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Review Article

When does an enlarged cervical lymph node in a child need excision? A systematic review

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ABSTRACT

Background: Palpable cervical lymphadenopathy is very common in children. The clinician's job is to exclude malignancy as a cause and reach a diagnosis. In children selected for open biopsy, reactive hyperplasia and other inflammatory causes are far more common as a final diagnosis than malignancy. Furthermore complications can occur after open biopsy.
Objective: To assess the diagnostic utility of clinical examination and investigations to exclude malignancy and other serious causes of paediatric cervical lymphadenopathy and minimise open biopsy.
Type of review: A systematic review of the literature with defined search strategy.
Search strategy: A structured search of Medline, Embase, CINAHL and Cochrane databases. The references within standard paediatric ENT and head and neck textbooks were also examined.
Results: The quality of evidence regarding predictors of malignancy is poor. Large lymph nodes and supraclavicular nodes are potential indicators of serious pathology. Fever, weight loss and organomegaly may be indicators but duration of symptoms and consistency are not. Abnormalities on chest X-ray are associated with serious causes but the diagnostic utility of routine chest X-ray is unknown. Ultrasound assessment of nodal architecture, margins, and shape (and possibly vascularity) shows considerable promise as a means of differentiating reactive hyperplasia from malignancy but further studies in children are required. Abnormalities in the full blood count (FBC) seem to be uncommon but when present are associated with serious causes of cervical lymphadenopathy, again the diagnostic utility is unclear. Serological testing may identify a specific cause and therefore avoid excision biopsy in around 10% of cases. Cutting needle biopsy requires further evaluation before it can be recommended. Fine needle aspiration cytology (FNAC) is very specific, but sensitivity varies in different studies to the extent that it cannot yet be relied upon to exclude malignancy.
Conclusions: Large and supraclavicular nodes should be biopsied. Ultrasound is likely to be useful but further study is required. FNAC cannot be relied upon to exclude malignancy in children. The diagnostic utility of chest X-ray and FBC are unclear. Work is required on multivariate predictive models.

Contents

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1. Introduction

The purpose of this systematic review is to identify the evidence for a management strategy for children up to 16 years of age who have been referred to hospital for investigation of one or more enlarged cervical lymph nodes where the likeliest diagnosis on clinical grounds is a reactive process but more serious causes need to be excluded. The interpretation is based on practice in a general paediatric ENT clinic in the United Kingdom.

Cervical lymphadenopathy is a common reason for referral to hospital and the commonest cause is reactive lymphadenopathy [1]. Only a small proportion will have serious pathology that requires treatment, such as malignancy [2]. Lymphoma is the third commonest childhood malignancy after leukaemia and central nervous system tumours, however it is the commonest malignancy of the head and neck [3,4]. The definitive way of confirming the diagnosis is excision biopsy therefore it is the gold standard. Unfortunately this has an associated morbidity (scar, bleeding, infection, possible accessory, hypoglossal or marginal mandibular nerve injury, risks of a general anaesthetic and the inconvenience of a hospital stay. It would be preferable to distinguish those children who are likely to have serious pathology and who require biopsy from those who have reactive hyperplasia and can be treated expectantly.

The questions that we wish to answer are:

- How common is cervical lymphadenopathy in children?
- How likely is serious pathology in children presenting with cervical lymphadenopathy?
- Can serious pathology be excluded on clinical grounds, serology, ultrasound, fine needle aspiration cytology (FNAC), core needle biopsy or with multivariate predictive models?

The clinical issue which we are addressing (cervical lymphadenopathy) is very different from the following clinical diagnoses which are managed differently and will therefore not be considered in our review:

1. Acute lymphadenitis, abscess formation or deep neck abscess (parapharyngeal, retropharyngeal)
2. Atypical mycobacterial infection
3. Large, rapidly growing neck mass which is highly suspicious of a tumour
4. Congenital lesions including vascular malformations and fibromatosis colli
5. Thyroid and salivary tumours, which most Otolaryngologists would feel comfortable distinguishing on clinical grounds (history and examination) from lymphadenopathy.

2. Method

A systematic review of the literature was performed. Textwords used in the searches were:

- Child, children, childhood, infant, infancy, paediatric, pediatric
- Neck, cervical
- Lump, node, swelling, mass, lymphadenopathy

Randomised controlled trials are often not helpful in addressing this type of question which is related to the diagnostic utility of investigations rather than the results of therapy. To identify systematic reviews we performed a comprehensive textword and subject heading search of the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effectiveness, and the American College of Physicians Journal Club from their inception date (1991) to the present day. We performed a comprehensive textword and subject heading search of Embase (1980-present), Pre-Medline, Medline and Medline-in-Process (1950-present) using Ovid (search date August 2012). A separate Pubmed search was not conducted as the studies should all be accessible via a Medline. We also identified references from the bibliographies of review articles and the relevant chapters in major textbooks of paediatric otolaryngology [5–8].

All the article titles and abstracts were examined independently by 2 of the authors to select papers for further study. Articles thought to be of interest were then obtained. Articles for inclusion were agreed upon by all authors.

In order to compare investigations a defined gold standard was required. The use of histology in all is not possible therefore we accept clinical follow up for 1 year as an alternative option for those not undergoing surgery. We consider a serious pathology to be a positive result, including:

- Lymphoma or other malignancy
- Non-malignant conditions that are serious and which require treatment (such as Langerhans cell histocytosis and tuberculosis)

Studies with acute infective pathologies, atypical mycobacterium, rapidly growing lesions, congenital, salivary gland and thyroid cases were excluded. Studies not principally concerned with cervical lymphadenopathy were also excluded.

We examined over 1700 article titles to identify approximately 250 abstracts of interest. From these the full text of 89 papers were selected and obtained of which 51 were relevant to the question and included. Papers in languages other than English were obtained and translated and no articles were excluded on language grounds. Unfortunately, we could not identify any individual researchers as having a specific interest to contact in order to request any unpublished data. Manual searching of the conference abstracts from The American Society for Pediatric Otolaryngology, The European Society for Pediatric Otolaryngology and the British Society for Paediatric Otolaryngology 2000–2012 yielded 1 additional publication. The studies were graded according to the Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence [9].

3. Results

Overall, the quality of studies was poor (Table 1). We found that few met the minimum standard for reporting. However, we felt that there was enough data to enable us to draw some limited conclusions as detailed below.

3.1. How common is cervical lymphadenopathy in children?

It is said that total mass of lymphoid tissue increases during development and is twice that of an adult at puberty [10]. Lymphadenopathy would appear to be common in apparently healthy children. Bamji et al. found in 548 children from birth to 1 year of age, examined on maternity ward or at routine health checks, palpable lymph nodes in the neck in 17% up to 4 weeks of age, 27% aged 1–6 months and 55% aged 6–12 months [11]. Herzog