterium tuberculosis	+	2–3+	2–3+
Atypical mycobacteria		2–3+	2–3+

Spirochetal			
Syphilis	2–3+	+	+
Lyme disease			+
Leptospirosis	3+	+	+
RICKETTSIA / CHLAMYDIA			
Lymphogranuloma venereum			3+
Ehrlichiosis	2–3+		
Rickettsia tsutsugamushi	3+	2–3+	3+
PROTOZOAN			
Toxoplasmosis	+	3+	+
Malaria	+		
PARASITIC (Toxocara canis, Toxocara cati, Baylisascaris pyocyonis, Trichinella spiralis, filiaris)	1–2+	+	1–2+
Myiasis		+	1–2+
FUNGAL			
Histoplasmosis	1–3+	+	1–2+
Coccidiomycosis	1–3+	+	1–2+
Tinea capitis			2–3+
IMMUNISATIONS			
Viral	+		+
Typhoid	+		+
Bacille Calmette-Guérin			1–3+
NEOPLASTIc			
Leukaemia	1–2+		
Lymphoma	1–3+	2–3+	2–3+
Hodgkin’s disease		2–3+	2–3+
Metastatic, solid tumours (neuroblastoma, Wilms tumour, Ewing sarcoma, rhabdomyosarcoma)	1–2+		1–2+
HISTIOCYTOSES			
Langerhans cell histiocytosis		1–3+	
Malignant histiocytosis		1–2+	1–2+
Sinus histiocytosis (Rosai-Dorfman disease)		3+	

Hemophagocytic syndromes	1–2+	2+	
IMMUNOLOGIC			
Deficiency syndromes	1–2+	1–2+	2–3+
Autoimmune lymphoproliferative syndrome	2–3+		
Serum sickness	2+	+	+
Ommen syndrome	1–2+	+	+
Juvenile rheumatoid arthritis	1–2+	+	+
Atopic disease, eczema	2–3+	2+	2–3+
Castleman disease	1–3+	3+	2–3+
MEDICATIONS (phenytoin and others)	1–2+		
STORAGE DISEASES (Gaucher, Niemann-Pick disease)	2–3+		1–3+
GRANULOCYTE DEFECTS			
Chronic granulomatous disease	+	1–2+	2–3+
Leukocyte adhesion deficiencies		1–3+	1–3+
Chédiak-Higashi anomaly		1–3+	1–3+
OTHER			
Kawasaki disease		2–3+	
Hemoglobinopathic conditions	+	1–2+	
Haemophilia with HIV	2–3+	+	+
Sarcoidosis	2–3+	+	1–2+
Gianotti-Crosti syndrome	3+	+	+
Necrotising lymphadenitis (Kikuchi lymphadenitis, Fujimoto necrotizing lymphadenitis)	+	2–3+	2–3+
Insect bites		+	+
Kimura		2–3+	1–2+
Addison disease	1–2+		
Hyperthyroidism	1–3+		

Investigations

To be undertaken by non-specialist practitioners (eg, General Practitioner (GP) Team) or by specialist practitioners (eg, Emergency Department / Paediatric / Paediatric Infectious Disease / Paediatric Haematology / Oncology Team(s)):

- Full blood count

- Acute phase reactants
  - C-reactive protein
  - Erythrocyte sedimentation rate
- Glandular fever screening tests
- Swabs, if appropriate
- Liver function tests

To be undertaken by specialist practitioners (eg, Emergency Department / Paediatric / Paediatric Infectious Disease / Paediatric Haematology / Oncology Team(s)):

- Imaging
  - Chest X-ray
  - Consider ultrasonography, CT, magnetic resonance imaging (MRI), nucleotide, or positron emission tomographic scanning
- Biopsy
  - For significantly enlarged, unexplained adenopathy
    - If no evidence of infection or other cause exists
    - If mediastinal or hilar nodes are enlarged
  - For suspicion of tuberculosis
    - Needle aspiration should be avoided to prevent spread of infection and creating a track.
    - Excisional biopsy is required.
      - Even in the absence of mediastinal or hilar adenopathy
- Precise diagnosis may require:
  - Immunophenotyping
  - Cytogenetic analysis
  - Molecular studies of gene rearrangement
  - Electron microscopy

Treatment Approach

To be undertaken by non-specialist practitioners (eg, GP Team) or by specialist practitioners (eg, Emergency Department / Paediatric / Paediatric Infectious Disease / Paediatric Haematology / Oncology Team(s)):

- Lymphadenitis
  - Therapy dependent on most likely cause
- Infection with group A β-haemolytic streptococci or *Staphylococcus aureus*
  - Antibiotics directed at group A streptococci and penicillinase-producing strains of *S. aureus* eg, phenoxymethylpenicillin, co-amoxiclav
    - For children beyond the neonatal period who have acute localised adenitis, particularly cervical adenitis

  - Oral therapy (adequate for most patients)
    - Typical length of treatment is 10–14 days.
    - Treatment should be continued for ≥ 5 days after signs of acute inflammation have subsided.
- Other infections
  - Therapy dependent on location of adenitis and type of organism
  - Penicillin
    - Most anaerobic infections of the cervical and submental areas are associated with mouth flora, and most are sensitive to penicillin.
  - Alternative therapy
    - Clindamycin
    - Co-amoxiclav
    - Metronidazole
    - Some cephalosporins

To be undertaken by specialist practitioners (eg, Emergency Department / Paediatric / Paediatric Infectious Disease / Paediatric Surgery / Paediatric Haematology / Oncology Team(s)):

- Infection with group A β-haemolytic streptococci or *S. aureus*
  - For patients who have suppurative adenitis, drainage is not only diagnostic (by culturing the exudate) but also therapeutic.
  - Parenteral antibiotic therapy is required in patients who do not respond to oral therapy.
    - Even with a drug to which the organism is sensitive
- *Mycobacterium tuberculosis* and atypical mycobacteria (may be difficult to differentiate)
  - Await culture and sensitivity results before starting anti-tubercular treatment.
    - Many strains of atypical mycobacteria are resistant to the usual antitubercular chemotherapy.
    - Adenitis that is thought to be tubercular should not be incised or drained.
    - Excisional biopsy may be required.
- Cat-scratch disease (Bartonella species, especially *B. henselae*) (usually self-limited)
  - Some antibiotics, alone or combined, may be of clinical benefit.
    - Azithromycin
    - Erythromycin
    - Rifampicin
    - Co-trimoxazole
    - Parenteral aminoglycosides

  - For markedly enlarged, tender, and fluctuant nodes:
    - Aspiration may help to relieve symptoms.
    - Incision and drainage should be avoided.
- Severe primary herpes simplex virus infection with localised adenitis (unusual)
  - Treatment with oral aciclovir to shorten the clinical course

When to Refer

Refer urgently to specialist practitioners (eg, Emergency Department / Paediatric / Paediatric Infectious Disease / Paediatric Surgery / Paediatric Haematology / Oncology Team(s)) if:

- History and physical examination do not suggest an infectious cause
- Potentially infectious nodes have not responded to a course of antibiotics
- Supraclavicular, mediastinal, or hilar adenopathy
- Biopsy is considered

'Safety Netting' Advice

Advise parents / carers to seek medical advice if:

- Potentially infectious nodes have not responded to a course of antibiotics
- 'Red flag' symptoms develop

Patient / Carer Information

Please note: whilst these resources have been developed to a high standard they may not be specific to children.

- Swollen glands (Web page), the NHS website
- Generalised lymphadenopathy (Web page), Patient

Resources

National Clinical Guidance

Suspected cancer: recognition and referral (Web page), NICE clinical guideline NG12, National Institute for Health and Care Excellence

Suggested Resources

Please note: these resources include links to external websites. These resources may not have national accreditation and therefore PCO UK cannot guarantee the accuracy of the content.

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