



Diagnostic biopsy of lymph nodes of the neck, axilla and groin: rhyme, reason or chance?

JAMES W MOOR¹, PATRICK MURRAY¹, JANE INWOOD¹, DAVID GOULDESBOUGH², CHRIS BEM¹

Departments of ¹Otorhinolaryngology Head and Neck Surgery and ²Histopathology, Bradford Royal Infirmary, Bradford, UK

ABSTRACT

INTRODUCTION Improving patient pathways of care is becoming increasingly important in the delivery of timely, appropriate surgical care. With this aim, we analysed the referral and management pathway of patients undergoing diagnostic superficial lymph node biopsy.

PATIENTS AND METHODS A retrospective review of case notes of patients undergoing diagnostic superficial lymph node biopsy over 3 years, 1998–2000 at the Bradford Hospitals NHS Trust. Indication for surgical biopsy was based on clinical suspicion following assessment in the out-patient clinic for the majority, and arrangement of investigations as deemed appropriate. There were no clinical algorithms in use during the study period.

RESULTS There was no evidence for the use of explicit protocols for referral or management. Biopsy was often delayed. Of 268 patients referred from primary care, referral was made to any of 14 hospital departments with 39% (105 of 268) attending more than one outpatient appointment, and 155 (41 of 268) attending more than one department. Eighteen percent (47 of 268) of patients were informed of their diagnosis within 6 weeks of referral and 42% (113 of 268) within 3 months of referral. Nine percent (24 of 268) underwent pre-operative fine needle aspiration cytology. Of patients with enlarged neck nodes, 29% (52/180) had examination of the upper aero-digestive tract.

CONCLUSIONS The study supports the introduction of co-ordinated problem-based referral and management pathways for the management of patients with enlarged superficial lymph nodes supported by regular audits of practice.

KEYWORDS

Lymph nodes – Diagnosis – Patient-centred care

CORRESPONDENCE TO

James Moor, Department of Otorhinolaryngology Head and Neck Surgery, Bradford Royal Infirmary, Duckworth Lane, Bradford BD9 6RJ, UK
M: +44 (0)7973 686926; F:+44 (0)7973 686926; E: jim@docmoor.freereserve.co.uk

Patients with enlarged superficial lymph nodes sometimes require surgical biopsy for diagnosis, and there have been many case series describing the pathology found at biopsy.^{1–11} Not all patients with palpable lymph nodes require biopsy, and the finding of benign disease requiring no further treatment is common.^{5,12,15} This has stimulated the development of clinical algorithms to assist the decision to carry out an open surgical biopsy,^{14–16} though these have not found general application, perhaps because patients may be referred to any one of a large number of specialist clinics. Awareness that patients, with enlarged superficial lymph nodes, are not being managed in a coherent manner in the UK has stimulated a call for the rationalisation of the referral and management of these patients.^{17–20} There have also been reports on the value of generic neck lump clinics.^{21–25} The scale and nature of the problem of referral

and management of patients with enlarged superficial lymph nodes, both those in the neck or elsewhere, has however not been closely investigated. We, therefore, examined the records of all patients who underwent superficial lymph node biopsy in our hospital over a 3-year period in order to characterise: (i) the patterns of referral from primary to secondary care; and (ii) the patient's pathway of care from the time of referral to being informed of a diagnosis.

Patients and Methods

The database of the Department of Histopathology for Bradford Hospitals was searched for details of patients whose diagnosis had been made by examination of lymphoid tissue received between 1 January 1998 and 31

December 2000. The clinical records of these patients were reviewed. Those patients who had undergone either excision of mediastinal or retroperitoneal nodes, or lymphadenectomy as radical treatment for carcinoma were excluded. Inclusion criteria were open excision or incision biopsy of lymphoid tissue from any superficial site. Data collected included dates of referral, out-patient clinics and surgery and investigations, which form the material for the present paper. Patients were analysed according to the following groups: adult cervical, adult axillary, adult groin and children (defined as those less than 16 years of age).

Results

There were 342 patients (308 adults and 34 children) who underwent diagnostic lymph node biopsy during 1998–2000, with 67% (228 of 342) classified as 'white' of UK origin and 30% (101 of 342) of Asian origin. The distribution of the site of biopsy (adults and children included) was cervical 63% (216 of 342), inguinal 22% (76 of 342) and axillary 17% (50 of 342). Overall, 34% (117 of 342) of biopsies showed malignant disease, either lymphoreticular (19%; 64 of 342) or metastatic (15%; 53 of 342), and 15% (52 of 342) tuberculous lymphadenitis. Forty-five percent (153 of 342) showed benign, non-specific, self-limiting disease (Table 1).

Of the 342 patients undergoing lymph node biopsy, 268 (78%) were referred from primary care, the remainder attending secondary care for follow-up of existing or previous disease.

Of those 268 patients referred from primary care, referral was made to any of 14 departments (12 for cervical nodes, 5 for axillary nodes, 8 for groin nodes and 6 for children), though most patients were referred to surgical spe-

cialities (203 of 268; 76%) and most of these to general surgery (158 of 268; 59%) or to the ear, nose and throat (ENT) department (33 of 268; 12%). Referral was initially made to non-surgical specialties in 24% cases (65 of 268) predominantly respiratory medicine 9% (25 of 268), general medicine 6% (15 of 268), and haematology 6% (15 of 268). Other departments receiving referrals were elderly medicine (5), thoracic surgery (4), maxillofacial surgery (4), dermatology (2), plastic surgery (2), paediatrics (2), rheumatology (1), obstetrics and gynaecology (1) and urology (1).

Arrangements for biopsy were made at the initial visit for 58% patients (156 of 268); this included 20 patients attending medical clinics and listed directly onto theatre lists for surgery (by ENT 13 of 20; general surgery 6 of 20, and thoracic surgery 1 of 20) and seven patients admitted directly from clinic for investigations. Thirty-nine percent of patients (105 of 268) attended more than one out-patient appointment prior to biopsy, 25% (68 of 268) attended out-patient appointments twice, and 14% (37 of 268) more than twice (no data on 7 patients). Of those attending more than one out-patient appointment, 39% (41 of 105) were referred on to a different department – 5 from a surgical to medical department, 7 between two different surgical departments (usually from general surgery to ENT), 28 from a medical to surgical department and 1 patient referred between two medical departments. Five of the 154 patients with cervical nodes attended three or more departments prior to biopsy. Of patients (adults and children) with enlarged neck nodes, 29% (52 of 180) were seen in the ENT department and underwent examination of the upper aerodigestive tract.

Eight departments carried out diagnostic lymph node biopsies. The majority were carried out by general surgery 71% (190 of 268) and ENT 21% (57/268). The other six

Table 1 Histology of lymph node biopsies in Bradford 1998–2000

	Adult cervical	Adult axillary	Adult Inguinal	Children all sites	All cases
Lymphoma	30 (16%)	12 (25%)	20 (27%)	2 (6%)	64 (19%)
Metastatic lymphadenopathy	35 (19%)	7 (15%)	11 (15%)	–	53 (15%)
Tuberculous lymphadenitis	45 (24%)	4 (8%)	1 (1%)	2 (6%)	52 (15%)
Specific non-tuberculous lymphadenitis ^a	14 (8%)	1 (2%)	1 (1%)	4 (12%)	20 (6%)
Non-specific lymphadenopathy ^b	61 (33%)	24 (50%)	42 (56%)	26 (76%)	153 (45%)
Total	185 (100%)	48 (100%)	75 (100%)	34 (100%)	342 (100%)

^aAdult nodes, cervical – Kikuchi's disease 5, sarcoidosis 4, toxoplasmosis 2, SLE lymphadenopathy 1, foreign body reaction 1, abscess 1; axillary nodes – sarcoidosis 1; inguinal nodes – infectious mononucleosis 1. Children's nodes – cat scratch disease 2, granulomatous inflammation (non-diagnostic) 1, toxoplasmosis 1.

^bNon-specific lymphadenopathy defined as non-specific follicular hyperplasia indicative of reactive hyperplasia or dermatopathic lymphadenopathy with no distinguishing histological feature.

departments involved were thoracic surgery 13 (5%), plastic surgery 3 (1%), maxillofacial 2, paediatric surgery 1, urology 1, and obstetrics and gynaecology 1.

Waiting times for first out-patient appoint and biopsy varied enormously, and only 18% (47 of 268) were informed of their diagnosis within 6 weeks of referral and 42% (113 of 268) within 3 months of referral. Patients on average waited 154 days from referral to being informed of their diagnosis (median time, 90 days; 75% range, 49–160 days), though those diagnosed with malignancy and tuberculous lymphadenitis has shorter waiting times on average (malignancy: mean, 65 days; median, 47 days; 75% range, 28–78 days; tuberculous lymphadenitis: mean, 115 days; median, 79 days; 75% range, 51–108 days). There was some limited evidence of accuracy in the referring clinician's clinical diagnostic acumen in that of 15 referrals to the haematology department, 10 showed lymphoma on biopsy and of 25 referrals to respiratory medicine (who supervise antituberculous therapy), 11 showed tuberculous lymphadenitis and 5 primary lung cancer. Overall, only 18% (10 of 55) of patients with lymphoma were referred initially to haematology and only 23% (11/47) of patients with tuberculous lymphadenitis were referred initially to respiratory medicine.

There did not appear to be any systematic procedure for evaluation of patients, and fine needle aspiration cytology

was used infrequently (Table 2). Overall, 33% (88 of 268) patients had no investigations carried out prior to biopsy.

Sixty-seven patients were already under review by secondary care at the time of their lymph node biopsy, of whom 54% (36 of 67) were under review for previous malignant disease with histology showing further malignancy in 26, of whom 4 had a new primary malignancy diagnosed. Among the remaining 31 patients with previous benign disease, histology showed a new metastatic disease in 4, lymphoma in 3 and tuberculous lymphadenitis in 5. If under a surgical department (58 patients), biopsy was carried out in a median time of 30 days (75% range, 15–56 days). If under a medical department (9 patients), biopsy was carried out in a median time of 31 days (75% range, 26–102 days).

Seven patients underwent 'opportunistic' lymph node biopsy of the groin at the time of varicose vein surgery (6 patients) or herniorrhaphy (1 patient) all of which showed non-specific lymphadenopathy.

Discussion

The study shows that, at Bradford during the period 1998–2000, there appeared to be little rhyme or reason in either the referral pattern or hospital management of patients undergoing diagnostic lymph node biopsy. Patients might attend one of a large number of departments. There appeared to be no systematic use of preliminary investigations. In particular, fine needle aspiration cytology was not routine and a minority of patients with cervical lymphadenopathy had examination by nasopharyngolaryngoscopy of the upper aerodigestive tract in the ENT department. Patients often waited a long time for biopsy and diagnosis. A significant proportion of patients, especially children, underwent biopsy showing non-specific lymphadenopathy or specific non-tuberculous lymphadenitis not requiring treatment.

Recent papers have shown the benefits of a dedicated neck lump clinic^{21–25} and found that neck nodes represented the commonest single reason for referral. Nodes accounted for 46 of 100 consecutive neck lumps in one study²⁵ and 45 of 110 in a second study,²⁶ but neither paper presented the context of pre-existing care in the absence of such a service. This was the subject of our study. We also addressed the management of patients with enlarged axillary and groin nodes. Our study, therefore, offers a unique analysis of the pathway of care for patients referred with superficial lymph node enlargement of the neck, axilla and groin who ultimately undergo open biopsy. It adds evidence to those authorities calling for the rationalisation of the referral and management of patients with lumps and bumps, particularly those with enlarged superficial nodes.^{17–20}

From our study, it would appear that the need to rationalise services was greatest for neck nodes, which showed the greatest variation in referral and management. Whilst

Table 2 Investigations into the cause of lymphadenopathy carried out prior to lymph node biopsy (patients referred from primary care)

Number of patients	Adults			Children All sites
	Cervical	Axillary	Groin	
Chest X-ray	77	16	15	14
Ultrasound examination	21	5	8	3
CT scan	27	6	8	–
MRI scan	1	–	–	–
Other X-rays/scans ^a	9	8	2	1
Other investigations ^b	10	2	6	–
Blood tests	48	7	8	10
Fine needle aspiration	21	–	1	2

^aCervical nodes – mammography 2, contrast swallow 1, contrast enema 1, sinus X-ray 1, bone scan 1, sialogram 1, venography 1, carotid angiography 1. Axillary nodes – mammography 6, X-ray lumbar spine 1, X-ray shoulder 1. Groin nodes – abdominal X-ray 1, arteriography 1. Children – OPG 1.

^bCervical nodes – bone marrow aspiration 4, OGD 2, Heaf test 2, punch biopsy 1, spirometry 1. Axillary nodes – bone marrow aspiration 2. Groin nodes – bone marrow aspiration 3, core biopsy 1, flexible oesophagogastrroduodenoscopy 1, colonoscopy 1.

most patients in Bradford were referred initially to general surgeons (51%) and only 17% to the ENT department, there are good reasons to suggest that patients with suspected neck lumps should be referred first to ENT as examination of the ear, nose, throat and larynx is important to exclude causes of reactive lymphadenitis (secondary to ENT infection) and primary upper aerodigestive tract malignancy.^{18,26,27} This is particularly true where the ENT service is part of a comprehensive Department of Head and Neck Surgery that includes maxillo-facial, plastic and thyroid surgery. With patients undergoing axillary and inguinal lymph node biopsy, where there was greater cohesion in referral and management, one in five patients still attended multiple departments prior to biopsy.

The study, therefore, confirms the need for clearly recognised diagnostic pathways from primary to secondary care and supports the concept of development of clinics organised around commonly presenting clinical problems served by multidisciplinary teams rather than the traditional model of clinics organised around specialist disciplines.

Specialist clinics, such as neck lump clinics, offer many advantages to patients, including clear referral pathways, rapid management by experienced multidisciplinary teams, facilitation of audit, implementation of protocols and concentration of resources. With increasing concentration of problem-specific clinics, the development of immediate on-site diagnostic facilities such as ultrasound scanning, fine needle aspiration cytology, out-patient laryngopharyngoscopy becomes efficient and cost-effective such that finally the clinic can become a one-stop diagnostic service for patients.²¹⁻²⁵ Clear pathways for onward referral once a diagnosis has been made further minimises delays in treatment. Rapid diagnosis clinics could also allow efficient integration of fast-track referrals with minimum disruption and greatest efficiency into clinic schedules.

The study also found that 45% of all lymph node biopsies showed non-specific lymphadenopathy not requiring further treatment. This raises the question whether this diagnosis could have been made on other, non-surgical grounds, such as clinical judgement, cytological analysis³⁰⁻³³ or by ultrasound scanning which is becoming an increasingly sophisticated and accurate diagnostic tool.³⁴⁻³⁷ The negative biopsy rate was particularly high amongst children (30 of 34; 85%), a group on whom unnecessary or inappropriate surgery should particularly be avoided. The study suggests that there is a case for each histopathology department to review periodically the rates for diagnosis of non-specific lymphadenopathy and for surgeons to review individual cases to confirm that there was a clear suspicion of risk of pathology. Small lymph nodes are frequently palpable in health in the jugulodigastric area in adults and additionally in the posterior neck in young children.^{58,59}

There have been attempts to develop protocols for management of enlarged superficial nodes¹⁴⁻¹⁶ but frequently

the most important diagnostic tool is examination by an experienced clinician since suspicion of pathology is multifactorial and determined by size, form, consistency, site, associated symptoms and signs, and risk factors for disease. Following history taking and close examination of the area of nodal drainage and of other lymph node sites, performed by a clinician knowledgeable of locoregional disease processes, any suspicious node is subjected to fine needle aspiration cytology.⁵⁰⁻⁵³ A normal full blood count excludes those patients with chronic lymphatic leukaemia presenting with lymphadenopathy. In the younger adult with neck nodes, screening for infectious mononucleosis, cat scratch disease and toxoplasmosis helps exclude these diseases that clinically can mimic a lymphoma.⁴⁰ Where there is clinical doubt as to the significance of a lymph node, ultrasound scanning is becoming a valuable screening tool.³⁴⁻³⁷ Cytology has high sensitivity for detecting metastatic nodal disease,⁵⁰⁻⁵³ though it is less useful for lymphomas and tuberculous lymphadenitis, where surgical biopsy is usually necessary to confirm the diagnosis, and additionally to identify the subtype of lymphoma or to provide material for culture and sensitivity for tuberculous lymphadenitis.

Our study is historical but may still represent the level of care within many hospitals in Britain even today. Even in Bradford, where a neck lump clinic was opened in 2003, early analysis for the three year period 2003-2005 shows no reduction in lymph node biopsies (349) although with fewer children (7%; 25 of 349) than before. Of 192 cervical lymph node biopsies, 69% (132 of 192) were performed by ENT surgeons and 69% of these (91 of 132) had been seen in the neck lump clinic.

Conclusions

This study shows the lack of a cohesive approach to the investigation and diagnosis of superficial lymphadenopathy in Bradford hospitals during the study period. The data lends support to the call for co-ordinated referral pathways for this group of patients to reduce the time taken to achieve a diagnosis and initiate treatment. The development of clinical algorithms, closer working practices of inter-departmental teams with improved lines of communication between primary and secondary care with regular prospective audit are recommended.

References

1. Karadeniz C, Oguz A, Ezer U, Oztürk G, Dursun A. The etiology of peripheral lymphadenopathy in children. *Pediatr Hematol Oncol* 1999; **16**: 525-31.
2. Friedig EE, McClure SP, Wilson WR, Banks PR, Washington JA. Clinico-histologic-microbiologic analysis of 419 lymph node biopsy specimens. *Rev Infect Dis* 1986; **8**: 322-8.
3. Doberneck RC. The diagnostic yield of lymph node biopsy. *Arch Surg* 1983; **118**: 1203-4.

4. Anthony PR, Knowles SS. Lymphadenopathy as a primary presenting sign: a clinico-pathological study of 228 cases. *Br J Surg* 1983; **70**: 412–4.
5. Lee YTN, Terry R, Lukes RJ. Biopsy of peripheral lymph nodes. *Am Surg* 1982; **48**: 536–9.
6. Lee YTN, Terry R, Lukes RJ. Lymph node biopsy for diagnosis: a statistical study. *J Surg Oncol* 1980; **14**: 53–60.
7. Lake AM, Oski FA. Peripheral lymphadenopathy in childhood. Ten years experience in excisional biopsy. *Am J Dis Child* 1978; **132**: 357–9.
8. Sinclair S, Beckman E, Ellman L. Biopsy of enlarged superficial lymph nodes. *JAMA* 1974; **228**: 602–3.
9. Barton LL, Feigin RD. Childhood cervical lymphadenopathy: a re-appraisal. *J Pediatr* 1974; **84**: 846–52.
10. Saltzstein SR. The fate of patients with non-diagnostic lymph node biopsy. *Surgery* 1963; **58**: 659–62.
11. Moore RD, Weisberger AS, Bowerfind ES. An evaluation of lymphadenopathy in systemic disease. *Arch Intern Med* 1957; **99**: 751–9.
12. Connolly AAP, MacKenzie K. Paediatric neck masses – a diagnostic dilemma. *J Laryngol Otol* 1997; **111**: 541–5.
13. Zuelzer WW, Kaplan J. The child with lymphadenopathy. *Semin Hematol* 1975; **12**: 323–4.
14. Vassilakopoulos TP, Pangalis GA. Application of a prediction rule to select which patients presenting with lymphadenopathy should undergo a lymph node biopsy. *Medicine* 2000; **79**: 338–47.
15. Slap GB, Brooks JS, Schwartz JS. When to perform biopsies of enlarged peripheral lymph nodes in young patients. *JAMA* 1984; **252**: 1321–6.
16. Greenfield S, Jordan MC. The clinical investigations of lymphadenopathy in primary care practice. *JAMA* 1978; **240**: 1388–93.
17. Bradley PJ, MacKenzie K. Head and neck cancer in the United Kingdom: the current documents. *Clin Otolaryngol* 2005; **30**: 452–7.
18. British Association of Otorhinolaryngologists Head and Neck Surgeons. *Effective Head and Neck Cancer Management*. Third Consensus document. 2002.
19. National Institute for Health and Clinical Excellence. *Guidance on cancer services improving outcomes in head and neck cancer. The manual*. London: NICE, 2004.
20. <www.lymphoma.org.uk> [Accessed 2006].
21. McCombe A, George E. One-stop neck lump clinic. *Clin Otolaryngol* 2002; **27**: 412.
22. Kishore A, Stewart CJR, McGarry GW, MacKenzie K. One stop neck lump clinic; phase 2 of audit. How are we doing? *Clin Otolaryngol* 2001; **26**: 495–7.
23. Murray A, Stewart CJR, McGarry GW, MacKenzie K. Patients with neck lumps: can they be managed in a 'one-stop' clinic setting? *Clin Otolaryngol* 2000; **25**: 471–5.
24. Smith OD, Ellis PDM, Bearcroft PWP, Berman LH, Grant JW, Jani P. Management of neck lumps – a triage model. *Ann R Coll Surg Engl* 2000; **82**: 223–6.
25. Vowles RH, Ghiacy S, Jefferis AF. A clinic for the rapid processing of patients with neck masses. *J Laryngol Otol* 1998; **112**: 1061–4.
26. Birchall MA, Walsh-Waring GP, Stafford ND. Malignant neck lumps: a measured approach. *Ann R Coll Surg Engl* 1991; **73**: 91–5.
27. Barakat M, Flood IM, Oswal VH, Ruckley RW. The management of a neck mass: presenting feature of an asymptomatic head and neck primary malignancy? *Ann R Coll Surg Engl* 1987; **69**: 181–4.
28. Department of Health. *Manual for cancer services*. London: DH, 2004.
29. Amir Z, Kwan SYL, Landes D, Feber T, Williams SA. Diagnostic delays in head and neck cancers. *Eur J Cancer Care* 1999; **8**: 198–203.
30. Schafernak KT, Kluskens LF, Ariga R, Reddy VB, Gattuso P. Fine-needle aspiration of superficial and deeply seated lymph nodes on patients with and without a history of malignancy: a review of 439 cases. *Diagn Cytopathol* 2003; **29**: 315–9.
31. Lioe TF, Elliott H, Allen DC, Spence RA. The role of fine needle aspiration cytology (FNAC) in the investigation of superficial lymphadenopathy; uses and limitations of the technique. *Cytopathology* 1999; **10**: 291–7.
32. Akhtar SS, Imran-Ul-Haq A, Faiz-U-Din M, Reves LM. Efficacy of fine-needle capillary biopsy in the assessment of patients with superficial lymphadenopathy. *Cancer* 1997; **85**: 27–80.
33. Layfield LJ. Fine-needle aspiration of the head and neck. *Pathology* 1996; **4**: 409–38.
34. Tschammier A, Beer M, Hahn D. Differential diagnosis of lymphadenopathy: power Doppler vs color Doppler sonography. *Eur Radiol* 2002; **12**: 1794–9.
35. Blum A, Schlagenhauff B, Stroebel W, Breuninger H, Rassner G, Garbe C. Ultrasound examination of regional lymph nodes significantly improves early detection of locoregional metastases during the follow-up of patients with cutaneous melanoma: results of a prospective study of 1288 patients. *Cancer* 2000; **88**: 2534–9.
36. Dragoni F, Cartoni C, Pescarmona E, Chiarotti F, Puopolo M. The role of high resolution pulsed and Doppler ultrasound in the differential diagnosis of benign and malignant lymphadenopathy: results of multivariate analysis. *Cancer* 1999; **85**: 2485–90.
37. Wu CH, Shih HC, Chang YL, Lee SY, Hsieh FJ. Two-dimensional and three-dimensional power Doppler sonographic classification of vascular patterns in cervical lymphadenopathies. *J Ultrasound Med* 1998; **17**: 459–64.
38. Larsson LO, Bentzon MW, Berg-Kelly K, Mellander L, Skoog BE. Palpable lymph nodes of the neck in Swedish school children. *Acta Paediatr* 1992; **83**: 1091–4.
39. Bamji J, Stone RK, Kaul A, Usmani G, Schachter FF, Wasserman E. Palpable lymph nodes in healthy newborns and infants. *Pediatrics* 1986; **78**: 573–5.
40. Leung AK, Robson WL. Childhood cervical lymphadenopathy. *J Pediatr Health Care* 2004; **18**: 3–7.